# Problem Formulations: Pathway Exclusion Text

**1-BP**
Intro: p. 13
Conceptual models: p. 45
Detailed discussion: p. 54+
*Exclusions:*
Land/disposal pathways

**1,4-dioxane**
Intro: p. 11
Conceptual models: p. 37
Detailed discussion: p. 42+
*Exclusions:*
Air
Water (except for env)
Land

**Carbon Tet**
Intro: p. 13
Conceptual models: pp. 42-44
Detailed discussion: pp. 48-51
*Exclusions:*
Ambient air pathway (CAA),
Drinking Water pathway (SDWA, NPDWR),
Ambient Water pathway for humans (recommended water quality criteria under CWA; still includes aquatic life but will not be further analyzed),
Biosolids (CWA),
Land/Disposal (RCRA, CAA, SDWA)

**DCM**
Intro: p. 15
Conceptual models: p. 46-47
Detailed discussion: pp. 52-57
*Exclusions:*
Ambient Air (CAA),
Drinking Water Pathway (SDWA, NPDWRs),
Ambient Water for humans (recommended water quality criteria under CWA but **i**ncludes for aquatic life),
Land/Disposal (RCRA, CAA, SDWA)

**NMP**
Intro: pp. 11-2
Conceptual models: pp. 41-42

Detailed discussion: p. 49-51
*Exclusions:*
Drinking water pathway (CCL),
Disposal pathway (RCRA, CAA, SDWA)

**Perc**
Intro: p. 15
Conceptual models: p. 54
Detailed discussion: p. 59+
*Exclusions:*
Air pathways
Water pathways (except for env)
Land/Disposal pathways

**HBCD:**
Intro: p. 13
Conceptual models: p. 44
Detailed discussion: p. 51
*Exclusions:*
Land/Disposal pathways

- Emissions from hazardous waste incinerators will not be included (because it is not a RCRA hazardous waste and this type of incineration is more expensive)
- Will not include on-site releases that go to underground injection
- Will not include on-site releases to land that go to Subtitle C hazardous waste landfills
- Will not include on-site releases to land from RCRA Subtitle D municipal solid waste landfills

**Asbestos**:
Intro: p. 11
Conceptual model: p. 36
Detailed discussion: p. 42-45
*Exclusions:*

- **Clean Air Act:** EPA does not plan to evaluate emission pathways to ambient air from commercial and industrial stationary sources or associated inhalation exposure of the general population or terrestrial species
- **Safe Drinking Water Act:** "[D]rinking water exposure pathway for asbestos is currently addressed in the SDWA regulatory analytical process for public water systems" it will not be included in the RE
- **Clean Water Act:**
    - Asbestos is a priority pollutant with recommended water quality criteria for protection of human health, EPA does not expect to include this pathway
    - EPA has not developed criteria for the protection of aquatic life, this pathway will be included in the RE
- **RCRA:**

- Does not expect to include on-site releases to land that go to underground injection
- Does not expect to include on-site release to land that go to Subtitle C hazardous waste landfills or D municipal solid waste landfills
- Combustion by-products from incineration treatment of asbestos wastes will not be included
- Industrial-non-hazardous and construction/demolition waste landfills (both generally regulated by states) are not included

**TCE:**
Intro: p. 13
Conceptual model: p. 46
Detailed discussion: p. 53-54
*Exclusions:*

- Air: commercial and industrial stationary sources of emission to general pop or terrestrial species (CAA)
- Water:
    - Drinking water (based on existence of MCL under SDWA)
    - Ambient water (based on TCE listing as a priority pollutant under CWA)
    - Will look at aquatic species exposure via contaminated surface water.
- Land:
    - On-site releases to land that go to underground injection (RCRA and SDWA)
    - Releases to land under RCRA Subtitle C hazardous waste landfills
    - On-site releases to RCRA subtitle D municipal solid waste landfills or exposures of the general population (including sus populations) or terrestrial species
    - On-site releases to land from industrial non-hazardous and construction/demolition waste landfills. (which are primarily regulated under state programs)

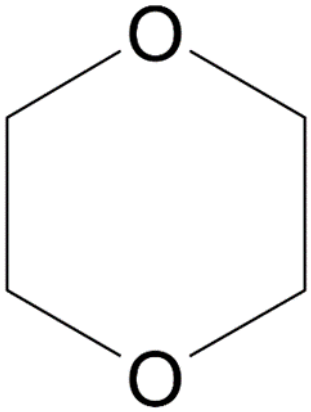
**Pigment Violet 29:**
Remains the same: “no conditions of use were excluded during problem formulation” p. 15-16
*No exclusions*

EPA Document# EPA-740-R1-7012
May 2018
Office of Chemical Safety and
Pollution Prevention

United States
Environmental Protection Agency

# Problem Formulation of the Risk Evaluation for 1,4-Dioxane

# CASRN: 123-91-1



*May, 2018*

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# ACKNOWLEDGEMENTS

This report was developed by the United States Environmental Protection Agency (U.S. EPA), Office of Chemical Safety and Pollution Prevention (OCSPP), Office of Pollution Prevention and Toxics (OPPT).

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**Docket**

Supporting information can be found in public docket: EPA-HQ-OPPT-2016-0723.

**Disclaimer**

Reference herein to any specific commercial products, process or service by trade name, trademark, manufacturer or otherwise does not constitute or imply its endorsement, recommendation or favoring by the United States Government.

# ABBREVIATIONS

| | |
|---|---|
| °C | Degrees Celsius |
| AAL | Allowable Ambient Level |
| ACGIH | American Conference of Government Industrial Hygienists |
| AEGL | Acute Exposure Guideline Level |
| AES | Alkyl Ethyl Sulphates |
| AMA | Ambient Monitoring Archive |
| AQS | Air Quality System |
| atm | Atmosphere(s) |
| ATSDR | Agency for Toxic Substances and Disease Registries |
| BAF | Bioaccumulation Factor |
| BCF | Bioconcentration Factor |
| BSER | Best System of Emission Reduction |
| CAA | Clean Air Act |
| CASRN | Chemical Abstracts Service Registry Number |
| CBI | Confidential Business Information |
| CCL | Candidate Contaminant List |
| CDR | Chemical Data Reporting |
| CERCLA | Comprehensive Environmental Response, Compensation and Liability Act |
| $cm^3$ | Cubic Centimeter(s) |
| COC | Concentration of Concern |
| COU | Conditions of Use |
| cP | Centipoise |
| CPCat | Chemical and Product Categories |
| CSCL | Chemical Substances Control Law |
| EC | European Commission |
| EPA | Environmental Protection Agency |
| EPCRA | Emergency Planning and Community Right-to-Know Act |
| EU | European Union |
| FDA | Food and Drug Administration |
| FFDCA | Federal Food, Drug and Cosmetic Act |
| g | Gram(s) |
| GACT | Generally Available Control Technology |
| HAP | Hazardous Air Pollutant |
| HHE | Health Hazard Evaluation |
| HPV | High Production Volume |
| IARC | International Agency for Research on Cancer |
| IRIS | Integrated Risk Information System |
| ISHA | Industrial Safety and Health Act |
| kg | Kilogram(s) |
| kPa | Kilopascal(s) |
| L | Liter(s) |
| lb | Pound |
| Log $K_{oc}$ | Logarithmic Soil Organic Carbon:Water Partitioning Coefficient |
| Log $K_{ow}$ | Logarithmic Octanol:Water Partition Coefficient |
| $m^3$ | Cubic Meter(s) |
| MACT | Maximum Achievable Control Technology |
| mg | Milligram(s) |

| | |
|---|---|
| µg | Microgram(s) |
| mmHg | Millimeter(s) of Mercury |
| MSDS | Material Safety Data Sheet |
| NAC | National Advisory Committee |
| NAICS | North American Industry Classification System |
| NATA | National Air Toxics Assessment |
| NCEA | National Center for Environmental Assessment |
| NEI | National Emissions Inventory |
| NESHAP | National Emission Standards for Hazardous Air Pollutants |
| NICNAS | National Industrial Chemicals Notification and Assessment Scheme |
| NIH | National Institute of Health |
| NIOSH | National Institute of Occupational Safety and Health |
| NOAEL | No-Observed-Adverse-Effect Level |
| NPRI | National Pollutant Release Inventory |
| NSPS | New Source Performance Standards |
| NTP | National Toxicology Program |
| OCSPP | Office of Chemical Safety and Pollution Prevention |
| OECD | Organisation for Economic Co-operation and Development |
| ONU | Occupational Non-User |
| OPPT | Office of Pollution Prevention and Toxics |
| OSHA | Occupational Safety and Health Administration |
| PBPK | Physiologically Based Pharmacokinetic |
| PEL | Permissible Exposure Limit |
| PESS | Potentially Exposed or Susceptible Subpopulations |
| PET | Polyethylene Terephthalate |
| POD | Point of Departure |
| POTW | Publicly Owned Treatment Works |
| ppm | Part(s) per Million |
| PWS | Public Water System |
| RCRA | Resource Conservation and Recovery Act |
| REL | Recommended Exposure Level |
| SDS | Safety Data Sheet |
| SDWA | Safe Drinking Water Act |
| SIDS | Screening Information Data Set |
| TCA | 1,1,1-Trichloroethane |
| TCCR | Transparent, Clear, Consistent and Reasonable |
| TLV | Threshold Limit Value |
| TRI | Toxics Release Inventory |
| TSCA | Toxic Substances Control Act |
| TWA | Time-Weighted Average |
| UCMR | Unregulated Contaminant Monitoring Rule |
| U.S. | United States |
| UV | Ultraviolet |
| VCCEP | Voluntary Children's Chemical Evaluation Program |
| VOC | Volatile Organic Compound |
| WHO | World Health Organisation |

# EXECUTIVE SUMMARY

TSCA § 6(b)(4) requires the United States Environmental Protection Agency (U.S. EPA) to establish a risk evaluation process. In performing risk evaluations for existing chemicals, EPA is directed to "determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of costs or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator under the conditions of use." In December of 2016, EPA published a list of 10 chemical substances that are the subject of the Agency's initial chemical risk evaluations (81 FR 91927), as required by TSCA § 6(b)(2)(A). 1,4-Dioxane was one of these chemicals.

TSCA § 6(b)(4)(D) requires that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use and potentially exposed or susceptible subpopulations that the Administrator expects to consider. In June 2017, EPA published the Scope of the Risk Evaluation for 1,4-Dioxane. As explained in the scope document, because there was insufficient time for EPA to provide an opportunity for comment on a draft of the scope, as EPA intends to do for future scope documents, EPA is publishing and taking public comment on a problem formulation document to refine the current scope, as an additional interim step prior to publication of the draft risk evaluation for 1,4-dioxane. Comments received on this problem formulation document will inform development of the draft risk evaluation.

This problem formulation document refines the conditions of use, exposures and hazards presented in the scope of the risk evaluation for 1,4-dioxane and presents refined conceptual models and analysis plans that describe how EPA expects to evaluate the risk for 1,4-dioxane.

1,4-Dioxane is a clear volatile liquid used primarily as a solvent and is subject to federal and state regulations and reporting requirements. 1,4-Dioxane has been a reportable Toxics Release Inventory (TRI) chemical under Section 313 of the Emergency Planning and Community Right-to-Know Act (EPCRA) since 1987. It is designated a Hazardous Air Pollutant (HAP) under the Clean Air Act (CAA), and listed as a waste under the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). It was listed on the Safe Drinking Water (SDWA) Candidate Contaminant List (CCL) and identified in the third Unregulated Contaminant Monitoring Rule (UCMR3).

Information on domestic manufacture, processing and use of 1,4-dioxane is available to EPA through its Chemical Data Reporting (CDR) Rule, issued under TSCA. In 2016, approximately 1 million pounds per year was reported to be manufactured in the U.S. (U.S. EPA, 2016c). 1,4-Dioxane is currently used in industrial processes and for industrial and commercial uses. Industrial processing uses include use as a processing aid and in functional fluids in open and closed systems. 1,4-Dioxane has uses as a laboratory chemical reagent, in adhesives and sealants and several other identified uses. Historically, 90% of 1,4-dioxane produced was used as a stabilizer in chlorinated solvents such as 1,1,1-trichloroethane (TCA). Use of 1,4-dioxane has decreased since TCA was phased out by the Montreal Protocol in 1996.

The most recent data on environmental releases, according to the Toxics Release Inventory (TRI), indicate that approximately 675,000 pounds of 1,4-dioxane were released to the environment in 2015 (U.S. EPA, 2017d). Releases are reported to all types of environmental media: air, water and land. The environmental fate of 1,4-dioxane is characterized by partitioning to the atmosphere, surface water and

groundwater, and degradation by atmospheric oxidation or biodegradation. It is expected to be moderately persistent in the environment and has a low bioaccumulation potential.

This document presents the potential exposures that may result from the conditions of use of 1,4-dioxane. Workers and occupational non-users may be exposed to 1,4-dioxane during industrial and commercial conditions of use such as manufacturing, processing, distribution, use and disposal. EPA plans to further analyze inhalation exposures to vapors and mists for workers and occupational non-users and dermal exposures for skin contact with liquids in occluded situations for workers in the risk evaluation. For environmental release pathways, EPA plans to include surface water exposure to aquatic vertebrates, invertebrates and aquatic plants, exposure to sediment organisms and exposure to 1,4-dioxane in land-applied biosolids in the risk evaluation.

1,4-Dioxane has been the subject of numerous human health reviews including EPA's Integrated Risk Information System (IRIS) Toxicological Review, Agency for Toxic Substances and Disease Registry's (ATSDR's) Toxicological Profile, Health Canada Screening Assessment, and Interim Acute Exposure Guideline Levels (AEGL). Many targets of toxicity from exposures to 1,4-dioxane have been identified in animal and human studies for both oral and inhalation exposures. EPA plans to evaluate all potential hazards for 1,4-dioxane, including any found in recent literature. Hazard endpoints identified in previous assessments include acute toxicity, non-cancer effects and cancer. Non-cancer effects include irritation of the eyes and respiratory tract, liver toxicity and kidney toxicity. Animals exposed to 1,4-dioxane by inhalation and oral exposure have also developed multiple types of cancer. If additional hazard concerns are identified during the systematic review of the literature, these will also be considered. These hazards will be evaluated based on the specific exposure scenarios identified.

The revised conceptual models presented in this problem formulation identify conditions of use; exposure pathways (e.g., media); exposure routes (e.g., inhalation, dermal, oral); potentially exposed or susceptible subpopulations; and hazards EPA expects to further analyze in the risk evaluation. The initial conceptual models provided in the scope document (U.S. EPA, 2017c) were revised during problem formulation based on evaluation of reasonably available information for physical and chemical properties, fate, exposures and hazards to indicate conditions of use, exposure pathways, exposure routes, and hazards, conditions of use and consideration of other statutory and regulatory authorities. In each problem formulation document for the first 10 chemical substances, EPA also refined the activities, hazards and exposure pathways that will be included in and excluded from the risk evaluation.

EPA's overall objectives in the risk evaluation process are to conduct timely, relevant, high-quality, and scientifically credible risk evaluations within the statutory deadlines, and to evaluate the conditions of use that raise greatest potential for risk 82 FR 33726, 33728 (July 20, 2017).

# 1 INTRODUCTION

This document presents for comment the problem formulation of the risk evaluation to be conducted for 1,4-dioxane under the Frank R. Lautenberg Chemical Safety for the 21st Century Act. The Frank R. Lautenberg Chemical Safety for the 21st Century Act amended the Toxic Substances Control Act (TSCA), the Nation's primary chemicals management law, on June 22, 2016. The new law includes statutory requirements and deadlines for actions related to conducting risk evaluations of existing chemicals.

In December of 2016, EPA published a list of 10 chemical substances that are the subject of the Agency's initial chemical risk evaluations (81 FR 91927), as required by TSCA § 6(b)(2)(A). These 10 chemical substances were drawn from the 2014 update of EPA's TSCA Work Plan for Chemical Assessments, a list of chemicals that EPA identified in 2012 and updated in 2014 (currently totaling 90 chemicals) for further assessment under TSCA. EPA's designation of the first 10 chemical substances constituted the initiation of the risk evaluation process for each of these chemical substances, pursuant to the requirements of TSCA § 6(b)(4).

TSCA § 6(b)(4)(D) requires that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use and potentially exposed or susceptible subpopulations that the Administrator expects to consider, within 6 months after the initiation of a risk evaluation. The scope documents for all first 10 chemical substances were issued on June 22, 2017. The first 10 problem formulation documents are a refinement of what was presented in the first 10 scope documents. TSCA § 6(b)(4)(D) does not distinguish between scoping and problem formulation, and requires EPA to issue scope documents that include information about the chemical substance, such as the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations that the Administrator expects to consider in the risk evaluation. In the future, EPA expects scoping and problem formulation to be completed prior to the issuance of scope documents and intends to issue scope documents that include problem formulation.

As explained in the scope document, because there was insufficient time for EPA to provide an opportunity for comment on a draft of the scope, as EPA intends to do for future scope documents, EPA is publishing and taking public comment on a problem formulation document to refine the current scope, as an additional interim step prior to publication of the draft risk evaluation for 1,4-dioxane. Comments received on this problem formulation document will inform development of the draft risk evaluation.

The Agency defines problem formulation as the analytical phase of the risk assessment in which "the purpose for the assessment is articulated, the problem is defined, and a plan for analyzing and characterizing risk is determined" (see section 2.2 of the *Framework for Human Health Risk Assessment to Inform Decision Making*, (U.S. EPA, 2014c). The outcome of problem formulation is a conceptual model(s) and an analysis plan. The conceptual model describes the linkages between stressors and adverse human health effects, including the stressor(s), exposure pathway(s), exposed life stage(s) and population(s), and endpoint(s) that will be addressed in the risk evaluation (U.S. EPA, 2014c). The analysis plan follows the development of the conceptual model(s) and is intended to describe the approach for conducting the risk evaluation, including its design, methods and key inputs and intended outputs as described in the EPA *Human Health Risk Assessment Framework* (U.S. EPA, 2014c). The problem formulation documents refine the initial conceptual models and analysis plans that were provided in the scope documents.

First, EPA has removed from the risk evaluation any activities and exposure pathways that EPA has concluded do not warrant inclusion in the risk evaluation. For example, for some activities that were listed as "conditions of use" in the scope document, EPA has insufficient information following the further investigations during problem formulation to find they are circumstances under which the chemical is actually "intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of."

Second, EPA also identified certain exposure pathways that are under the jurisdiction of regulatory programs and associated analytical processes carried out under other EPA-administered environmental statutes – namely, the Clean Air Act (CAA), the Safe Drinking Water Act (SDWA), the Clean Water Act (CWA), and the Resource Conservation and Recovery Act (RCRA) – and which EPA does not expect to include in the risk evaluation.

As a general matter, EPA believes that certain programs under other Federal environmental laws adequately assess and effectively manage the risks for the covered exposure pathways. To use Agency resources efficiently under the TSCA program, to avoid duplicating efforts taken pursuant to other Agency programs, to maximize scientific and analytical efforts, and to meet the three-year statutory deadline, EPA is planning to exercise its discretion under TSCA 6(b)(4)(D) to focus its analytical efforts on exposures that are likely to present the greatest concern and consequently merit a risk evaluation under TSCA, by excluding, on a case-by-case basis, certain exposure pathways that fall under the jurisdiction of other EPA-administered statutes.[1] EPA does not expect to include any such excluded pathways in the risk evaluation as further explained below. The provisions of various EPA-administered environmental statutes and their implementing regulations represent the judgment of Congress and the Administrator, respectively, as to the degree of health and environmental risk reduction that is sufficient under the various environmental statutes.

Third, EPA identified any conditions of use, hazards, or exposure pathways which were included in the scope document and that EPA expects to include in the risk evaluation but which EPA does not expect to further analyze in the risk evaluation. EPA expects to be able to reach conclusions about particular conditions of use, hazards or exposure pathways without further analysis and therefore plans to conduct no further analysis on those conditions of use, hazards or exposure pathways in order to focus the Agency's resources on more extensive or quantitative analyses. Each risk evaluation will be "fit-for-purpose," meaning not all conditions of use will warrant the same level of evaluation and the Agency may be able to reach some conclusions without comprehensive or quantitative risk evaluations. 82 FR 33726, 33734, 33739 (July 20, 2017).

EPA received comments on the published scope document for 1,4-dioxane and has considered the comments specific to 1,4-dioxane in this problem formulation document. EPA is soliciting public comments on this problem formulation document and when the draft risk evaluation is issued the Agency intends to respond to comments that are submitted. In its draft risk evaluation, EPA may revise the conclusions and approaches contained in this problem formulation, including the conditions of use and pathways covered and the conceptual models and analysis plans, based on comments received.

[1]As explained in the final rule for chemical risk evaluation procedures, "EPA may, on a case-by case basis, exclude certain activities that EPA has determined to be conditions of use in order to focus its analytical efforts on those exposures that are likely to present the greatest concern, and consequently merit an unreasonable risk determination." [82 FR 33726, 33729 (July 20, 2017)].

## 1.1 Regulatory History

EPA conducted a search of existing domestic and international laws, regulations and assessments pertaining to 1,4-dioxane. EPA compiled this summary from data available from federal, state, international and other government sources, as cited in Appendix A. As noted in public comments to the scope document, the NESHAP for Rubber Manufacturing does not apply to 1,4-dioxane and has been removed from Table_Apx A-1. EPA evaluated and considered the impact of existing laws and regulations in the problem formulation step to determine what, if any further analysis might be necessary as part of the risk evaluation. Consideration of the nexus between these existing regulations and TSCA uses may additionally be made as detailed/specific conditions of use and exposure scenarios are developed in conducting the analysis phase of the risk evaluation.

***Federal Laws and Regulations***

1,4-Dioxane is subject to federal statutes or regulations, other than TSCA, that are implemented by other offices within EPA and/or other federal agencies/departments. A summary of federal laws, regulations and implementing authorities is provided in Appendix A.1.

***State Laws and Regulations***

1,4-Dioxane is subject to state statutes or regulations implemented by state agencies or departments. A summary of state laws, regulations and implementing authorities is provided in Appendix A.2.

***Laws and Regulations in Other Countries and International Treaties or Agreements***

1,4-Dioxane is subject to statutes or regulations in countries other than the United States and/or international treaties and/or agreements. A summary of these laws, regulations, treaties and/or agreements is provided in Appendix A.3.

## 1.2 Assessment History

EPA has identified assessments conducted by other EPA Programs and other organizations (see Table 1-1). Depending on the source, these assessments may include information on conditions of use, hazards, exposures and potentially exposed or susceptible subpopulations. Table 1-1 shows the assessments that have been conducted. EPA found no additional assessments beyond those listed in the Scope document.

In addition to using this information, EPA intends to conduct a full review of the relevant data/information collected in the initial comprehensive search (see *1,4-Dioxane (CASRN 123-91-1) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0723) following the literature search and screening strategies documented in the *Strategy for Conducting Literature Searches for 1,4-Dioxane: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0723. This will ensure that EPA considers data/information that has been made available since these assessments were conducted.

**Table 1-1. Assessment History of 1,4-Dioxane**

| Authoring Organization | Assessment |
|---|---|
| **EPA assessments** | |
| EPA, Office of Chemical Safety and Pollution Prevention (OCSPP), Office of Pollution Prevention and Toxics (OPPT) | TSCA Work Plan Chemical Problem Formulation and Initial Assessment: 1,4-Dioxane (CASRN 123-91-1) (2015c) |
| EPA, National Center for Environmental Assessment (NCEA) | Toxicological Review of 1,4-Dioxane (With Inhalation Update) (CASRN 123-91-1) (2013c) |
| EPA, NCEA | Toxicological review of 1,4-Dioxane (CAS No. 123-91-1) (2010) |
| EPA, Office of Water (OW) | Drinking Water Health Advisory (2012a) |
| **Other U.S.-based organizations** | |
| National Toxicology Program (NTP) | Report on Carcinogens, Fourteenth Edition, 1,4-Dioxane (2016) |
| Agency for Toxic Substances and Disease Registry (ATSDR) | Toxicological Profile for 1,4-Dioxane (2012) |
| National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances (NAC/AEGL Committee) | Interim Acute Exposure Guideline Levels (AEGL) for 1,4-Dioxane (CAS Reg. No. 123-91-1) (2005b) |
| **International** | |
| International Cooperation on Cosmetics Regulation | Report of the ICCR Working Group: Considerations on Acceptable Trace Level of 1.4-Dioxane in Cosmetic Products (2017) |
| International Agency for Research on Cancer (IARC) | IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 71 (1999) |
| Government of Canada, Environment Canada, Health Canada | Screening Assessment for the Challenge. 1,4-Dioxane. CASRN 123-91-1 (2010) |
| Research Center for Chemical Risk Management, National Institute of Advanced Industrial Science and Technology, Japan | Estimating Health Risk from Exposure to 1,4-Dioxane in Japan (2006) |
| World Health Organisation (WHO) | 1,4-Dioxane in Drinking-water (2005) |
| Employment, Social Affairs, and Inclusion, European Commission (EC) | Recommendation from the Scientific Committee on Occupational Exposure Limits for 1,4-dioxane (2004) |
| European Chemicals Bureau, Institute for Health and Consumer Protection | European Union Risk Assessment Report. 1,4-dioxane. CASRN 123-91-1. EINECS No: 204-661-8. (2002) |

| Authoring Organization | Assessment |
|---|---|
| National Industrial Chemicals Notification and Assessment Scheme (NICNAS), Australian Government | 1,4-Dioxane. Priority Existing Chemical No. 7. Full Public Report (1998) |
| Organisation for Economic Co-operation and Development (OECD), Screening Information Data Set (SIDS) | 1,4-Dioxane. SIDS initial assessment profile (1999) |

## 1.3 Data and Information Collection

EPA/OPPT generally applies a systematic review process and workflow that includes: (1) data collection, (2) data evaluation and (3) data integration of the scientific data used in risk evaluations developed under TSCA. Scientific analysis is often iterative in nature as new knowledge is obtained. Hence, EPA/OPPT expects that multiple refinements regarding data collection may occur during the process of risk evaluation.

***Data Collection: Data Search***

EPA/OPPT conducted chemical-specific searches for data and information on: physical and chemical properties; environmental fate and transport; conditions of use information; environmental exposures, human exposures, including potentially exposed or susceptible subpopulations; ecological hazard, human health hazard, including potentially exposed or susceptible subpopulations.

EPA/OPPT designed its initial data search to be broad enough to capture a comprehensive set of sources containing data and/or information potentially relevant to the risk evaluation. Generally, the search was not limited by date and was conducted on a wide range of data sources, including but not limited to: peer-reviewed literature and gray literature (e.g., publicly-available industry reports, trade association resources, government reports). For human health hazard, EPA/OPPT relied on the search strategies from recent assessments, such as EPA Integrated Risk Information System (IRIS) assessments and the NTP *Report on Carcinogens*, to identify relevant information published after the end date of the previous search to capture more recent literature. The *Strategy for Conducting Literature Searches for 1,4-Dioxane: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0723) provides details about the data and information sources and search terms that were used in the literature search.

***Data Collection: Data Screening***

Following the data search, references were screened and categorized using selection criteria outlined in the *Strategy for Conducting Literature Searches for 1,4-Dioxane: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0723). Titles and abstracts were screened against the criteria as a first step with the goal of identifying a smaller subset of the relevant data to move into the subsequent data extraction and data evaluation steps. Prior to full-text review, EPA/OPPT anticipates refinements to the search and screening strategies, as informed by an evaluation of the performance of the initial title/abstract screening and categorization process.

The categorization scheme (or tagging structure) used for data screening varies by scientific discipline (i.e., physical and chemical properties; environmental fate and transport; chemical use/conditions of use information; environmental exposures, human exposures, including potentially exposed or susceptible subpopulations identified by virtue of greater exposure; human health hazard, including potentially exposed or susceptible subpopulations identified by virtue of greater susceptibility; and ecological

hazard). However, within each data set, there are two broad categories or data tags: (1) o*n-topic* references or (2) *off-topic* references. *On-topic* references are those that may contain data and/or information relevant to the risk evaluation. O*ff-topic* references are those that do not appear to contain data or information relevant to the risk evaluation. The supplemental document, *Strategy for Conducting Literature Searches for 1,4-Dioxane: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0723) discusses the inclusion and exclusion criteria that EPA/OPPT used to categorize references as *on-topic* or *off-topic*.

Additional data screening using sub-categories (or sub-tags) was also performed to facilitate further sorting of data/information. For example, identifying references by source type (e.g., published peer-reviewed journal article, government report); data type (e.g., primary data, review article); human health hazard (e.g., liver toxicity, cancer, reproductive toxicity); or chemical-specific and use-specific data or information. These sub-categories are described in the supplemental document, *Strategy for Conducting Literature Searches for 1,4-Dioxane: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0723) and will be used to organize the different streams of data during the stages of data evaluation and data integration steps of systematic review.

Results of the initial search and categorization can be found in the *1,4-Dioxane* (*CASRN 123-91-1) Bibliography: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0723). This document provides a comprehensive list (bibliography) of the sources of data identified by the initial search and the initial categorization for *on-topic* and *off-topic* references. Because systematic review is an iterative process, EPA/OPPT expects that some references may move from the *on-topic* to the *off-topic* categories, and vice versa. Moreover, targeted supplemental searches may also be conducted to address specific needs for the analysis phase (e.g., to locate specific data needed for modeling); hence, additional *on-topic* references not initially identified in the initial search may be identified as the systematic review process proceeds.

## 1.4 Data Screening During Problem Formulation

EPA/OPPT is in the process of completing the full text screening of the on-topic references identified in the *1,4-Dioxane* (*CASRN 123-91-1) Bibliography: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0723). The screening process at the full-text level is described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a). Appendix F provides the inclusion and exclusion criteria applied at the full text screening. The eligibility criteria are guided by the analytical considerations in the revised conceptual models and analysis plan, as discussed in the problem formulation document. Thus, it is expected that the number of data/information sources entering evaluation is reduced to those that are relevant to address the technical approach and issues described in the analysis plan of this document. Following the screening process, the quality of the included data/information sources will be assessed using the evaluation strategies that are described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a).

# 2 PROBLEM FORMULATION

As required by TSCA, the scope of the risk evaluation identifies the conditions of use, hazards, exposures and potentially exposed or susceptible subpopulations that the Administrator expects to consider. To communicate and visually convey the relationships between these components, EPA included in the scope document a life cycle diagram and conceptual models that describe the actual or potential relationships between 1,4-dioxane and human and ecological receptors. During the problem formulation, EPA revised the conceptual models based on further data gathering and analysis as presented in this Problem Formulation document. An updated analysis plan is also included which identifies, to the extent feasible, the approaches and methods that EPA may use to assess exposures, effects (hazards) and risks under the conditions of use of 1,4-dioxane.

## 2.1 Physical and Chemical Properties

Physical-chemical properties influence the environmental behavior and the toxic properties of a chemical, thereby informing the potential conditions of use, exposure pathways and routes and hazards that EPA intends to consider. For scope development, EPA considered the measured or estimated physical-chemical properties set forth in Table 2-1 and EPA found no additional information during problem formulation that would change these values.

**Table 2-1. Physical and Chemical Properties of 1,4-Dioxane**

| Property | Value [a] | References |
|---|---|---|
| Molecular formula | $C_4H_8O_2$ | |
| Molecular weight | 88.1 g/mole | (Howard, 1990) |
| Physical form | Clear liquid | (O'Neil et al., 2001) |
| Melting point | 11.75°C | (Haynes, 2014) |
| Boiling point | 101.1°C | (O'Neil et al., 2006) |
| Density | 1.0329 g/cm$^3$ | (O'Neil et al., 2006) |
| Vapor pressure | 40 mm Hg at 25°C | (Lewis, 2000) |
| Vapor density | Not readily available | |
| Water solubility | >8.00 × 10$^2$ g/L | (Yalkowsky et al., 2010) |
| Octanol:water partition | -0.27 (estimated) | (Hansch et al., 1995) |
| Henry's Law constant | 4.8 × 10$^{-6}$ atm-m$^3$/mole at 25°C | (Sander, 2017); (Howard, 1990); (Atkins, 1986) |
| Flash point | 18.3°C (open cup) | (Lewis, 2012) |
| Autoflammability | Not readily available | |
| Viscosity | 0.0120 cP at 25°C | (O'Neil, 2013) |
| Refractive index | 1.4224 at 20°C | (Haynes, 2014) |
| Dielectric constant | 2.209 | (Bruno and Svoronos, 2006) |

[a] Measured unless otherwise noted

## 2.2 Conditions of Use

TSCA § 3(4) defines the conditions of use as "the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of."

### 2.2.1 Data and Information Sources

In the scope documents, EPA identified, based on reasonably available information, the conditions of use for the subject chemicals. As further described in this document, EPA searched a number of available data sources (e.g. *Use and Market Profile for 1,4-Dioxane*, (EPA-HQ-OPPT-2016-0723). Based on this search, EPA published a preliminary list of information and sources related to chemical conditions of use (see *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: 1,4-Dioxane*, EPA-HQ-OPPT-2017-0723-0003) prior to a February 2017 public meeting on scoping efforts for risk evaluations convened to solicit comment and input from the public. EPA also convened meetings with companies, industry groups, chemical users and other stakeholders to aid in identifying conditions of use and verifying conditions of use identified by EPA. The information and input received from the public and stakeholder meetings has been incorporated into this problem formulation document to the extent appropriate. Thus, EPA believes the identified manufacture, processing, distribution, use and disposal activities constitute the intended, known, and reasonably foreseeable activities associated with the subject chemical, based on reasonably available information.

### 2.2.2 Identification of Conditions of Use

To determine the current conditions of use of 1,4-dioxane and inversely, conditions of use that are no longer ongoing, EPA conducted extensive research and outreach. This included EPA's review of published literature and online databases including the most recent data available from EPA's Chemical Data Reporting program (CDR) and Safety Data Sheets (SDSs). EPA also conducted online research by reviewing company websites of potential manufacturers, importers, distributors, retailers, or other users of 1,4-dioxane and queried government and commercial trade databases. EPA also received comments on the Scope of the Risk Evaluation for 1,4-Dioxane (EPA-HQ-OPPT-2016-0723) that were used to determine the current conditions of use. In addition, EPA convened meetings with companies, industry groups, chemical users, states, environmental groups, and other stakeholders to aid in identifying conditions of use and verifying conditions of use identified by EPA. Those meetings included a February 14, 2017 public meeting with such entities and a September 15, 2017 meeting with several representatives from trade associations.

EPA has removed from the risk evaluation activities that EPA concluded do not constitute conditions of use – for example because EPA has insufficient information to find certain activities are circumstances under which the chemical is actually "intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used or disposed of." EPA has also identified any conditions of use that EPA does not plan to include in the risk evaluation. As explained in the final rule for Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act, TSCA section 6(b)(4)(D) requires EPA to identify "the hazards, exposures, conditions of use and the potentially exposed or susceptible subpopulations that the Agency expects to consider in a risk evaluation," suggesting that EPA may exclude certain activities that EPA has determined to be conditions of use on a case-by-case basis (82 FR 33736, 33729; July 20, 2017). For example, EPA may exclude conditions of use that the Agency has sufficient basis to conclude would present only de minimis exposures or otherwise insignificant risks (such as use in a closed system that effectively precludes exposure or as an intermediate).

The activities that EPA no longer believes are conditions of use or were otherwise excluded during problem formulation are described in Section 2.2.2.1. The conditions of use included in the scope of the risk evaluation are summarized in Section 2.2.2.2.

#### 2.2.2.1 Categories and Subcategories Determined Not to be Conditions of Use During Problem Formulation

For 1,4-dioxane, EPA has reviewed reasonably available information about 1,4-dioxane conditions of use. EPA did not find evidence of any current consumer uses (U.S. EPA, 2016c) for 1,4-dioxane and is excluding consumer uses from the scope of the risk evaluation as explained in the Scope document (U.S. EPA, 2017c). As described in the Scope, contamination of industrial, commercial and consumer products are not intended conditions of use for 1,4-dioxane and will not be evaluated. For fuels and fuel additives (Other uses category), EPA contacted several racing authorities that indicated that their organizations banned the use of dioxane in competitions. The organizations also could not provide credible information on whether or how often dioxane was used prior to their bans nor whether it is currently used at all. Based on the lack of information confirming that 1,4-dioxane is currently used as a fuel or fuel additive and the fact that racing authorities have prohibited this use, use in fuels and fuel additives is not a condition of use under which EPA will evaluate 1,4-dioxane.

**Table 2-2. Categories and Subcategories Determined Not to Be Conditions of Use During Problem Formulation**

| Life Cycle Stage | Category | Subcategory | References |
|---|---|---|---|
| Industrial use, potential commercial use | Other Uses | Fuels and fuel additives | Use document, EPA-HQ-OPPT-2016-0723-0003 |

#### 2.2.2.2 Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation

For 1,4-dioxane, EPA has conducted public outreach and literature searches to collect information about conditions of use and has reviewed reasonably available information obtained or possessed by EPA concerning activities associated with 1,4-dioxane.

1,4-Dioxane is currently manufactured, processed, distributed and used in industrial processes and for industrial and commercial uses. Manufacturing sites produce 1,4-dioxane in liquid form at concentrations greater or equal to 90% (EPA-HQ-OPPT-2016-0723-0012; BASF (2017). Industrial processing uses included in the scope include processing as a reactant or intermediate, non-incorporative processing, repackaging and recycling. Uses include processing aids (not otherwise listed), functional fluids in open and closed systems, laboratory chemicals, adhesives and sealants, other uses (spray polyurethane foam, printing and printing compositions) and disposal. Note that during problem formulation, EPA determined that some subcategories, such as cutting and tapping fluid, may also be used in open systems and is including these uses. Activities related to distribution (e.g., loading, unloading) will be considered throughout the 1,4-dioxane life cycle, rather than as a single distribution scenario. Also included in the scope are 1,4-dioxane use as a laboratory chemical reagent and use in adhesives and sealants in industrial and/or commercial settings and use in laboratory reference materials or standards containing 1,4-dioxane. Searches identified two products with greater than 5% of 1,4-dioxane that are included: a professional film cement and a chemiluminescent laboratory reagent. Other uses included are spray polyurethane foam; and printing and printing compositions.

Table 2-3 summarizes each life cycle stage and the corresponding categories and subcategories of conditions of use for 1,4-dioxane that EPA is including in the scope of the risk evaluation. Using the 2016 CDR (U.S. EPA, 2016c), EPA identified industrial processing or use activities, industrial function categories and commercial use product categories. EPA identified the subcategories by supplementing CDR data with other published literature and information obtained through stakeholder consultations. For this risk evaluation, EPA intends to consider each life cycle stage (and corresponding use categories and subcategories) and assess certain relevant potential sources of release and human exposure associated with that life cycle stage.

Beyond the uses identified in the *Scope of the Risk Evaluation for 1,4-Dioxane* (U.S. EPA, 2017c), EPA has received no additional information identifying additional current conditions of use for 1,4-dioxane from public comment and stakeholder meetings.

**Table 2-3. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation**

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| Manufacture | Domestic manufacture | Domestic manufacture | Use document, EPA-HQ-OPPT-2016-0723-0003; Public Comment, EPA-HQ-OPPT-2016-0723-0012 |
| | Import | Import | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| Processing | Processing as a reactant | Pharmaceutical intermediate | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Polymerization catalyst | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | Non-incorporative | Pharmaceutical and medicine manufacturing (process solvent) | Public Comment, EPA-HQ-OPPT-2016-0723-0012 |
| | | Basic organic chemical manufacturing (process solvent) | Public Comment, EPA-HQ-OPPT-2016-0723-0012 |
| | Repackaging | Bulk to packages, then distribute | Public Comment, EPA-HQ-OPPT-2016-0723-0012 |
| | Recycling | Recycling | (U.S. EPA, 2017d) |
| Distribution in commerce | Distribution | Distribution | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| Industrial use | Intermediate use | Agricultural chemical intermediate | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Plasticizer intermediate | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Catalysts and reagents for anhydrous acid reactions, | Use document, EPA-HQ-OPPT-2016-0723-0003 |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| | | brominations and sulfonations | |
| | Processing aids, not otherwise listed | Wood pulping | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Extraction of animal and vegetable oils | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Wetting and dispersing agent in textile processing | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Polymerization catalyst | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Purification of pharmaceuticals | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Etching of fluoropolymers | Public Comment, EPA-HQ-OPPT-2016-0723-0012 |
| | Functional fluids (open and closed system); refer to section 2.5.1 below for details | Polyalkylene glycol lubricant | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Synthetic metalworking fluid | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Cutting and tapping fluid | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Hydraulic fluid | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| Industrial use, potential commercial use | Laboratory chemicals | Chemical reagent | Use document, EPA-HQ-OPPT-2016-0723-0003; Public Comment, EPA-HQ-OPPT-2016-0723-0009 |
| | | Reference material | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Spectroscopic and photometric measurement | Use document, EPA-HQ-OPPT-2016-0723-0003; Public Comment, EPA-HQ-OPPT-2016-0723-0009 |
| | | Liquid scintillation counting medium | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Stable reaction medium | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Cryoscopic solvent for molecular mass determinations | Use document, EPA-HQ-OPPT-2016-0723-0003 |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| | | Preparation of histological sections for microscopic examination | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | Adhesives and sealants | Film cement | Use document, EPA-HQ-OPPT-2016-0723-0003; Public Comment, EPA-HQ-OPPT-2016-0723-0021 |
| | Other uses | Spray polyurethane foam<br>Printing and printing compositions | Use document, EPA-HQ-OPPT-2016-0723-0003; Public Comment, EPA-HQ-OPPT-2016-0723-0012 |
| Disposal | Disposal | Industrial pre-treatment | (U.S. EPA, 2017d) |
| | | Industrial wastewater treatment | |
| | | Publicly owned treatment works (POTW) | |
| | | Underground injection | |
| | | Municipal landfill | |
| | | Hazardous landfill | |
| | | Other land disposal | |
| | | Municipal waste incinerator | |
| | | Hazardous waste incinerator | |
| | | Off-site waste transfer | |

[a] These categories of conditions of use appear in the initial life cycle diagram, reflect CDR codes and broadly represent conditions of use for 1,4-dioxane in industrial and/or commercial settings.
[b] These subcategories reflect more specific uses of 1,4-dioxane.

#### 2.2.2.3 Overview of Conditions of Use and Lifecycle Diagram

The life cycle diagram provided in Figure 2-1 depicts the conditions of use that are considered within the scope of the risk evaluation during various life cycle stages including manufacturing, processing, distribution, use (industrial, commercial; when distinguishable) and disposal. Additions or changes to conditions of use based on additional information gathered or analyzed during problem formulation were described in Section 2.2.2.1 and 2.2.2.2. The activities that EPA determined are out of scope during problem formulation are not included in the life cycle diagram. The information is grouped according to Chemical Data Reporting (CDR) processing codes and use categories (including functional use codes for industrial uses and product categories for commercial and consumer uses), in combination with other data sources (e.g., published literature and consultation with stakeholders), to provide an overview of conditions of use. EPA notes that some subcategories may be grouped under multiple CDR categories.

Use categories include the following: "industrial use" means use at a site at which one or more chemicals or mixtures are manufactured (including imported) or processed. "Commercial use" means the use of a chemical or a mixture containing a chemical (including as part of an article) in a commercial enterprise providing saleable goods or services (U.S. EPA, 2016c).

To understand conditions of use relative to one another and associated potential exposures under those conditions of use, the life cycle diagram includes the production volume associated with each stage of the life cycle, as reported in the 2016 CDR reporting (U.S. EPA, 2016c), when the volume was not claimed confidential business information (CBI).

The 2016 CDR reporting data for 1,4-dioxane are provided in Table 2-4 for 1,4-dioxane from EPA's CDR database (U.S. EPA, 2016c). This information has not changed from that provided in the scope document.

**Table 2-4. Production Volume of 1,4-Dioxane in Chemical Data Reporting (CDR) Reporting Period (2012 to 2015) [a]**

| Reporting Year | 2012 | 2013 | 2014 | 2015 |
|---|---|---|---|---|
| Total Aggregate Production Volume (lbs) | 894,505 | 1,043,627 | 474,331 | 1,059,980 |

[a] The CDR data for the 2016 reporting period is available via ChemView (https://java.epa.gov/chemview) (U.S. EPA, 2014a). Because of an ongoing CBI substantiation process required by amended TSCA, the CDR data available in the scope document is more specific than currently in ChemView.

According to data collected in EPA's 2016 Chemical Data Reporting (CDR) Rule, over one million pounds of 1,4-dioxane were produced or imported in the U.S. in 2015 (U.S. EPA, 2016c). Data reported indicate that there was one manufacturer of 1,4-dioxane in the U.S. in 2015. The total volume (in lbs) of 1,4-dioxane manufactured (including imported) in the U.S. from 2012 to 2015 indicates that production has varied over that time period. Historically, the main use (90%) of 1,4-dioxane was as a stabilizer of chlorinated solvents such as 1,1,1 trichloroethane (TCA) (ATSDR, 2012). Use of TCA was phased out under the 1995 Montreal Protocol and the use of 1,4-dioxane as a solvent stabilizer was terminated (NTP, 2011; ECJRC, 2002). Lack of recent reports for other previously reported uses (Sapphire Group, 2007) suggest that many other industrial, commercial and consumer uses were also stopped.

Descriptions of the industrial, commercial and consumer use categories identified from the 2016 CDR (U.S. EPA, 2016a) and included in the life cycle diagram . Descriptions in Appendix B contain detailed descriptions (e.g., process descriptions, worker activities, process flow diagrams, equipment illustrations) for each manufacture, processing, distribution, use and disposal category. The descriptions are primarily based on the corresponding industrial function category and/or commercial and consumer product category descriptions from the 2016 CDR and can be found in EPA's *Instructions for Reporting 2016 TSCA Chemical Data Reporting* (U.S. EPA, 2016b).

Figure 2-1 depicts the life cycle diagram of 1,4-dioxane from manufacture to the point of disposal. Activities related to distribution (e.g., loading, unloading) will be considered throughout the 1,4-dioxane life cycle, rather than using a single distribution scenario.

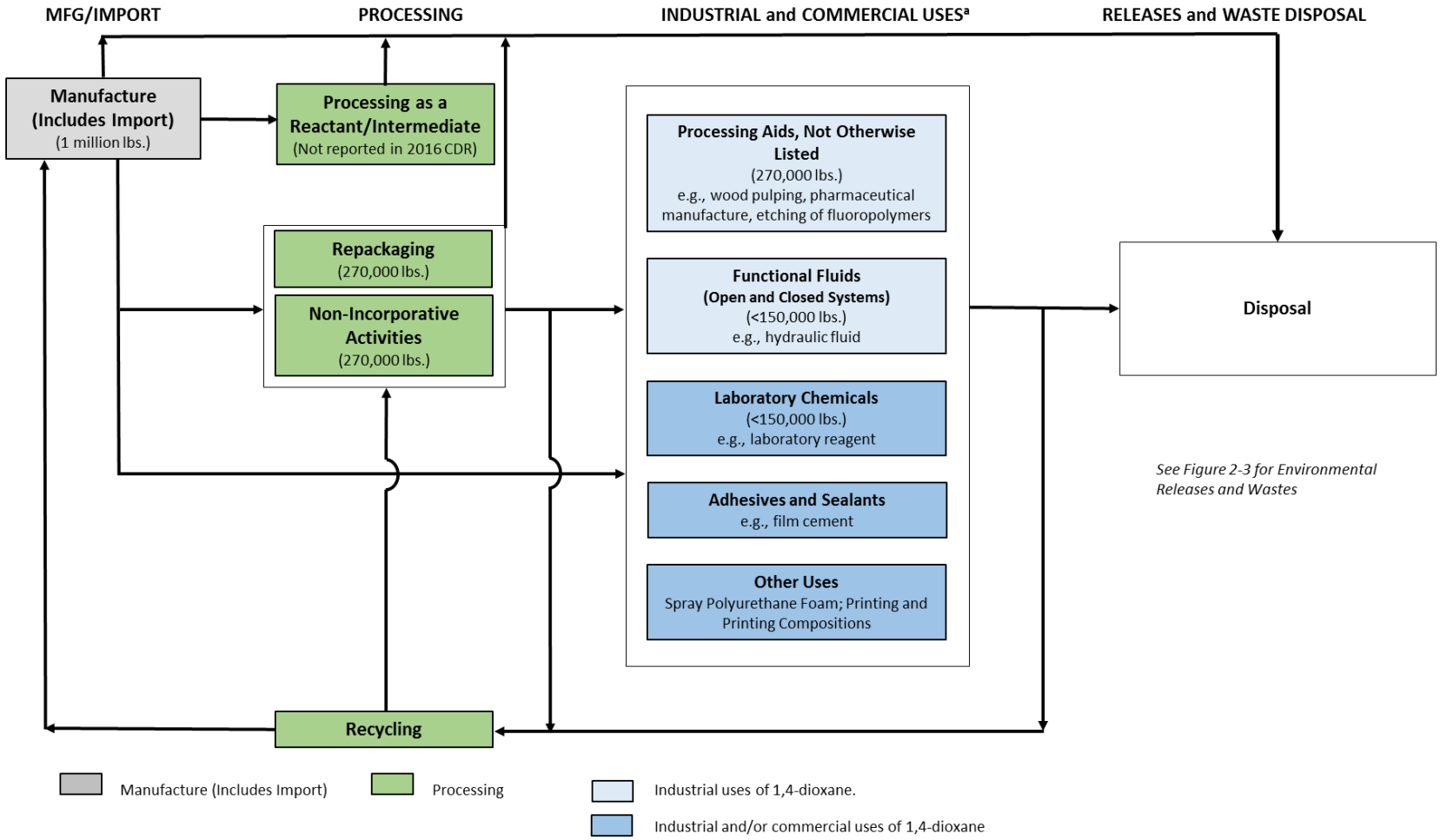


Figure 2-1. 1,4-Dioxane Life Cycle Diagram

The life cycle diagram depicts the conditions of use that are within the scope of the risk evaluation during various life cycle stages including manufacturing, processing, use (industrial or commercial) and disposal. The production volumes shown are for reporting year 2015 from the 2016 CDR reporting period (U.S. EPA, 2016c). Activities related to distribution (e.g., loading, unloading) will be considered throughout the 1,4-dioxane life cycle, rather than using a single distribution scenario.

[a] See Table 2-3 for additional uses not mentioned specifically in this diagram.

## 2.3 Exposures

For TSCA exposure assessments, EPA expects to evaluate exposures and releases to the environment resulting from the conditions of use applicable to 1,4-dioxane. Post-release pathways and routes will be described to characterize the relationship between the conditions of use of 1,4-dioxane and the exposure to human receptors, including potentially exposed or susceptible subpopulations, and ecological receptors. EPA will take into account, where relevant, the duration, intensity (concentration), frequency and number of exposures in characterizing exposures to 1,4-dioxane.

### 2.3.1 Fate and Transport

Environmental fate includes both transport and transformation processes. Environmental transport is the movement of the chemical within and between environmental media. Transformation occurs through the degradation or reaction of the chemical with other species in the environment. Hence, knowledge of the environmental fate of the chemical informs the determination of the specific exposure pathways and potential human and environmental receptors EPA expects to consider in the risk evaluation. Table 2-5 provides environmental fate data that EPA identified and considered in developing the scope for 1,4-dioxane. This information has not changed from that provided in the scope document.

Fate data including volatilization during wastewater treatment, volatilization from lakes and rivers, biodegradation rates, and organic carbon:water partition coefficient (log $K_{OC}$) were used when considering changes to the conceptual models. Systematic literature review is currently underway, so model results and basic principles were used to support the fate data used in problem formulation.

EPI Suite™ (U.S. EPA, 2012c) modules were used to predict volatilization of 1,4-dioxane from wastewater treatment plants, lakes, and rivers and to confirm the data showing slow biodegradation. The EPI Suite™ module that estimates chemical removal in sewage treatment plants ("STP" module) was run using default settings to evaluate the potential for 1,4-dioxane to volatilize to air or adsorb to sludge during wastewater treatment. The STP module estimates that 0.27% of 1,4-dioxane in wastewater will be removed by volatilization while 1.75% of 1,4-dioxane will be removed by adsorption.

The EPI Suite™ module that estimates volatilization from lakes and rivers ("Volatilization" module) was run using default settings to evaluate the volatilization half-life of 1,4-dioxane in surface water. The volatilization module estimates that the half-life of 1,4-dioxane in a model river will be 4.8 days and the half-life in a model lake will be 56 days.

The EPI Suite™ module that predicts biodegradation rates ("BIOWIN" module) was run using default settings to estimate biodegradation rates of 1,4-dioxane in soil and sediment. Three of the models built into the BIOWIN module (BIOWIN 1, 2, and 5) estimate that 1,4-dioxane will not rapidly biodegrade in aerobic environments, while a fourth (BIOWIN 6) estimates that 1,4-dioxane will rapidly biodegrade in aerobic environments. These results support the biodegradation data presented in the 1,4-dioxane scope document, which demonstrate slow biodegradation under aerobic conditions. The model that estimates anaerobic biodegradation (BIOWIN 7) predicts that 1,4-dioxane will not rapidly biodegrade under anaerobic conditions. Further, previous assessments of 1,4-dioxane found that biodegradation was slow or negligible (ATSDR, 2012; NTP, 2011; Health Canada, 2010; ECJRC, 2002; NICNAS, 1998).

The log $K_{OC}$ reported in the 1,4-dioxane scoping document was predicted using EPI Suite™. That value (0.4) is supported by the basic principles of environmental chemistry which states that the $K_{OC}$ is typically within one order of magnitude (one log unit) of the octanol:water partition coefficient ($K_{OW}$).

Indeed, the log $K_{OW}$ reported for 1,4-dioxane in the scoping document was -0.27, which is within the expected range. Further, the $K_{OC}$ could be approximately one order of magnitude larger than predicted by EPI Suite™ before sorption would be expected to significantly impact the mobility of 1,4-dioxane in groundwater. The log $K_{OC}$ reported in previous assessments of 1,4-dioxane were in the range of 0.4 – 1.23 (U.S. EPA, 2013b; ATSDR, 2012; U.S. EPA, 2010; ECJRC, 2002; NICNAS, 1998) and all values within that range would be associated with low sorption to soil and sediment (ECJRC, 2002; NICNAS, 1998), and all values within that range would be associated with low sorption to soil and sediment.

**Table 2-5. Environmental Fate Characteristics of 1,4-Dioxane**

| Property or Endpoint | Value [a] | References |
|---|---|---|
| Direct photodegradation | Not expected to undergo direct photolysis | (U.S. EPA, 2015c) |
| Indirect photodegradation | 4.6 hours (estimated for atmospheric degradation) | (U.S. EPA, 2015c) |
| Hydrolysis half-life | Does not undergo hydrolysis | (U.S. EPA, 2015c) |
| Biodegradation | <10% in 29 days (aerobic in water, OECD 301F)<br><5% in 60 days (aerobic in water, OECD 310)<br>0% in 120 days, 60% in 300 days (aerobic in soil microcosm) | (U.S. EPA, 2015c) |
| Bioconcentration factor (BCF) | 0.2-0.7 (OECD 305C) | (U.S. EPA, 2015c) |
| Bioaccumulation factor (BAF) | 0.93 (estimated) | (U.S. EPA, 2015c) |
| Organic carbon:water partition coefficient (log $K_{oc}$) | 0.4 (estimated) | (U.S. EPA, 2015c) |

[a] Measured unless otherwise noted.

1,4-Dioxane is expected to volatilize from dry surfaces and dry soil due to its vapor pressure of 40 mm Hg at 25°C (Table 2-1). It reacts with hydroxyl radicals (OH•) in the atmosphere with an estimated indirect photolysis half-life on the order of hours. 1,4-Dioxane is not expected to be susceptible to direct photolysis under environmental conditions since this compound lacks functional groups that absorb light at visible-ultraviolet (UV) light wavelengths.

Due to its water solubility (>800 g/L; Table 2-1) and Henry's Law constant ($4.8 \times 10^{-6}$ atm-$m^3$/mole at 25°C; Table 2-1), 1,4-dioxane is expected to demonstrate limited volatility from water surfaces and moist soil. Once it enters the environment, 1,4-dioxane is expected to be mobile in soil based on its organic carbon partition coefficient (estimated log $K_{oc}$ = 0.4) and may therefore migrate to surface waters and groundwater. 1,4-Dioxane will not hydrolyze in water because it does not have functional hydrolyzable groups.

In experimental studies, 1,4-dioxane has been demonstrated to be not readily biodegradable but was subject to biodegradation after acclimation in a soil microcosm. Measured bioconcentration factors for 1,4-dioxane are 0.7 or below and the estimated bioaccumulation factor is 0.93. Therefore, 1,4-dioxane has low bioaccumulation potential.

### 2.3.2 Releases to the Environment

Releases to the environment from conditions of use (e.g., industrial and commercial processes, commercial or consumer uses resulting in down-the-drain releases) are one component of potential exposure and may be derived from reported data that are obtained through direct measurement, calculations based on empirical data and/or assumptions and models.

Under the Emergency Planning and Community Right-to-Know Act (EPCRA) Section 313 rule, 1,4-dioxane is a TRI-reportable substance effective January 1, 1987. During problem formulation EPA further analyzed the TRI data and examined the definitions of elements in the TRI data to determine the level of confidence that a release would result from certain types of disposal to land (i.e. RCRA Subtitle C hazardous landfill and Class I underground Injection wells) and incineration. EPA also examined how many facilities recycle 1,4 dioxane, and how it is treated at industrial facilities.

Table 2-6 provides production-related waste managed data (also referred to as waste managed) for 1,4-dioxane reported by industrial facilities to the TRI program for 2015. Table 2-7 provides more detailed information on the quantities released to air or water or disposed of on land.

**Table 2-6. Summary of 1,4-Dioxane TRI Production-Related Waste Managed in 2015 (lbs)**

| Number of Facilities | Recycling | Energy Recovery | Treatment | Releases [a,b,c] | Total Production Related Waste |
|---|---|---|---|---|---|
| 49 | 4,292 | 1,591,064 | 1,923,623 | 705,691 | 4,224,670 |

Data source: 2015 TRI Data (updated March 2017) (U.S. EPA, 2017d).
[a] Terminology used in these columns may not match the more detailed data element names used in the TRI public data and analysis access points.
[b] Does not include releases due to one-time event not associated with production such as remedial actions or earthquakes.
[c] Counts all releases including release quantities transferred and release quantities disposed of by a receiving facility reporting to TRI.

**Table 2-7. Summary of 1,4-Dioxane TRI Releases to the Environment in 2015 (lbs)**

| | Number of Facilities | Air Releases | | Water Releases | Land Disposal | | | Other Releases [a] | Total On- and Off-site Disposal or Other Releases [b,c] |
|---|---|---|---|---|---|---|---|---|---|
| | | Stack Air Releases | Fugitive Air Releases | | Class I Under-ground Injection | RCRA Subtitle C Landfills | All other Land Disposal [a] | | |
| Subtotal | | 46,219 | 16,377 | | 563,976 | 13,376 | 49 | | |
| Totals | 49 | 62,596 | | 35,402 | 577,400 | | | 0 | 675,399 |

Data source: 2015 TRI Data (updated March 2017) (U.S. EPA, 2017d).
[a] Terminology used in these columns may not match the more detailed data element names used in the TRI public data and analysis access points.
[b] These release quantities include releases due to one-time events not associated with production such as remedial actions or earthquakes.
[c] Counts release quantities once at final disposition, accounting for transfers to other TRI reporting facilities that ultimately dispose of the chemical waste.

Facilities are required to report if they manufacture (including import) or process more than 25,000 pounds of 1,4-dioxane, or if they otherwise use more than 10,000 pounds of 1,4-dioxane. In 2015, 49 facilities reported a total of 4.2 million pounds of 1,4-dioxane waste managed. Of this total, over 4 thousand pounds were recycled, 1.6 million pounds were recovered for energy, 1.9 million pounds were treated and 700 thousand pounds were released to the environment. No TRI facilities reported recycling

1,4-dioxane on-site, but one reported transferring it off-site for recycling, specifically for solvents/organics recovery.

Of the almost 700 thousand pounds of total releases, there were stack and fugitive air releases, water releases, Class I underground injection, release to Resource Conservation and Recovery Act (RCRA) Subtitle C landfills and other land disposal (Table 2-7). For stack releases, multiple types of facilities report on incineration destruction, including hazardous waste facilities, and facilities that perform other industrial activities and may be privately or publically (i.e., federal, state or municipality) owned or operated. Approximately 46,000 lbs of 1,4-dioxane releases were reported to TRI as on-site stack releases, and account for any incineration destruction. Stack releases reported to TRI represent the total amount of 1,4 dioxane being released to the air at the facility from stacks, confined vents, ducts, pipes or other confined air streams.

In 2015, 205,725 pounds of 1,4-dioxane were released on-site, and 469,674 pounds were released off-site. Of the on-site releases, 52% (107,726 pounds) went to land disposal, 30% (62,596 pounds) went to air, including stack and fugitive releases, and 17% (35,402 pounds) was discharged to water. Of the on-site land disposal, most went to Class I underground injection wells or RCRA Subtitle C Landfills. Just 47 pounds went to on-site landfills other than RCRA Subtitle C Landfills, and none was disposed of in on-site Class II-V underground injection wells, on-site land treatment, or on-site surface impoundments. Of the off-site releases, the vast majority (469,672 lb) went to Class I underground injection wells. Very small amounts were transferred off-site to RCRA Subtitle C Landfills (0.31 lb), landfills other than RCRA Subtitle C Landfills (0.1 lb), and other types of land disposal (1.65 lb) and are considered of negligible concern for exposure.

While most 1, 4-dioxane going to land disposal went to highly regulated land disposal units in 2015, in past years, the TRI data show 1,4-dioxane going to other types of land disposal as well. From 1989 to 2002 the data show thousands of pounds of 1,4-dioxane disposed of via on-site land treatment. From 2009 to 2011, hundreds of pounds were disposed of in on-site landfills other than RCRA Subtitle C Landfills. There was also off-site disposal, with thousands of pounds disposed of off-site in landfills other than RCRA Subtitle C from 2002 to 2005. The volumes then decreased from hundreds, to tens, to almost no pounds disposed of off-site in landfills other than RCRA Subtitle C from 2006 to 2015.

While the volume of production-related waste managed shown in Table 2-6 excludes any quantities reported as catastrophic or one-time releases (TRI section 8 data), release quantities shown in Table 2-7 includes both production-related and non-routine quantities (TRI section 5 and 6 data). As a result, release quantities may differ slightly and may reflect differences in TRI calculation methods for reported release range estimates (U.S. EPA, 2017d).

EPA's *Compilation of Air Pollutant Emission Factors*, AP-42 section 6.13 on pharmaceuticals production provides general process and emissions information and the ultimate disposition of 1,4-dioxane (air, sewer, incineration, solid waste, product) by pharmaceutical manufacturers. Other sources of information provide evidence of releases of 1,4-dioxane, including National Emission Standards for Hazardous Air Pollutants (NESHAPs) promulgated under the Clean Air Act (CAA) or other EPA standards and regulations that set legal limits on the amount of 1,4-dioxane that can be emitted to a particular media.

### 2.3.3 Presence in the Environment and Biota

Monitoring studies or a collection of relevant and reliable monitoring studies provide(s) information that can be used in an exposure assessment. Monitoring studies that measure environmental concentrations or concentrations of chemical substances in biota provide evidence of exposure. Monitoring data were identified in EPA's data search for 1,4-dioxane.

Monitoring data (measured) from EPA's Air Quality System (AQS) and the open literature, as well as modeled estimates based on the National Air Toxics Assessment (NATA) and TRI emissions data suggest that 1,4-dioxane is present in ambient air. Monitored and modeled air concentrations from these sources suggest that many air concentrations may be low (i.e., <1 μg/m$^3$) and appear to have been higher in the past, possibly reflecting past uses (U.S. EPA, 2015a, 2011a). Recent (2015) air monitoring data). Recent (2015) air monitoring data were extracted from the Ambient Monitoring Archive (AMA). Of a total of 1397 collected samples, there were 948 non-detects (68%) and 449 detections (32%), which ranged from 0.005 to 0.96 ppb. All non-detects and detections for this chemical were sampled in four states: MI, OH, NC, and IN.

Indoor air monitoring data are available. One recent study reported annual average concentrations of 1,4-dioxane ranging from 0.01 to 0.11 μg/m$^3$ in several hundred homes in Germany (Wissenbach et al., 2016). Older indoor air monitoring studies are summarized in the U.S. EPA Voluntary Children's Chemical Evaluation Program (VCCEP) submission and report slightly higher concentrations, possibly reflecting past uses (Sapphire Group, 2007).

EPA's third Unregulated Contaminant Monitoring Rule (UCMR 3), published in 2012, required monitoring for 1,4-dioxane, along with 29 other contaminants. Over 28,000 drinking water samples were collected for chemicals suspected to be present in drinking water that lack health-based standards under the Safe Drinking Water Act.

Reported levels of 1,4-dioxane in groundwater range from 3 to 31,000 μg/L (ATSDR, 2012; USGS, 2002). Such instances of ground water contamination with 1,4-dioxane are documented in the states of California and Michigan. These data provide a basis for including groundwater in the scope of the 1,4dioxane risk evaluation from manufacturing, processing, distribution and use unless otherwise regulated or managed.

There are relatively fewer data available on 1,4-dioxane levels in surface water, though some studies of groundwater contamination also reported levels in nearby surface water. 1,4-Dioxane is released into surface water and some studies have examined 1,4-dioxane levels in sewage treatment or chemical plant effluent, combined collection treatments from apartment homes, and in river basin systems (ATSDR, 2012). 1,4-Dioxane has also been detected in landfill leachate (ATSDR, 2012).

1,4-Dioxane has not been measured and is unlikely to be present at elevated levels in sediment, sludge, soil or dust, based on its physical and chemical properties. Note, 1,4 dioxane is expected to be present in the water within the biosolids and the porewater within the soil. 1,4-Dioxane has a low bioaccumulation potential for accumulation in aquatic organisms and is short-lived in humans and few biomonitoring data are available.

### 2.3.4 Environmental Exposures

The manufacturing, processing, use and disposal of 1,4-dioxane can result in releases to the environment. In this section, EPA presents exposures to aquatic and terrestrial organisms.

***Aquatic Environmental Exposures***

EPA identified and reviewed national scale monitoring data to support this problem formulation. Based on national-scale monitoring data from EPA's STOrage and RETreival (STORET) and National Water Information System (NWIS) for the past ten years, 1,4-dioxoane is detected in surface water. The data points showed a detection rate of approximately 6% for this media, with detections ranging from 0.568 to 100 µg/L.

While recent monitoring data on ambient surface water levels indicate relatively low levels, EPA has used release estimates and measured effluent concentrations from EPA's Toxic Release Inventory (TRI) and Discharge Monitoring Report (DMR) Pollutant Loading Tool, respectively, to predict surface water concentrations near such discharging facilities for this problem formulation. To examine whether near-facility surface water concentrations could approach 1,4-dioxane's concentrations of concern, EPA employed a conservative approach, using readily-available modeling tools and data, as well as conservative assumptions. EPA's Exposure and Fate Assessment Screening Tool (U.S. EPA, 2014b) was used to estimate site-specific surface water concentrations based on estimated loadings of 1,4-Dioxane into receiving water bodies or reported on-site releases to surface waters for DMR and TRI facilities. The estimated loadings for the DMR facilities are calculated by the DMR Tool by combining the reported effluent concentrations with facility effluent flows. For TRI, the reported releases are based on monitoring, emission factors, mass balance and/or other engineering calculations. E-FAST 2014 incorporates stream dilution using stream flow information contained within the model. E-FAST also incorporates wastewater treatment removal efficiencies. Wastewater treatment removal is assumed to be 0% for this exercise, as reported loadings/releases are assumed to account for any treatment. To ensure this effort was likely to capture high-end surface water concentrations, loading data from the top ten dischargers from each data source were modeled for the last two years of complete datasets (2014-2015 for TRI sites and 2015-2016 for DMR facilities). Furthermore, as days of release and operation are not reported in these sources, EPA assumed a range of possible release days (i.e., 1, 20, and 250 days/year for facilities and 250 days/year for wastewater treatment plants or POTWs). Refer to the E-FAST 2014 Documentation Manual for equations used in the model to estimate surface water concentrations (U.S. EPA, 2007). Based on availability of site-specific flow data within E-FAST 2014 and scenario results, refinements were made to clarify or confirm the receiving water body and/or likely days of release.

High-end surface water concentrations (i.e., those obtained assuming low receiving water body stream flows) from all E-FAST 2014 runs ranged from 0.006 µg/L to 11,500 µg/L, with the minimum of 0.006 µg/L associated with a chronic release scenario (i.e., more than 20 days of release per year assumed) and the maximum of 11,500 µg/L associated with an acute release scenario (i.e., fewer than 20 days of release per year assumed). The maximum acute scenario high-end concentration was 11,500 µg/L and the maximum chronic scenario high-end concentration was 5,762 µg/. Results based on TRI release estimates were within the same range as those based on DMR annual loading values for the top ten dischargers and the reporting years covered. For a full table of results, see Appendix E.

***Terrestrial Environmental Exposures***

Based on its fate properties, 1,4-dioxane is not expected to reside in soil because it will either volatilize from dry surfaces and dry soil or move through the soil column with pore water.

### 2.3.5 Human Exposures

In this section, EPA presents occupational and general population exposures. Subpopulations, including potentially exposed and susceptible subpopulations, within these exposure categories are also presented.

#### 2.3.5.1 Occupational Exposures

Exposure pathways and exposure routes are listed below for worker activities under the various conditions of use described in Section 2.2. In addition, exposures to occupational non-users who do not directly handle the chemical but perform work in an area where the chemical is present are listed. Engineering controls and/or personal protective equipment may impact the occupational exposure levels.

Workers and occupational non-users may be exposed to 1,4-dioxane when performing activities associated with the conditions of use described in Section 2.2, including, but not limited to:

- Unloading and transferring 1,4-dioxane to and from storage containers to process vessels.
- Using 1,4-dioxane in process equipment.
- Cleaning and maintaining equipment.
- Sampling chemical, formulations or products containing 1,4-dioxane for quality control.
- Repackaging chemicals, formulations or products containing 1,4-dioxane.
- Handling, transporting and disposing waste containing 1,4-dioxane.
- Performing other work activities in or near areas where 1,4-dioxane is used.

***Key Data***

Key data that inform occupational exposure assessment include: the OSHA Chemical Exposure Health Data (CEHD) and NIOSH Health Hazard Evaluation (HHE) program data. OSHA data are workplace monitoring data from OSHA inspections. The inspections can be random or targeted, or can be the result of a worker complaint. OSHA data can be obtained through the OSHA Integrated Management Information System (IMIS) at https://www.osha.gov/oshstats/index.html. Table_Apx B-1 in Appendix B.1.3 provides a summary of industry sectors with 1,4-dioxane personal monitoring air samples obtained from OSHA inspections conducted between 2002 and 2016. NIOSH HHEs are conducted at the request of employees, union officials, or employers and help inform potential hazards at the workplace. HHEs can be downloaded at https://www.cdc.gov/niosh/hhe/.

***Inhalation***

Based on these activities, inhalation exposure to vapors and mists are expected for workers and occupational non-users. There is potential for spray application of some products containing 1,4-dioxane so exposures to mists are also expected for workers and will be incorporated into the worker inhalation exposure. See section 2.5.1 for additional details on the pathways EPA expects to analyze for occupational exposures.

The United States has several regulatory and non-regulatory exposure limits for 1,4-dioxane: An Occupational Safety and Health Administration (OSHA) Permissible Exposure Limit (PEL) of 100 ppm 8-hour time-weighted average (TWA) (360 mg/m$^3$) with a skin notation, a National Institute of Occupational Safety and Health (NIOSH) Recommended Exposure Limit (REL) of 1 ppm (3.6 mg/m$^3$) as a 30-minute ceiling and an American Conference of Government Industrial Hygienists (ACGIH) Threshold Limit Value (TLV) of 20 ppm TWA (72 mg/m$^3$) (OSHA, 2005). The influence of these exposure limits on occupation exposures will be considered in the occupational exposure assessment.

***Dermal***

Based on the conditions of use, EPA expects dermal exposure for workers and occupational non-users, including skin contact with vapors, liquids and mists. Occupational non-users do not handle the chemical directly, so dermal exposure from liquids containing 1,4-dioxane are not expected.

***Oral***
Worker exposure via the oral route is not expected. For some uses (described in Section 2.5.1), there are potential worker exposures through mists that deposit in the upper respiratory tract. Based on physical chemical properties, mists of 1,4-dioxane will likely be rapidly absorbed in the respiratory tract and will be considered as an inhalation exposure.

#### 2.3.5.2 Consumer Exposures

As stated in the Scope document (U.S. EPA, 2017c) and Section 2.2.2.1, there are no current consumer uses for 1,4-dioxane in the U.S.

#### 2.3.5.3 General Population Exposures

Wastewater/liquid wastes, solid wastes or air emissions of 1,4-dioxane could result in potential pathways for oral, dermal or inhalation exposure to the general population.

***Inhalation***
The general population may be exposed to 1,4-dioxane through inhalation of ambient air and indoor air. Ambient air exposures may occur from releases from industrial/commercial sources. Indoor air exposures may occur from infiltration from ambient air or emissions from tap water during activities such as showering and bathing. Based on the relatively high water solubility and relatively low Henry's law constant for 1,4-dioxane, EPA expects that volatilization would be low for many indoor uses. However, increased water temperature during bathing and showering can increase volatilization. The Henry's Law constant for 1,4-dioxane is appreciably higher at 40°C ($4.9 \times 10^{-4}$ atm-$m^3$/mole) than 25°C ($4.8 \times 10^{-6}$ atm-$m^3$/mole). Furthermore, smaller droplets of water created by some indoor uses (e.g., showering) have a larger surface area from which 1,4-dioxane may volatize.

Vapor intrusion and volatilization from wastewater treatment are not considered significant sources of exposure to the general population because the Henry's Law constant ($4.8 \times 10^{-6}$ atm-$m^3$/mole) and high water solubility of 1,4-dioxane (>800 g/L) indicate that 1,4-dioxane will primarily remain in the aqueous phase (wastewater or groundwater) and that volatilization from water to air will be limited. Estimated volatilization from the sewage treatment plant (STP) module in EPI Suite™ found that 0.27% of 1,4-dioxane in wastewater would be removed by volatilization during wastewater treatment.

***Oral***
The general population may ingest 1,4-dioxane via contaminated drinking water. Based on reported uses, down-the-drain sources may contribute to surface water and drinking water levels. Therefore, there is potential oral exposure to 1,4-dioxane by ingestion of drinking water from surface water and ground water sources to municipal drinking water.

***Dermal***
Dermal exposure via water may occur through extended contact with tap water containing 1,4-dioxane during washing and bathing. The source of the contaminated water may be either contaminated surface or ground waters used as a source of municipal drinking water.

#### 2.3.5.4 Potentially Exposed or Susceptible Subpopulations

TSCA requires that the determination of whether a chemical substance presents an unreasonable risk to "a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation" by EPA. TSCA § 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." General population is "the total of individuals inhabiting an area or making up a whole group" and refers here to the U.S. general population (U.S. EPA, 2011a).

As part of the Problem Formulation, EPA identified potentially exposed and susceptible subpopulations for further analysis during the development and refinement of the life cycle, conceptual models, exposure scenarios and analysis plan. In this section, EPA addresses the potentially exposed or susceptible subpopulations identified as relevant based on greater exposure. EPA will address the subpopulations identified as relevant based on greater susceptibility in the hazard section.

EPA identifies the following as potentially exposed or susceptible subpopulations due to their *greater exposure*:

- Workers and occupational non-users.
- Other groups of individuals within the general population who may experience greater exposures due to their proximity to conditions of use identified in Section 2.2 that result in releases to the environment and subsequent exposures (e.g., individuals who live or work near manufacturing, processing, distribution, use or disposal sites).

In developing exposure scenarios, EPA will analyze available data to ascertain whether some human receptor groups may be exposed via exposure pathways that may be distinct to a particular subpopulation or lifestage and whether some human receptor groups may have higher exposure via identified pathways of exposure due to unique characteristics (e.g., activities, duration or location of exposure) when compared with the general population (U.S. EPA, 2006).

In summary, in the risk evaluation for 1,4-dioxane, EPA plans to analyze the following potentially exposed groups of human receptors: workers, occupational non-users and the general population. EPA may also identify additional potentially exposed or susceptible subpopulations that will be considered based on greater exposure.

## 2.4 Hazards (Effects)

For scoping, EPA conducted comprehensive searches for data on hazards of 1,4-dioxane, as described in *Strategy for Conducting Literature Searches for 1,4-Dioxane: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0723). Based on initial screening, EPA plans to analyze the hazards of 1,4-dioxane identified in this problem formulation document. However, when conducting the risk evaluation, the relevance of each hazard within the context of a specific exposure scenario will be judged for appropriateness. For example, hazards that occur only as a result of chronic exposures may not be applicable for acute exposure scenarios. This means that it is unlikely that every identified hazard will be analyzed for every exposure scenario.

### 2.4.1 Environmental Hazards

During problem formulation, EPA analyzed potential environmental health hazards associated with 1,4-dioxane. EPA identified the following sources of environmental hazard data for 1,4-dioxane: (Health

Canada, 2010; ECJRC, 2002; OECD, 1999; NICNAS, 1998); and the European Chemicals Agency (ECHA) Database. Studies published since 2003 were identified in the literature search for 1,4-dioxane (*1,4-Dioxane (CASRN 123-91-1) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0723) and were reviewed as described in *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a) and *Strategy for Assessing Data Quality in TSCA Risk Evaluations* (U.S. EPA, 2018b). Only the *on-topic* references listed in the Ecological Hazard Literature Search Results were considered as potentially relevant data/information sources for the risk evaluation. Inclusion criteria were used to screen the results of the ECOTOX literature search (as explained in the *Strategy for Conducting Literature Searches for 1-4-Dioxane: Supplemental Document to the TSCA Scope Document, CASRN:123-91-1*). Data from the screened literature are summarized below (Table 2-8) as ranges (min-max). EPA plans to complete review of these data/information sources during risk evaluation using the data quality review evaluation metrics and the rating criteria described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a).

***Toxicity to Aquatic Organisms***

EPA identified 1,4-dioxane environmental hazard data for fish, aquatic invertebrates and aquatic plants exposed under acute and chronic exposure conditions. Aquatic toxicity studies are summarized in Table 2-8.

**Table 2-8. Ecological Hazard Characterization of 1,4-Dioxane**

| Duration | Test organism | Endpoint | Hazard value(s)[a] | Units | Effect(s) | Citation(s) |
|---|---|---|---|---|---|---|
| **Aquatic Organisms** | | | | | | |
| Acute | Fish | $LC_{50}$ | >100 – 67,000 | mg/L | Mortality | (Geiger et al., 1990) |
| | Aquatic invertebrates | $EC_{50}$ | >299 - >1,000 | mg/L | Immobilization | (Dow Chemical Company, 1989) as cited in (ECJRC, 2002) |
| | Algae | $EC_{50}$ | 575 - 5600 | mg/L | Inhibition | (Bringman and Kuhn, 1977) |
| | | | 580 | mg/L | Biomass | (ECHA, 2014b) |
| | | | >1,000 | mg/L | Biomass | (ECHA, 2014b) |
| | **Acute COC = 60 mg/L** | | | | | |
| Chronic | Fish | NOEC[b] | 565 | mg/L | Carcinogenicity | (Johnson et al., 1993) |
| | | MATC[c] | >145 | | Development, Hatching, Survival | (TSCATS, 1989) as cited in (ECJRC, 2002) |
| | Aquatic invertebrates | NOEC | 1,000 | mg/L | Reproduction | (ECHA, 2014a) |
| | **Chronic COC = 15 mg/L** | | | | | |
| **Terrestrial Organisms** | | | | | | |
| Chronic | Terrestrial Plant | $EC_{50}$ | 1,450 | mg/L | Germination/Root Elongation | (Reynolds, 1989) |

[a]Values in the tables are presented as reported by the study authors.
[b]NOEC: No Observable Effect Concentration,
[c]MATC, Maximum Acceptable Toxicant Concentration; Calculated using the geometric mean of LOEC and NOEC values (as described in (U.S. EPA, 2013a)

The acute 96-hour $LC_{50}$ values for fish range from >100 mg/L (highest concentration tested) for fathead minnow (*Pimephales promelas*) to 67,000 mg/L for inland silversides (*Menidia beryllina*). Two studies on the acute ecotoxicity to aquatic invertebrates (*Daphnia magna* and *Ceridodaphnia dubia*) indicate that the 48-hour $EC_{50}$ is >1,000 mg/L (highest concentration tested) (ECJRC, 2002) and >299 mg/L (highest concentration tested; (Dow Chemical Company, 1989)).

In a chronic study, Medaka (*Oryzias latipes*) were exposed to measured concentrations of 1,4-dioxane ranging from 565 to 6,933 mg/L for 28 days under flow-through conditions. There were effects on growth and survival (Johnson et al., 1993). A no observed effect concentration (NOEC) of 565 mg/L was reported. In another study, fathead minnows (*P. promelas*) were exposed to 1,4-dioxane for 32 days to mean measured concentrations of 27.6, 40.3, 65.3, 99.7 and 145 mg/L to observe the effects on embroyonic development (i.e., hatching, larval development, and larval survival) under flow-through conditions. No effects were observed. A NOEC of >103 mg/L based on larval survival and a maximum acceptable toxicant concentration (MATC) of 145 mg/L was calculated (NOEC=MATC/√2) (ECJRC, 2002).

In a study on the chronic toxicity of 1,4-dioxane to aquatic invertebrates, water fleas (*D. magna*) were exposed to unspecified concentrations of 1,4-dioxane in a 21-day reproduction test. The exposure conditions were not reported. The highest exposure concentration tested was 1,000 mg/L. No effects on reproduction, survival, or growth were reported. A 21-day NOEC of >1,000 mg/L was reported (ECHA, 2014a).

Three studies have characterized the toxicity of 1,4-dioxane to aquatic plants. In one study, green algae (*Pseudokirchnerella subcapitata*) were exposed to unspecified concentrations of 1,4-dioxane for 72-hours under static conditions. No effects were observed on growth rate or biomass at 1,000 mg/L, the highest concentration tested. A 72-hour $EC_{50}$ (growth rate and biomass) of > 1,000 mg/L was reported. A NOEC (biomass) of 580 mg/L and a NOEC (growth rate) of 1,000 mg/L was reported (ECHA, 2014b). Also, two short-term toxicity studies in *Microcystis aeruginosa* and *Scenedesmus quadricauda* reported $EC_{50}$ cell inhibition of 575 and 5,600 mg/L after eight days of exposure to 1,4-dioxane (Bringman and Kuhn, 1977).

***Toxicity to Sediment and Terrestrial Organisms***

In one study, lettuce (*Actuca sativa*) were exposed to 1,4-dioxane in a germination/root elongation toxicity test for 3-days. An EC50 of 1,450 mg/L was reported for germination (Reynolds, 1989).

There are no available acute or chronic toxicity studies that characterize the hazard of 1,4-dioxane to sediment organisms. However, available hazard, fate and exposure characteristics (Sections 2.3.1 and 2.3.3) suggest that sediment organisms are not at risk from 1,4-dioxane exposures.

***Concentrations of Concern (COC)***

The concentrations of concern (COCs) for aquatic species were calculated based on the summarized environmental hazard data for 1,4-dioxane. The analysis of the environmental COCs are described in Appendix C and are based on EPA/OPPT methods (U.S. EPA, 2013a, 2012d). The acute and chronic COC for 1,4-dioxane are based on the lowest toxicity value in the dataset. For a particular environment (e.g., aquatic environment), the COC is based on the most sensitive species or the species with the lowest toxicity value reported in that environment.

The acute concentration of concern for 1,4-dioxane is based on a 96-hour fish toxicity study where the $LC_{50}$ is >100 mg/L (ECHA, 2014a; Geiger et al., 1990) and the chronic COC is based on a 32-day MATC fish toxicity value of 145 mg/L (Brooke, 1987). The acute and chronic COCs for 1,4-dioxane are 59,800 ppb and 14,500 ppb, respectively.

### 2.4.2 Human Health Hazards

1,4-Dioxane has an existing EPA IRIS Assessment (U.S. EPA, 2013c, 2010), an ATSDR Toxicological Profile (ATSDR, 2012), a Canadian Screening Assessment (Health Canada, 2010), a European Union (EU) Risk Assessment Report (ECJRC, 2002) and an Interim AEGL (U.S. EPA, 2005b); hence, many of the hazards of 1,4-dioxane have been previously compiled and reviewed. EPA expects to use these previous analyses as a starting point for identifying key and supporting studies to inform the human health hazard assessment, including dose-response analysis. The relevant studies will be evaluated using the data quality criteria in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a). EPA also plans to analyze other studies (e.g., more recently published, alternative test data) that have been published since these reviews, as identified in the literature search conducted by the Agency for 1,4-dioxane (*1,4-Dioxane* (*CASRN 123-91-1*) *Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0723). Based on reasonably available information, the following sections describe the potential hazards associated with 1,4-dioxane.

#### 2.4.2.1 Non-Cancer Hazards

***Acute Toxicity***

Effects following acute exposures were evaluated (U.S. EPA, 2005b). The Interim AEGLs (U.S. EPA, 2005b) evaluated the data on acute toxicity and irritation and concluded that, in animals, acute toxic effects of 1,4-dioxane include central nervous system depression, kidney and liver damage and irritation. Humans acutely exposed to 1,4-dioxane experienced irritation of the eyes, nose and throat, nausea and vomiting, coma and death. Also, 1,4-dioxane can cause narcosis in animals inhaling very high concentrations (U.S. EPA, 2005b).

***Irritation***

Acute inhalation studies in human volunteers noted irritation of the eyes, nose and throat (U.S. EPA, 2005b). In rats, 2 years of inhalation exposure to 1,4-dioxane, resulted in metaplasia, hyperplasia, atrophy, hydropic change, vacuolic change and preneoplastic cell proliferation in the nasal cavity (U.S. EPA, 2013c).

***Liver Toxicity***

In subchronic and chronic repeated exposure studies conducted in rats and mice by the oral (via drinking water) and inhalation routes, evidence shows that 1,4-dioxane is toxic to the liver (U.S. EPA, 2013c). Chronic administration of 1,4-dioxane via the drinking water resulted in hepatocellular degeneration and preneoplastic changes. Inhalation exposure to 1,4-dioxane resulted in necrosis of the centrilobular region and preneoplastic changes in the liver.

***Kidney Toxicity***

In subchronic and chronic repeated exposure studies conducted in rats and mice by the oral (via drinking water) and inhalation routes, evidence shows that 1,4-dioxane is toxic to the kidney (U.S. EPA, 2013c). Kidney damage following drinking water exposure to 1,4-dioxane includes degeneration of cortical tubule cells, necrosis with hemorrhage and glomerulonephritis.

#### 2.4.2.2 Genotoxicity and Cancer Hazards

U.S. EPA (2013c) concluded that overall, the available literature indicates that 1,4-dioxane is nongenotoxic or weakly genotoxic. Per EPA's Cancer Guidelines (U.S. EPA, 2005a), EPA concluded "there is insufficient biological support for potential key events and to have reasonable confidence in the sequence of events and how they relate to the development of nasal tumors following exposure to 1,4-dioxane". No single mode of action (MOA) accounts for the formation of liver, nasal, peritoneal (mesotheliomas), and mammary gland tumors seen in laboratory animals exposed to 1,4-dioxane. Some data support a non-linear MOA for liver tumorigenesis, but currently available data do not support non-linearity for the remaining tumor types.

EPA evaluated the weight of the evidence for cancer in humans and animals and concluded that 1,4-dioxane is "likely to be carcinogenic to humans" based on evidence of carcinogenicity in several 2-year bioassays (oral and inhalation) conducted in four strains of rats, two strains of mice and in guinea pigs (U.S. EPA, 2013c). The National Toxicology Program classified 1,4-dioxane as "reasonably anticipated to be a human carcinogen" (NTP, 2016), and NIOSH has classified it as a "potential occupational carcinogen" (ATSDR, 2012). Human occupational studies into the association between 1,4-dioxane exposure and increased cancer risk are inconclusive because they are limited by small cohort size and a small number of reported cancer cases.

#### 2.4.2.3 Potentially Exposed or Susceptible Subpopulations

TSCA requires that the determination of whether a chemical substance presents an unreasonable risk include consideration of unreasonable risk to "a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation" by EPA. TSCA § 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." In developing the hazard assessment, EPA will analyze available data to ascertain whether some human receptor groups may have greater susceptibility than the general population to the chemical's hazard(s).

## 2.5 Conceptual Models

EPA risk assessment guidance ((U.S. EPA, 2014c, 1998)), defines Problem Formulation as the part of the risk assessment framework that identifies the factors to be considered in the assessment. It draws from the regulatory, decision-making and policy context of the assessment and informs the assessment's technical approach.

A conceptual model describes the actual or predicted relationships between the chemical substance and receptors, either human or environmental. These conceptual models are integrated depictions of the conditions of use, exposures (pathways and routes), hazards and receptors. The initial conceptual models describing the scope of the assessment for 1,4-dioxane, have been refined during problem formulation. The changes to the conceptual models in this problem formulation are described along with the rationales.

In this section EPA outlines those pathways that will be included and further analyzed in the risk evaluation; will be included but will not be further analyzed in risk evaluation; and will not be included in the TSCA risk evaluation and the underlying rationale for these decisions.

EPA determined as part of problem formulation that it is not necessary to conduct further analysis on certain exposure pathways that were identified in the 1,4-dioxane scope document and that remain in the risk evaluation. Each risk evaluation will be "fit-for-purpose," meaning not all conditions of use will warrant the same level of evaluation and the Agency may be able to reach some conclusions without comprehensive risk evaluations. 82 FR 33726, 33734, 33739 (July 20, 2017).

As part of this problem formulation, EPA also identified t exposure pathways under other environmental statutes, administered by EPA, which adequately assess and effectively manage exposures and for which long-standing regulatory and analytical processes already exist, i.e., the Clean Air Act (CAA), the Safe Drinking Water Act (SDWA), the Clean Water Act (CWA) and the Resource Conservation and Recovery Act (RCRA). OPPT worked closely with the offices within EPA that administer and implement the regulatory programs under these statutes. In some cases, EPA has determined that chemicals present in various media pathways (i.e., air, water, land) fall under the jurisdiction of existing regulatory programs and associated analytical processes carried out under other EPA-administered statutes and have been assessed and effectively managed under those programs. EPA believes that the TSCA risk evaluation should focus on those exposure pathways associated with TSCA uses that are not subject to the regulatory regimes discuss above because these pathways are likely to represent the greatest areas of concern to EPA. As a result, EPA does not plan to include in the risk evaluation certain exposure pathways identified in the 1,4-dioxane scope document.

### 2.5.1 Conceptual Model for Industrial and Commercial Activities and Uses: Potential Exposures and Hazards

The revised conceptual model (Figure 2-2) describes the pathways of exposure from industrial and commercial activities and uses of 1,4-dioxane that EPA plans to include in the risk evaluation. There are exposures to workers and occupational non-users via dermal and inhalation routes during manufacturing, processing, use and disposal of 1,4-dioxane for all uses identified in the scope, except for distribution in commerce. During distribution, 1,4-dioxane is contained in closed systems (e.g. drums, pails, bottles) so releases and exposures are not expected. Any associated open system loading and unloading activities into these containers will be analyzed for the condition of use.

The description for uses of 1,4-dioxane as Functional Fluids has been refined to include both open and closed systems. When the scope of the risk evaluation was determined, the information available to EPA suggested that 1,4-dioxane was used as Functional Fluids only in closed systems. However, during problem formulation, EPA determined that some of the subcategories of uses, such as cutting and tapping fluid, may also include uses in open systems. This change is reflected in the conceptual model ( Figure 2-2).

***Inhalation***

EPA expects that for workers and occupational non-users, exposure via inhalation will be the most significant route of exposure for most exposure scenarios. EPA plans to further analyze inhalation exposures to vapors and mists for workers and occupational non-users in the risk evaluation.

EPA reviewed the potential for occupational exposures associated with subcategories of conditions of use where a mist may be generated. EPA determined that most subcategories will not produce a mist during their typical use and, for these, EPA concludes that exposure to 1,4-dioxane would be negligible and does not plan further analysis. For subcategories of uses where either a spray application or rotary equipment is likely, EPA determined that these conditions of use may produce a mist that could result in exposures for workers when the mist is inhaled and subsequently swallowed and EPA plans to analyze

exposures associated with these uses. EPA will also evaluate subcategories of uses where EPA is uncertain whether a mist is likely to be produced during use. EPA expects to further evaluate exposure via a mist for the uses listed in Table 2-9.

**Table 2-9. 1,4-Dioxane Conditions of Use that May Produce a Mist**

| Life Cycle Stage | Category | Subcategory |
|---|---|---|
| Processing | Recycling | Recycling |
| Industrial use | Processing aids, not otherwise listed | Wood pulping<br>Extraction of animal and vegetable oils<br>Wetting and dispersing agent in textile processing<br>Etching of fluoropolymers |
| Industrial use | Functional fluids (open and closed system) | Polyalkylene glycol lubricant<br>Synthetic metalworking fluid<br>Cutting and tapping fluid<br>Hydraulic fluid |
| Industrial use, potential commercial use | Other uses | Spray polyurethane foam<br>Printing and printing compositions |

***Dermal***

There is the potential for dermal exposures to 1,4-dioxane in many worker scenarios. Dermal exposure from contact with liquids containing 1,4-dioxane are expected primarily for workers, such as operators, directly involved in working with these liquids. Where workers may be exposed to 1,4-dioxane, the OSHA standard requires that workers are protected from contact (e.g. gloves) (29 CFR 1910.1052). Occupational non-users are not directly handling 1,4-dioxane; therefore, skin contact with liquid 1,4-dioxane is not expected for occupational non-users and will not be further analyzed in the risk evaluation. EPA plans to further analyze dermal exposures for skin contact with liquids in occluded situations for workers.

Workers and occupational non-users can have skin contact with 1,4-dioxane vapor concurrently with inhalation exposures. The parameters determining the absorption of 1,4-dioxane vapor are based on the concentration of the vapor, the duration of exposure and absorption. The concentration of the vapor and the duration of exposure are the same for concurrent dermal and inhalation exposures. Therefore, the differences between dermal and inhalation exposures depend on the absorption. The dermal absorption can be estimated from the skin permeation coefficient (0.00043 cm/hr from a water solution; (Bronaugh, 1982)) and exposed skin surface area (on the order of 0.2 $m^2$, (U.S. EPA, 2011a)). The absorption of inhaled vapors can be estimated from the volumetric inhalation rate (approximately 1.25 $m^3$/hr for a person performing light activity, (U.S. EPA, 2011a)) adjusted by a retention factor such as 0.75. Based on these parameters the absorption of 1,4-dioxane vapor via skin will be orders of magnitude lower than via inhalation and will not be further analyzed.

***Oral***

There are potential worker exposures through mists that deposit in the upper respiratory tract. Based on physical chemical properties, mists of 1,4-dioxane will likely be rapidly absorbed in the respiratory tract

or evaporate and contribute to the amount of 1,4-dioxane vapor in the air. Furthermore, if 1,4-dioxane mists were ingested orally the available toxicological data do not suggest significantly different toxicity from considering the mists as an inhalation exposure.

***Waste Handling, Treatment and Disposal***

Figure 2-2 shows that waste handling, treatment and disposal is expected to lead to the same pathways as other industrial and commercial activities and uses. The path leading from the "Waste Handling, Treatment and Disposal" box to the "Hazards Potentially Associated with Acute and/or Chronic Exposures See Section 2.4.2" box was re-routed to accurately reflect the expected exposure pathways, routes, and receptors associated with these conditions of use of 1,4-dioxane.

For each condition of use identified in Table 2-3, a determination was made as to whether each unique combination of exposure pathway, route, and receptor will be evaluated further in the risk evaluation. The results of that analysis along with the supporting rationale are presented in Appendix D and Appendix E.

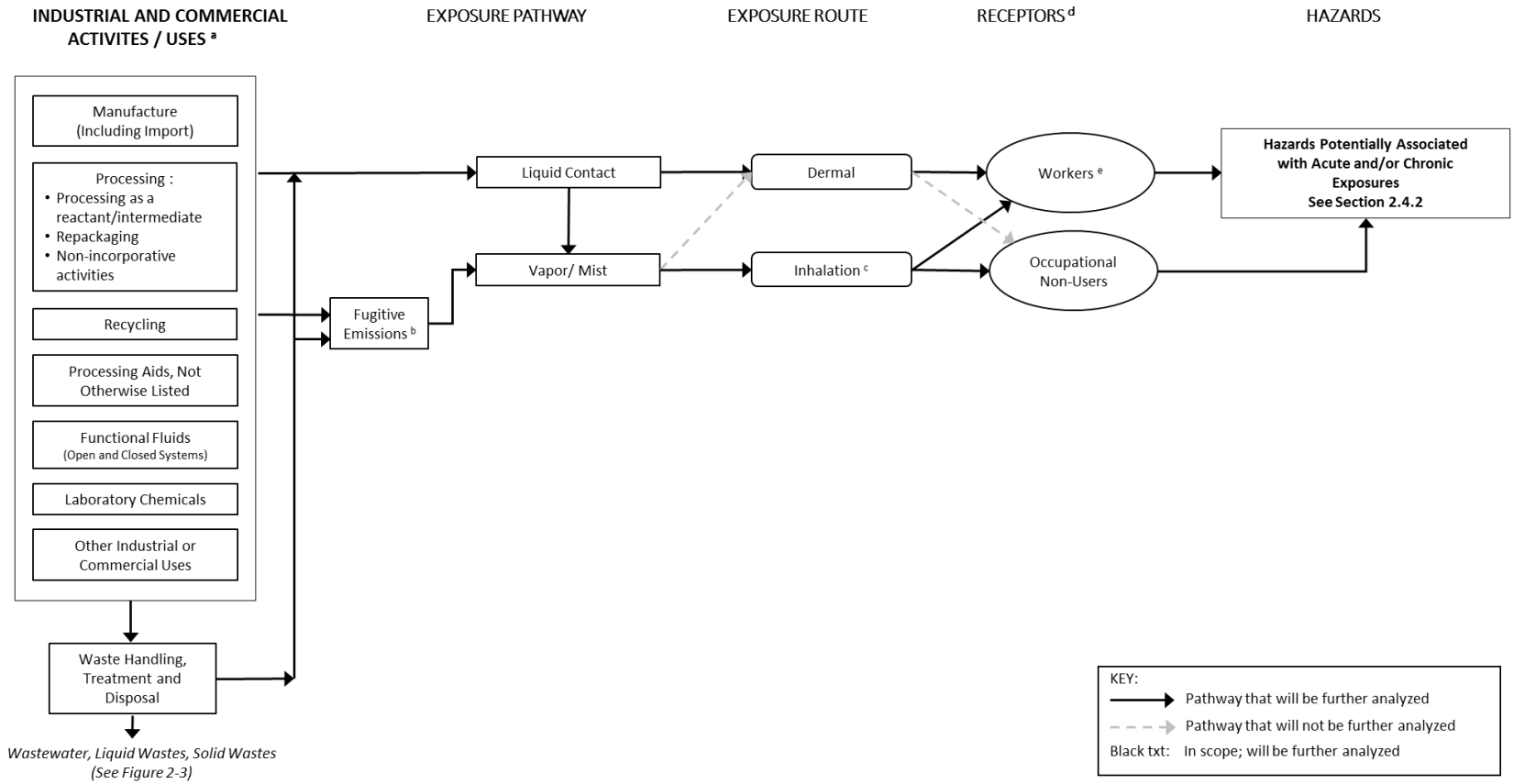


**Figure 2-2. 1,4-Dioxane Conceptual Model for Industrial and Commercial Activities and Uses: Potential Exposures and Hazards**

The conceptual model presents the exposure pathways, exposure routes and hazards to human receptors from industrial and commercial activities and uses of 1,4-dioxane that EPA plans to analyze.

[a] Additional uses of 1,4-dioxane are included in Table 2-3.

[b] Fugitive air emissions are those that are not stack emissions (emissions that occur through stacks, confined vents, ducts, pipes or other confined air streams), and include fugitive equipment leaks from valves, pump seals, flanges, compressors, sampling connections, open-ended lines; evaporative losses from surface impoundment and spills; and releases from building ventilation systems.

[c] Based on physical chemical properties, 1,4-dioxane in mists that deposit in the upper respiratory tract will likely be rapidly absorbed in the respiratory tract or evaporate and may be considered an inhalation exposure.

[d] Receptors include potentially exposed or susceptible subpopulations.

[e] When data and information are available to support the analysis, EPA also considers the effect that engineering controls and/or personnel protective equipment have on occupational exposure levels.

### 2.5.2 Conceptual Model for Consumer Activities and Uses: Potential Exposures and Hazards

The 1,4-dioxane life cycle diagram (Figure 2-1) indicates that no uses of 1,4-dioxane were identified in consumer products. EPA did not receive data, information or comments that informed a change was necessary to the scope. Therefore, EPA does not plan to evaluate use of 1,4-dioxane in consumer products and there is no conceptual model provided for consumer activities and uses.

### 2.5.3 Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards

The revised conceptual model (Figure 2-2) illustrates the expected exposure pathways to human and ecological receptors from environmental releases and waste stream associated with industrial and commercial activities for 1,4-dioxane. The pathways that EPA plans to include but not analyze further in risk evaluation are described in Section 2.5.3.2 and shown in the conceptual model. The pathways that EPA does not plan to include in the risk evaluation are described in Section 2.5.3.2.

#### 2.5.3.1 Pathways That EPA Plans to Include and Further Analyze in the Risk Evaluation

There are no environmental release and waste pathways for the environment or general populations that EPA plans to include and further analyze in the risk evaluation (see Figure 2-3).

#### 2.5.3.2 Pathways that EPA Plans to Include in the Risk Evaluation But Not Further Analyze

The pathways that EPA plans to include in the risk evaluation but not further analyze are ambient water exposure to aquatic vertebrates, invertebrates and aquatic plants, sediment and land-applied biosolids.

***Aquatic Pathways***

EPA analyzed risks to aquatic organisms exposed to 1,4-dioxane in surface water based on the relatively high potential for release, fate properties, and the availability of environmental monitoring data and hazard data. Based on 2015 TRI reporting, an estimated 35,402 lb of 1,4-dioxane was released to water from industrial sources. 1,4-Dioxane has high water solubility and slow removal from surface water due lack of hydrolysis (no hydrolyzable groups) and slow biodegradation (< 10% degradation in 29 days). Monitored concentrations in surface water from STORET/NWIS are as high as 100 µg/L and predicted concentrations in surface water for acute and chronic scenarios are up to 11,500 µg/L and 5,762 µg/L, respectively (Section 2.3.4). Measured and estimated levels of 1,4-dioxane in the environment are sufficiently below the acute and chronic aquatic COCs of 20,000 µg/L and 14,500 µg/L (See Environmental Hazards, Section 2.4.1 and Analysis of the Environmental Concentrations of Concern, Appendix C). EPA is including the analysis of risks to aquatic invertebrates and aquatic plants from exposures to 1,4-dioxane in surface waters in the evaluation, but will not further analyze the data.

***Sediment Pathways***

EPA does not plan to further analyze 1,4-dioxane pathways to sediment. 1,4-Dioxane is expected to remain in aqueous phases and not adsorb to sediment due to its water solubility (> 800 g/L) and low partitioning to organic matter (log KOC = 0.4). Limited sediment monitoring data for 1,4-dioxane that are available suggest that 1,4-dioxane is present in sediments, but because 1,4-dioxane does not partition to organic matter (log KOC = 0.4) and biodegrades slowly [<10% biodegradation in 29 days (ECHA, 1996)], 1,4-dioxane concentrations in sediment pore water are expected to be similar to the concentrations in the overlying water. Thus, the 1,4-dioxane detected in sediments is likely from the

pore water and not 1,4-dioxane that was sorbed to the sediment solids. While no ecotoxicity studies were available for sediment organisms, the toxicity of 1,4-dioxane to sediment invertebrates is expected to be similar to the toxicity to aquatic invertebrates.

***Land-Applied Biosolids Pathway***

EPA does not plan to further analyze other releases to land during risk evaluation, including biosolids application to soil. EPA expects releases of 1,4-dioxane to wastewater treatment plants (WWTP), resulting in biosolids that can be land-applied. Species in the environment including aquatic organisms, amphibians and terrestrial organisms may come into contact with 1,4-dioxane-contaminated biosolids and soil pore water when the biosolids are land applied. However, the release of 1,4-dioxane from land-applied biosolids represents a negligible fraction of its overall environmental release, due to its physical-chemical properties.

1,4-Dioxane is not expected to adsorb to soil and sediment due to its low partitioning to organic matter (estimated log $K_{oc}$ = 0.4), so 1,4-dioxane in biosolids is expected to be in the aqueous phase associated with the biosolids rather than adsorbed to the organic matter. The aqueous phase represents > 95% of biosolids, or ≥ 70% if the biosolids are dewatered, and at the time of removal the water in the biosolids will contain the same concentration of 1,4-dioxane as the rest of the wastewater at the activated sludge stage of treatment. However, the volume of water removed with biosolids represents < 2% of wastewater treatment plant influent volume (U.S. EPA, 1974), and is < 1% of influent volume when the sludge is dewatered and the excess water is returned to treatment, a process that is commonly used (NRC, 1996). Thus, the water released from a treatment plant via biosolids is negligible compared to that released as effluent. By extension the 1,4-dioxane released from wastewater treatment via biosolids is expected to be negligible compared to the 1,4-dioxane released with effluents: of the 1,4-dioxane in influent wastewater, it is expected that approximately 2% will be removed via adsorption to sludge or volatilization to air, < 2% will be removed with biosolids-associated water, and > 95% will be present in the effluent (see Section 2.3.1, Fate and Transport). Further, the concentrations of 1,4-dioxane in biosolids may decrease through volatilization to air during transport, processing (including dewatering and digestion), handling, and application to soil (which may include spraying). When 1,4-dioxane is released in the environment, it is expected to be mobile in soil and migrate to surface waters and groundwater or volatilize to air. 1,4-Dioxane is expected to volatilize readily from dry soil and surfaces due to its vapor pressure (40 mm Hg). Overall, the exposures to surface water from biosolids will be negligible compared to the direct release of WWTP effluent to surface water, and therefore exposures of aquatic organisms from surface water due to land-applied biosolids will not be further analyzed.

#### 2.5.3.3 Pathways That EPA Does Not Plan to Include in the Risk Evaluation

Exposures to receptors (i.e. general population) may occur from industrial and/or commercial uses; industrial releases to air, water or land; and other conditions of use. As described in section 2.5, pathways under other environmental statutes, administered by EPA, which adequately assess and effectively manage exposures and for which long-standing regulatory and analytical processes already exist will not be included in the risk evaluation. These pathways are described below.

***Ambient Air Pathway***

The Clean Air Act (CAA) contains a list of hazardous air pollutants (HAP), including 1,4-dioxane, and provides EPA with the authority to add to that list pollutants that present, or may present, a threat of adverse human health effects or adverse environmental effects. For stationary source categories emitting HAP, the CAA requires issuance of technology-based standards and, if necessary, additions or revisions to address developments in practices, processes, and control technologies, and to ensure the standards

adequately protect public health and the environment. The CAA thereby provides EPA with comprehensive authority to regulate emissions to ambient air of any HAP.

1,4-Dioxane is a HAP. EPA has issued a number of technology-based standards for source categories that emit 1,4-dioxane to ambient air and, as appropriate, has reviewed, or is in the process of reviewing remaining risks. Because stationary source releases of 1,4-dioxane to ambient air are adequately assessed and any risks effectively managed when under the jurisdiction of the CAA, EPA does not plan to evaluate emission pathways to ambient air from commercial and industrial stationary sources or associated inhalation exposure of the general population or terrestrial species in this TSCA evaluation.

***Drinking Water Pathway***

EPA has regular analytical processes to identify and evaluate drinking water contaminants of potential regulatory concern for public water systems under the Safe Drinking Water Act (SDWA). Under SDWA, EPA must also review and revise "as appropriate" existing drinking water regulations every 6 years.

The Contaminant Candidate List (CCL) is a list of unregulated contaminants that are known or anticipated to occur in public water systems and that may require regulation. EPA must publish a CCL every 5 years and make Regulatory Determinations (RegDet) to regulate (or not) at least five CCL contaminants every 5 years. To regulate a contaminant EPA must conclude the contaminant may have adverse health effects, occurs or is substantially likely to occur in public water systems at a level of concern and that regulation, in the sole judgement of the Administrator, presents a meaningful opportunity for health risk reduction.

Currently, there is no National Primary Drinking Water regulation for 1,4-Dioxane under SDWA. 1,4-dioxane released to surface water can contribute to levels of the chemical in drinking water. EPA's Office of Water has established a Health Advisory level of 35 µg/L (which corresponds to a 1 in ten thousand lifetime cancer risk) for 1,4-Dioxane. 1,4-Dioxane is also currently listed on EPA's Fourth Contaminant Candidate List (CCL 4) and was subject to occurrence monitoring in public water systems under the third Unregulated Contaminants Monitoring Rule (UMCR 3). Under UMCR 3, water systems were monitored for 1,4-dioxane during 2013-2015. Of the 4,915 water systems monitored, 1,077 systems had detections of 1,4-dioxane in at least one sample. None of the systems measured levels greater than the Health Advisory level, however, 341 systems (6.9%) had results at or above 0.35 µg/L (which corresponds to a 1 in a million-lifetime cancer risk). In accordance with EPA-OW's process, 1,4-dioxane is currently being evaluated under the fourth Regulatory Determination process under SDWA.

Hence, because the drinking water exposure pathway for 1,4-dioxane is being addressed under the regular analytical processes to identify and evaluate drinking water contaminants of potential regulatory concern for public water systems under SDWA, EPA does not plan to include this pathway in the risk evaluation for 1,4-dioxane under TSCA. EPA's Office of Water and Office of Pollution Prevention and Toxics will continue to work together providing understanding and analysis of the SDWA regulatory analytical processes for public water systems and to exchange information related to toxicity and occurrence data on chemicals undergoing risk evaluation under TSCA.

***Ambient Water Pathways***

EPA develops recommended water quality criteria under section 304(a) of the CWA for pollutants in surface water that are protective of aquatic life or human health designated uses. A criterion is a hazard assessment only; i.e. there is no exposure assessment or risk estimation. When states adopt criteria that

EPA approves as part of state's regulatory water quality standards, exposure is considered when state permit writers determine if permit limits are needed and at what level for a specific discharger of a pollutant to ensure protection of the designated uses of the receiving water. This is the process used under the CWA to address risk to human health and aquatic life from exposure to a pollutant in ambient waters.

EPA has not developed CWA section 304(a) recommended water quality criteria for the protection of aquatic life for 1,4-dioxane, so there are no national recommended criteria for this use available for adoption into state water quality standards and available for use in NPDES permits. Currently, only one state (Colorado) includes human health criteria for 1,4-dioxane in their water quality standards and none include aquatic life criteria for 1,4-dioxane. As a result, this pathway will undergo aquatic life risk evaluation under TSCA (see Section 2.5.3.2). EPA may publish CWA section 304(a) aquatic life criteria for 1,4-dioxane in the future if it is identified as a priority under the CWA.

***Disposal Pathways***

1,4-Dioxane is included on the list of hazardous wastes pursuant to RCRA 3001 (40 CFR §§ 261.33) as a listed waste on the F and U lists. The general RCRA standard in section 3004(a) for the technical (regulatory) criteria that govern the management (treatment, storage, and disposal) of hazardous waste (i.e., Subtitle C) are those "necessary to protect human health and the environment," RCRA 3004(a). The regulatory criteria for identifying "characteristic" hazardous wastes and for "listing" a waste as hazardous also relate solely to the potential risks to human health or the environment. 40 C.F.R. §§ 261.11, 261.21-261.24. RCRA statutory criteria for identifying hazardous wastes require EPA to "tak[e] into account toxicity, persistence, and degradability in nature, potential for accumulation in tissue, and other related factors such as flammability, corrosiveness, and other hazardous characteristics." Subtitle C controls cover not only hazardous wastes that are landfilled, but also hazardous wastes that are incinerated (subject to joint control under RCRA Subtitle C and the Clean Air Act (CAA) hazardous waste combustion MACT) or injected into UIC Class I hazardous waste wells (subject to joint control under Subtitle C and the Safe Drinking Water Act (SDWA)).

Emissions to ambient air from municipal and industrial waste incineration and energy recovery units will not be included in the risk evaluation, as they are regulated under section 129 of the Clean Air Act. CAA section 129 also requires EPA to review and, if necessary, add provisions to ensure the standards adequately protect public health and the environment. Thus, combustion by-products from incineration treatment of 1,4 dioxane wastes (the majority of the 46,000 lbs identified as treated in Table 2-6) would be subject to these regulations, as would 1,4 dioxane burned for energy recovery (1.6 million lbs).

EPA does not plan to include on-site releases to land that go to underground injection in its risk evaluation. TRI data (U.S. EPA, 2015b) indicate that 94,304 lb of 1,4-dioxane was disposed of on-site to Class I underground injection wells and no releases to underground injection wells of Classes II-VI. Environmental disposal of 1,4-dioxane injected into Class I well types are managed and prevented from further environmental release by RCRA and SDWA regulations. Therefore, disposal of 1,4-dioxane via underground injection is not likely to result in environmental and general population exposures.

EPA does not plan to include on-site releases to land that go to RCRA Subtitle C hazardous waste landfills or RCRA Subtitle D municipal solid waste (MSW) landfills in its risk evaluation. TRI data (U.S. EPA, 2015b) indicate that RCRA Subtitle C Landfills received 13,375 lb of 1,4-dioxane, with a small amount of 1,4-dioxane (47 lb) reported to on-site landfills other than RCRA Subtitle C Landfills. Design standards for Subtitle C landfills require double liner, double leachate collection and removal

systems, leak detection system, run on, runoff, and wind dispersal controls, and a construction quality assurance program. They are also subject to closure and post-closure care requirements including installing and maintaining a final cover, continuing operation of the leachate collection and removal system until leachate is no longer detected, maintaining and monitoring the leak detection and groundwater monitoring system. Bulk liquids may not be disposed in Subtitle C landfills. Subtitle C landfill operators are required to implement an analysis and testing program to ensure adequate knowledge of waste being managed, and to train personnel on routine and emergency operations at the facility. Hazardous waste being disposed in Subtitle C landfills must also meet RCRA waste treatment standards before disposal. Given these controls, general population exposure to 1,4-dioxane in groundwater from Subtitle C landfill leachate is not expected to be a significant pathway.

EPA does not plan to include on-site releases to land from RCRA Subtitle C hazardous waste landfills or RCRA Subtitle D municipal solid waste landfills or exposures of the general population (including susceptible populations) or terrestrial species from such releases in the TSCA evaluation. While permitted and managed by the individual states, municipal solid waste (MSW) landfills are required by federal regulations to implement some of the same requirements as Subtitle C landfills. MSW landfills generally must have a liner system with leachate collection and conduct groundwater monitoring and corrective action when releases are detected. MSW landfills are also subject to closure and post-closure care requirements, and must have financial assurance for funding of any needed corrective actions. MSW landfills have also been designed to allow for the small amounts of hazardous waste generated by households and very small quantity waste generators (less than 220 lbs per month). Bulk liquids, such as free solvent, may not be disposed of at MSW landfills.

EPA does not expect to include on-site releases to land from industrial non-hazardous and construction/demolition waste landfills. Industrial non-hazardous and construction/demolition waste landfills are primarily regulated under state regulatory programs. States must also implement limited federal regulatory requirements for siting, groundwater monitoring, and corrective action, and a prohibition on open dumping and disposal of bulk liquids. States may also establish additional requirement such as for liners, post-closure and financial assurance, but are not required to do so. Therefore, EPA does not expect to include this pathway in the risk evaluation.

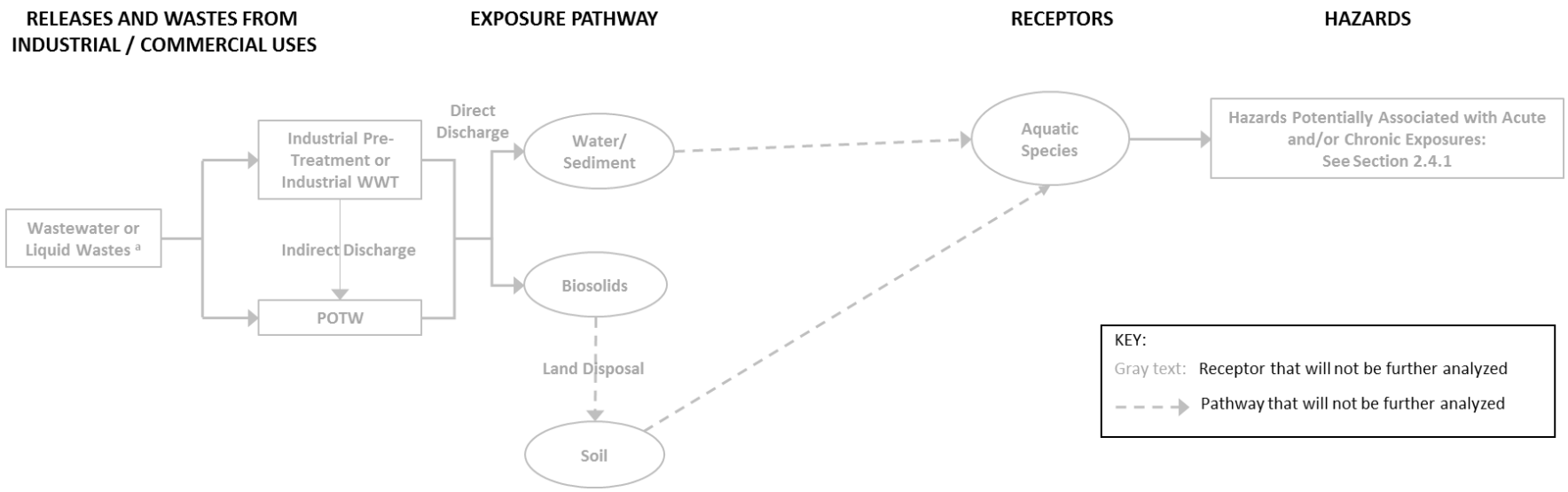


**Figure 2-3. 1,4-Dioxane Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards**
The conceptual model presents the exposure pathways, exposure routes and hazards to human and environmental receptors from environmental releases and wastes of 1,4-dioxane that EPA plans to analyze.

[a] Industrial wastewater or liquid wastes may be treated on-site and then released to surface water (direct discharge), or pre-treated and released to POTW (indirect discharge). Drinking water will undergo further treatment in drinking water treatment plants. Ground water may also be a source of drinking water.

## 2.6 Analysis Plan

The analysis plan presented in the problem formulation elaborates on the initial analysis plan that was published in the *Scope of the Risk Evaluation for 1,4-Dioxane* (U.S. EPA, 2017c).

The analysis plan is based on the conditions of use of 1,4-dioxane, as described in Section 2.2 of this problem formulation. EPA is implementing systematic review approaches and/or methods to identify, select, assess, integrate and summarize the findings of studies supporting the TSCA risk evaluation. The analytical approaches and considerations in the analysis plan are used to frame the scope of the systematic review activities for this assessment. The supplemental document, *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a), provides additional information about the criteria, approaches and/or methods that have been and will be applied to the first ten chemical risk evaluations. This supplemental document will be published in early 2018.

While EPA has conducted a search for reasonably available information as described in the *Scope of the Risk Evaluation for 1,4-Dioxane* (U.S. EPA, 2017c), EPA encourages submission of additional existing data, such as full study reports or workplace monitoring from industry sources, that may be relevant for refining conditions of use, exposures, hazards and potentially exposed or susceptible subpopulations during the risk evaluation. EPA will continue to consider new information submitted by the public until the end of the public comment period in 2018.

During the risk evaluation, EPA will rely on the search results [*1, 4-Dioxane (CASRN 123-91-1) Bibliography: Supplemental File for the TSCA Scope Document*; (U.S. EPA, 2017a)] or perform supplemental searches to address specific questions. Further, EPA may consider any relevant CBI information in the risk evaluation in a manner that protects the confidentiality of the information from public disclosure. The analysis plan is based on EPA's knowledge of 1,4-dioxane to date which includes partial, but not complete review of identified information. Should additional data or approaches become available, EPA may refine its analysis plan based on this information.

### 2.6.1 Exposure

For 1,4-dioxane, EPA does not plan to further analyze background levels for ambient air, indoor air, groundwater, and drinking water.

#### 2.6.1.1 Environmental Releases, Fate and Exposures

EPA does not plan to further analyze environmental releases to environmental media based on information described in Section 2.5. For the purposes of developing estimates of occupational exposure, EPA may use release related data collected under selected data sources such as the Toxics Release Inventory (TRI) and National Emissions Inventory (NEI) programs. Analyses conducted using physical and chemical properties, fate information and TRI/DMR show that TSCA-related environmental releases for 1,4-dioxane do not result in significant exposure to aquatic species through water and sediment exposure pathways (see Section 2.5.3.3). For the pathways of exposures for the general population and terrestrial species, EPA has determined that the existing regulatory programs and associated analytical processes have addressed or are in the process of addressing potential risks of chemicals that may be present in other media pathways. For these cases, EPA believes that the TSCA

risk evaluation should focus not on those exposure pathways, but rather on exposure pathways associated with TSCA uses that are not subject to those regulatory processes.

EPA does not plan to further analyze the environmental fate of 1,4-dioxane based on the conceptual models described in Section 2.5.2 and Section 2.5.3.

EPA does not plan to further analyze environmental exposures to 1,4-dioxane based on the exposure assessment presented in Section 2.3.4.

#### 2.6.1.2 Occupational Exposures

EPA expects to evaluate both worker and occupational non-user exposures as follows:

1) Review reasonably available exposure monitoring data for specific condition(s) of use.

Exposure data to be reviewed may include workplace monitoring data collected by government agencies such as OSHA and the NIOSH, and monitoring data found in published literature [e.g., personal exposure monitoring data (direct measurements) and area monitoring data (indirect measurements)]. Studies will be evaluated using the evaluation strategies laid out in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a).

EPA will evaluate applicable regulatory and non-regulatory exposure limits. Available data sources that may contain relevant monitoring data for the various conditions of use are listed in Table 2-10.

**Table 2-10. Potential Sources of 1,4-Dioxane Occupational Exposure Data**

| |
|---|
| The 2002 ECJRC Summary Risk Assessment Report: 1,4-Dioxane (ECJRC, 2002) |
| Health Canada Screening Assessment for the Challenge: 1,4-Dioxane (Health Canada, 2010) |
| U.S. NIOSH Health Hazard Evaluation (HHE) Program reports (NIOSH, 1987, 1982, 1980) |
| U.S. OSHA Chemical Exposure Health Data (CEHD) program data (OSHA, 2017b) |
| Industry workplace exposure monitoring data submitted to EPA by BASF Corporation and the American Chemistry Council (ACC) (BASF, 2017; ACC, 2015) |
| U.S. EPA Generic Scenarios (https://www.epa.gov/tsca-screening-tools/using-predictive-methods-assess-exposure-and-fate-under-tsca#fate) |
| OECD Emission Scenario Documents (OECD, 2015, 2011) |
| Buffler, P. A., Wood, S. M., Suarez, L., Kilian, D. J. Mortality follow-up of workers exposed to 1,4-dioxane. Journal of Occupational and Environmental Medicine. 1978. 20:255-259. |
| Jezewska, A., Szewczyńska, M., Woźnica, A. Occupational exposure to airborne chemical substances in paintings conservators. Medycyna Pracy. 2014. 65:33-41. |
| Kupczewska-Dobecka, M., Czerczak, S., Jakubowski, M., Maciaszek, P., Janasik, B. Application of predictive model to estimate concentrations of chemical substances in the work environment. Medycyna Pracy. 2010. 61:307-314. |

**2) For conditions of use where data are limited or not available, review existing exposure models that may be applicable in estimating exposure levels.**

EPA has identified potentially relevant OECD ESDs and EPA GS corresponding to some conditions of use. For example, the GS for Synthetic Fiber Manufacture, the GS on Lubricant Additives, the ESD on the Use of Metalworking Fluid, and the ESD on the Use of Adhesives are some of the ESDs and GS's that EPA may use to estimate occupational exposures for conditions of use such as use as a

wetting and dispersing agent in textile manufacturing, use in hydraulic fluids, and use in film cement. EPA will need to critically review these generic scenarios and ESDs to determine their applicability to the conditions of use assessed. EPA was not able to identify ESDs or GS's corresponding to several conditions of use, including solvent recycling, distribution, wood pulping, animal and vegetable oil extraction, fluoropolymer etching, and use as a fuel additive. EPA will perform additional targeted research, such as consulting Kirk-Othmer, in order to better understand those conditions of use, which may inform the identification of exposure scenarios. EPA may also need to perform targeted research to identify applicable models that may be used to estimate exposures for certain conditions of use.

**3) Review reasonably available data that may be used in developing, adapting or applying exposure models to the particular risk evaluation.**

If necessary, EPA will evaluate relevant data to determine whether the data can be used to develop, adapt, or apply models for specific conditions of use and corresponding exposure scenarios.

**4) Consider and incorporate applicable engineering controls and/or personal protective equipment into exposure scenarios.**

EPA will review potential data sources on engineering controls and personal protective equipment as identified in Table 2-10 to determine their applicability and incorporation into exposure scenarios during risk evaluation. Studies will be evaluated using the evaluation strategies laid out in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a).

**5) Evaluate the weight of the evidence of occupational exposure data.**

EPA will rely on the weight of the scientific evidence when evaluating and integrating occupational exposure data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

**6) Map or group each condition of use to occupational exposure assessment scenario(s).**

EPA has identified release/occupational exposure scenarios and mapped them to relevant conditions of use in Appendix D. As presented in the fourth column of the table in this appendix, EPA has grouped the uses into 23 representative release/exposure scenarios each with 5-6 unique combinations of exposure pathway, route, and receptor that will be further evaluated. EPA may further refine the mapping/grouping of occupational exposure scenarios based on factors (e.g., process equipment and handling, magnitude of production volume used, and exposure/release sources) corresponding to conditions of use as additional information is identified during risk evaluation. Consumer Exposures EPA does not expect to consider and analyze consumer exposures in the risk evaluation as described in the *Scope of the Risk Evaluation for 1,4-Dioxane* (U.S. EPA, 2017c).

#### 2.6.1.3 General Population

EPA does not expect to consider and analyze general population exposures in the risk evaluation for 1,4-dioxane based on Section 2.5.3.3. EPA has determined that the existing regulatory programs and associated analytical processes have addressed or are in the process of addressing potential risks of 1,4-dioxane that may be present in various media pathways (e.g., air, water, land) for the general population.

For these cases, EPA believes that the TSCA risk evaluation should focus not on those exposure pathways, but rather on exposure pathways associated with TSCA uses that are not subject to those regulatory processes.

### 2.6.2 Hazard

#### 2.6.2.1 Environmental Hazards

EPA does not plan to further analyze environmental hazards to 1,4-dioxane based on the hazard assessment presented in Section 2.4.1.

#### 2.6.2.2 Human Health Hazards

EPA expects to evaluate human health hazards as follows:

1) **Review reasonably available human health hazard data, including data from alternative test methods (e.g., computational toxicology and bioinformatics; high-throughput screening methods; data on categories and read-across; *in vitro* studies; systems biology).**

   For the 1,4 dioxane risk evaluation, EPA will evaluate information in the IRIS assessment and human health studies using OPPT's structured process described in the document, *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a). Human, animal and mechanistic data will be identified and included as described in Appendix F.3. EPA plans to prioritize the evaluation of mechanistic evidence. Specifically, EPA does not plan to evaluate mechanistic studies unless needed to clarify questions about associations between 1,4-dioxane and health effects and its relevance to humans. The protocol describes how studies will be evaluated using specific data evaluation criteria and a predetermined systematic approach. Study results will be extracted and presented in evidence tables by hazard endpoint. EPA plans to evaluate key studies used in the Integrated Risk Information System (IRIS) Toxicological Review of 1,4-Dioxane (U.S. EPA, 2013c, 2010), the TSCA Work Plan Problem Formulation and Initial Assessment (U.S. EPA, 2015c) and studies published after 2010 (oral) and 2013 (inhalation) that were captured in the comprehensive literature search conducted by the Agency for 1,4 Dioxane (*1, 4-Dioxane (CASRN 123-91-1) Bibliography: Supplemental File for the TSCA Scope Document*; (U.S. EPA, 2017a)). EPA intends to review studies published after the IRIS assessment to ensure that EPA is considering information that has been made available since these assessments were conducted.

2) **In evaluating reasonably available data, determine whether particular human receptor groups may have greater susceptibility to the chemical's hazard(s) than the general population.**

   Reasonably available human health hazard data will be evaluated to ascertain whether some human receptor groups may have greater susceptibility than the general population to 1,4-dioxane hazard(s). Susceptibility of particular human receptor groups to 1,4-dioxane will be determined by evaluating information on factors that influence susceptibility.

3) **Conduct hazard identification (the qualitative process of identifying non-cancer and cancer endpoints) and dose-response assessment (the quantitative relationship between hazard and exposure) for all identified human health hazard endpoints.**

Human health hazards from acute and chronic exposures will be identified by evaluating the human and animal data that meet the systematic review data quality criteria described in the *Application of Systematic Review in TSCA Risk Evaluations* document (U.S. EPA, 2018a). Data quality evaluation will be performed on key studies identified from the IRIS assessments (U.S. EPA, 2013b, 2010), the *TSCA Work Plan Problem Formulation and Initial Assessment* (U.S. EPA, 2015c) and studies published after 2010 (oral) and 2013 (inhalation) that were captured in the comprehensive literature search. Hazards identified by studies meeting data quality criteria will be grouped by routes of exposure relevant to humans (oral, dermal, inhalation) and by cancer and noncancer endpoints.

Dose-response assessment will be performed in accordance with EPA guidance (U.S. EPA, 2012b, 2011b, 1994). Dose-response analyses performed for the IRIS oral and inhalation reference dose determinations (U.S. EPA, 2013c, 2010) may be used if the data meet data quality criteria and if additional information on the identified hazard endpoints are not available or would not alter the analysis.

The cancer mode of action (MOA) determines how cancer risks can be quantitatively evaluated. EPA will evaluate information on genotoxicity and the mode of action for all tumor types to determine the appropriate approach for quantitative cancer assessment in accordance with the U.S. EPA *Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 2005a).

**4) Derive points of departure (PODs) where appropriate; conduct benchmark dose modeling depending on the available data. Adjust the PODs as appropriate to conform (e.g., adjust for duration of exposure) to the specific exposure scenarios evaluated.**

Hazard data will be evaluated to determine the type of dose-response modeling that is applicable. Where modeling is feasible, a set of dose-response models that are consistent with a variety of potentially underlying biological processes will be applied to empirically model the dose-response relationships in the range of the observed data consistent with the EPA *Benchmark Dose Technical Guidance Document* (U.S. EPA, 2012b). Where dose-response modeling is not feasible, NOAELs or LOAELs will be identified.

EPA will evaluate whether the available PBPK and empirical kinetic models are adequate for route-to-route and interspecies extrapolation of the POD, or for extrapolation of the POD to standard exposure durations (e.g., lifetime continuous exposure). If application of the PBPK model is not possible, oral PODs may be adjusted by $BW^{3/4}$ scaling in accordance with (U.S. EPA, 2011b), and inhalation PODs may be adjusted by exposure duration and chemical properties in accordance with (U.S. EPA, 1994).

**5) Consider the route(s) of exposure (oral, inhalation, dermal), available route-to-route extrapolation approaches, available biomonitoring data and available approaches to correlate internal and external exposures to integrate exposure and hazard assessment.**

EPA believes there are sufficient data to conduct dose-response analysis and/or benchmark dose modeling for both inhalation and oral routes of exposure.

If sufficient dermal toxicity studies are not identified in the literature search to assess risks from dermal exposures, then a route-to-route extrapolation from the inhalation and oral toxicity studies would be needed to assess systemic risks from dermal exposures. Without an adequate PBPK model,

the approaches described in the EPA guidance document *Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part E, Supplemental Guidance for Dermal Risk Assessment)* could be applied. These approaches may be able to further inform the relative importance of dermal exposures compared with other routes of exposure.

**6) Evaluate the weight of the evidence of human health hazard data.**

EPA will rely on the weight of the scientific evidence when evaluating and integrating human health hazard data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

### 2.6.3 Risk Characterization

Risk characterization is an integral component of the risk assessment process for both ecological and human health risks. EPA will derive the risk characterization in accordance with EPA's *Risk Characterization Handbook* (U.S. EPA, 2000). As defined in EPA's Risk Characterization Policy, "the risk characterization integrates information from the preceding components of the risk evaluation and synthesizes an overall conclusion about risk that is complete, informative and useful for decision makers." Risk characterization is considered to be a conscious and deliberate process to bring all important considerations about risk, not only the likelihood of the risk but also the strengths and limitations of the assessment, and a description of how others have assessed the risk into an integrated picture.

Risk characterization at EPA assumes different levels of complexity depending on the nature of the risk assessment being characterized. The level of information contained in each risk characterization varies according to the type of assessment for which the characterization is written. Regardless of the level of complexity or information, the risk characterization for TSCA risk evaluations will be prepared in a manner that is transparent, clear, consistent and reasonable (TCCR) (U.S. EPA, 2000). EPA will also present information in this section consistent with approaches described in the *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act* (82 FR 33726). For instance, in the risk characterization summary, EPA will further carry out the obligations under TSCA section 26; for example, by identifying and assessing uncertainty and variability in each step of the risk evaluation, discussing considerations of data quality such as the reliability, relevance and whether the methods utilized were reasonable and consistent, explaining any assumptions used, and discussing information generated from independent peer review. EPA will also be guided by EPA's *Information Quality Guidelines* (U.S. EPA, 2002) as it provides guidance for presenting risk information. Consistent with those guidelines, in the risk characterization, EPA will also identify: (1) Each population addressed by an estimate of applicable risk effects; (2) the expected risk or central estimate of risk for the potentially exposed or susceptible subpopulations affected; (3) each appropriate upper-bound or lower bound estimate of risk; (4) each significant uncertainty identified in the process of the assessment of risk effects and the studies that would assist in resolving the uncertainty; and (5) peer reviewed studies known to the Agency that support, are directly relevant to, or fail to support any estimate of risk effects and the methodology used to reconcile inconsistencies in the scientific information.

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# APPENDICES

# Appendix A REGULATORY HISTORY

## A.1 Federal Laws and Regulations

**Table_Apx A-1. Federal Laws and Regulations**

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| **EPA Regulations** | | |
| TSCA – Section 6(b) | EPA is directed to identify and begin risk evaluations on 10 chemical substances drawn from the 2014 update of the TSCA Work Plan for Chemical Assessments. | 1,4-Dioxane is on the initial list of chemicals to be evaluated for risk under TSCA (81 FR 91927, December 19, 2016). |
| TSCA – Section 8(a) | The TSCA section 8(a) CDR Rule requires manufacturers (including importers) to give EPA basic exposure-related information on the types, quantities and uses of chemical substances produced domestically and imported into the United States. | 1,4-Dioxane manufacturing (including importing), processing distribution and use information is reported under the CDR rule information about chemicals in commerce in the United States. |
| TSCA – Section 8(b) | EPA must compile, keep current and publish a list (the TSCA Inventory) of each chemical substance manufactured or processed in the United States. | 1,4-Dioxane was on the initial TSCA Inventory and therefore was not subject to EPA's new chemicals review process. |
| TSCA – Section 8(e) | Manufacturers (including importers), processors and distributors must immediately notify EPA if they obtain information that supports the conclusion that a chemical substance or mixture presents a substantial risk of injury to health or the environment. | Ten substantial risk reports from 1989 to 2004 U.S. EPA (2014a) Accessed April 13, 2017. |
| EPCRA – Section 313 | Requires annual reporting from facilities in specific industry sectors that employ 10 or more full time equivalent employees | 1,4-Dioxane is a listed substance subject to reporting requirements under 40 CFR 372.65 effective as of January 01, 1987. |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | and that manufacture, process or otherwise use a TRI-listed chemical in quantities above threshold levels. | |
| Federal Food, Drug, and Cosmetic Act (FFDCA) – Section 408 | FFDCA governs the allowable residues of pesticides in food. Section 408 of the FFDCA provides EPA with the authority to set tolerances (rules that establish maximum allowable residue limits) or exemptions from the requirement of a tolerance, for all residues of a pesticide (including both active and inert ingredients) that are in or on food. Prior to issuing a tolerance or exemption from tolerance, EPA must determine that the tolerance or exemption is "safe." Sections 408(b) and (c) of the FFDCA define "safe" to mean the Agency has reasonable certainty that no harm will result from aggregate exposures to the pesticide residue, including all dietary exposure and all other exposure (e.g., non-occupational exposures) for which there is reliable information. Pesticide tolerances or exemptions from tolerance that do not meet the FFDCA safety standard are subject to revocation. In the absence of a tolerance or an exemption from tolerance, a food containing a pesticide residue is considered adulterated and may not be distributed in interstate commerce. | In 1998, 1,4-dioxane was removed from the list of pesticide product inert ingredients because it was no longer being used in pesticide products. 1,4-Dioxane is also no longer exempt from the requirement of a tolerance (the maximum residue level that can remain on food or feed commodities under 40 CFR Part 180, Subpart D). |
| CAA – Section 111(b) | Requires EPA to establish new source performance standards (NSPS) for any category of new or modified stationary sources that EPA determines causes, or | 1,4-Dioxane is subject to the NSPS for equipment leaks of volatile organic compounds (VOCs) in the synthetic organic chemicals manufacturing industry for which construction, |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | contributes significantly to, air pollution, which may reasonably be anticipated to endanger public health or welfare. The standards are based on the degree of emission limitation achievable through the application of the best system of emission reduction (BSER) which (taking into account the cost of achieving reductions and environmental impacts and energy requirements) EPA determines has been adequately demonstrated. | reconstruction or modification began after 1/5/1981 and on or before 11/7/2006 (40 CFR Part 60, Subpart VV). |
| CAA – Section 112(b) | Defines the original list of 189 hazardous air pollutants (HAP). Under 112(c) of the CAA, EPA must identify and list source categories that emit HAP and then set emission standards for those listed source categories under CAA section 112(d). CAA section 112(b)(3)(A) specifies that any person may petition the Administrator to modify the list of HAP by adding or deleting a substance. | 1,4-Dioxane is listed as a HAP under section 112 (42 U.S.C. § 7412) of the CAA. |
| CAA – Section 112(d) | Section 112(d) states that the EPA must establish (NESHAPs for each category or subcategory of major sources and area sources of HAPs [listed pursuant to Section 112(c)]. The standards must require the maximum degree of emission reduction that the EPA determines to be achievable by each particular source category. Different criteria for maximum achievable control technology (MACT) apply for new and existing sources. Less stringent standards, known as generally available | There are a number of source-specific NESHAPs that are applicable to 1,4-dioxane, including:<br>Organic Hazardous Air Pollutants from the Synthetic Organic Chemical Manufacturing Industry (40 CFR Part 63, Subpart F),<br>Organic Hazardous Air Pollutants from the Synthetic Organic Chemical Manufacturing Industry for Process Vents, Storage Vessels, Transfer Operations, and Wastewater (40 CFR Part 63, Subpart G) |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | control technology (GACT) standards, are allowed at the Administrator's discretion for area sources. | Off-Site Waste and Recovery Operations (40 CFR Part 63, Subpart DD),<br>Wood Furniture Manufacturing Operations (40 CFR Part 63, Subpart JJ),<br>Pharmaceuticals Production (40 CFR Part 63, Subpart GGG),<br>Group IV Polymers and Resins (thermoplastic product manufacturing) (40 CFR Part 63, Subpart JJJ),<br>Organic Liquids Distribution (Non-gasoline) (40 CFR Part 63, Subpart EEEE),<br>Miscellaneous Organic Chemical Manufacturing (40 CFR Part 63, Subpart FFFF),<br>Site Remediation (40 CFR Part 63, Subpart GGGGG), and<br>Miscellaneous Coating Manufacturing (40 CFR Part 63, Subpart HHHHH). |
| Comprehensive Environmental Response, Compensation and Liability Act (CERCLA) – Sections 102(a) and 103 | Authorizes EPA to promulgate regulations designating as hazardous substances those substances which, when released into the environment, may present substantial danger to the public health or welfare or the environment. EPA must also promulgate regulations establishing the quantity of any hazardous substance the release of which must be reported under Section 103.<br>Section 103 requires persons in charge of vessels or facilities to report to the National Response Center if they have knowledge of a release of a hazardous substance above the reportable quantity threshold. | 1,4-Dioxane is a hazardous substance under CERCLA. Releases of 1,4-dioxane in excess of 100 pounds must be reported (40 CFR 302.4). |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| Safe Drinking Water Act (SDWA) – Section 1412(b) | Every 5 years, EPA must publish a list of contaminants that: (1) are currently unregulated, (2) are known or anticipated to occur in public water systems (PWSs) and (3) may require regulations under SDWA. EPA must also determine whether to regulate at least five contaminants from the list every 5 years. | 1,4-dioxane was identified on both the Third (2009) and Fourth (2016) Contaminant Candidate List (CCL) (74 FR 51850, October 8, 2009) (81 FR 81099, November 17, 2016). |
| SDWA – Section 1445(a) | Every 5 years, EPA must issue a new list of no more than 30 unregulated contaminants to be monitored by PWSs. The data obtained must be entered into the National Drinking Water Contaminant Occurrence Database. | 1,4-dioxane was identified in the third Unregulated Contaminant Monitoring Rule (UCMR3), issued in 2012 (77 FR 26072, May 2, 2012). |
| RCRA – Section 3001 | Directs EPA to develop and promulgate criteria for identifying the characteristics of hazardous waste, and for listing hazardous waste, taking into account toxicity, persistence, and degradability in nature, potential for accumulation in tissue and other related factors such as flammability, corrosiveness, and other hazardous characteristics. | In 1980, 1,4-dioxane became a listed hazardous waste in 40 CFR 261.33 - Discarded commercial chemical products, off-specification species, container residues, and spill residues thereof (U108) (45 FR 33084). |
| **Other federal regulations** | | |
| FFDCA | Provides the U.S. Food and Drug Administration (FDA) with authority to oversee the safety of food, drugs and cosmetics. | FDA established a limit of 10 mg/kg on the amount of 1,4dioxane that can be present in the food additive glycerides and polyglycides of hydrogenated vegetable oils (21 CFR 172.736 and 71 FR 12618, March 13, 2006). |
| Occupational Safety and Health Act | Requires employers to provide their workers with a place of employment free from recognized hazards to safety and health, such as exposure to toxic chemicals, excessive noise | In 1989, OSHA established a PEL for 1,4-dioxane of 100 ppm or 360 mg/$m^3$ as an 8-hour, TWA (29 CFR 1910.1001).<br>While OSHA has established a PEL for 1,4-dioxane, OSHA has recognized |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | levels, mechanical dangers, heat or cold stress or unsanitary conditions.<br>Under the Act, OSHA can issue occupational safety and health standards including such provisions as PELs, exposure monitoring, engineering and administrative control measures and respiratory protection. | that many of its PELs are outdated and inadequate for ensuring the protection of worker health. 1,4-Dioxane appears in OSHA's annotated PEL tables, wherein OSHA recommends that employers follow the California OSHA limit of 0.28 ppm, the NIOSH REL of 1 ppm as a 30-minute ceiling or the ACGIH TLV of 20 ppm (8-hour TWA). |
| Atomic Energy Act | The Atomic Energy Act authorizes the Department of Energy to regulate the health and safety of its contractor employees | 10 CFR 851.23, Worker Safety and Health Program, requires the use of the 2005 ACGIH TLVs if they are more protective than the OSHA PEL. |
| Federal Hazardous Materials Transportation Act | Section 5103 of the Act directs the Secretary of Transportation to:<br>Designate material (including an explosive, radioactive material, infectious substance, flammable or combustible liquid, solid or gas, toxic, oxidizing or corrosive material and compressed gas) as hazardous when the Secretary determines that transporting the material in commerce may pose an unreasonable risk to health and safety or property.<br>Issue regulations for the safe transportation, including security, of hazardous material in intrastate, interstate and foreign commerce. | The Department of Transportation (DOT) has designated 1,4-dioxane as a hazardous material, and there are special requirements for marking, labeling and transporting it (49 CFR Part 171, 40 CFR 173.202 and 40 CFR 173.242). |

## A.2 State Laws and Regulations

**Table_Apx A-2. State Laws and Regulations**

| State Actions | Description of Action |
|---|---|
| State PELs | California PEL: 0.28 ppm (Cal Code Regs. Title 8, § 5155). |
| State Right-to-Know Acts | New Jersey (8:59 N.J. Admin. Code § 9.1), Pennsylvania (34 Pa. Code § 323). |
| State air regulations | Allowable Ambient Levels (AAL): New Hampshire (RSA 125-I:6, ENV-A Chap. 1400), Rhode Island (12 R.I. Code R. 031-022). |
| State drinking/ground water limits | Massachusetts (310 Code Mass. Regs. § 22.00), Michigan (Mich. Admin. Code r.299.44 and r.299.49, 2017). |
| Chemicals of high concern to children | Several states have adopted reporting laws for chemicals in children's products that include 1,4-dioxane, such as Oregon (Toxic-Free Kids Act, Senate Bill 478, 2015) Vermont (Code Vt. R. § 13-140-077) and Washington State (Wash. Admin. Code § 173-334-130). |
| Other | In California, 1,4-dioxane was added to the Proposition 65 list in 1988 (Cal. Code Regs. title 27, § 27001). |

## A.3 International Laws and Regulations

**Table_Apx A-3. Regulatory Actions by other Governments and Tribes**

| Country/Organization | Requirements and Restrictions |
|---|---|
| Canada | 1,4-Dioxane is on the Cosmetic Ingredient Hotlist as a substance prohibited for use in cosmetics. 1,4-Dioxane is also included in Canada's National Pollutant Release Inventory (NPRI), the publicly-accessible inventory of pollutants released, disposed of and sent for recycling by facilities across the country [Government of Canada (2010) *1,4-Dioxane*. Accessed April 18, 2017]. |
| Australia | In 1994, 1,4-dioxane was assessed. A workplace product containing more than 0.1% 1,4-dioxane is classed as a hazardous substance. 1,4-Dioxane is in Class 3, (Packing Group II) under the Australian Dangerous Goods Code (1,4-Dioxane. Priority Existing Chemical No. 7. Full Public Report (1998)). |
| Japan | 1,4-dioxane is regulated in Japan under the following legislation:<br>• Act on the Evaluation of Chemical Substances and Regulation of Their Manufacture, etc. (Chemical Substances Control Law; CSCL)<br>• Act on Confirmation, etc. of Release Amounts of Specific Chemical Substances in the Environment and Promotion of Improvements to the Management Thereof |

| Country/Organization | Requirements and Restrictions |
|---|---|
| | • Industrial Safety and Health Act (ISHA)<br>• Air Pollution Control Law<br>• Water Pollution Control Law<br>(National Institute of Technology and Evaluation (NITE) Chemical Risk Information Platform (CHIRP)(NITE, 2015), Accessed April 18, 2017). |
| Republic of Korea | The Ministry of the Environment recently adopted a provisional water quality standard for human health of 50 µg/L 1,4-dioxane in drinking water (An et al., 2014). |
| Australia, Austria, Belgium, Canada, Denmark, European Union (EU), Finland, France, Germany, Hungary, Ireland, Italy, Japan, Latvia, New Zealand, People's Republic of China, Poland, Singapore, South Korea, Spain, Sweden, Switzerland, The Netherlands, Turkey, United Kingdom | Occupational exposure limits for 1,4-dioxane (Insitut fur Arbeitsschutz der (IFA) Deutschen Gesetzlichen Unfallversicherung, 2017)(GESTIS International limit values for chemical agents (Occupational exposure limits, OELs) database. Accessed April 18, 2017). |
| WHO | Established a tolerable daily intake of 16 µg 1,4-dioxane/kg body weight based on a no-observed-adverse-effect level (NOAEL) of 16 mg/kg body weight per day for hepatocellular tumors observed in a long-term drinking-water study in rats. The WHO water quality guideline is 0.05 mg/L 1,4-dioxane in drinking water (WHO, 2005). |

# Appendix B PROCESS, RELEASE AND OCCUPATIONAL EXPOSURE INFORMATION

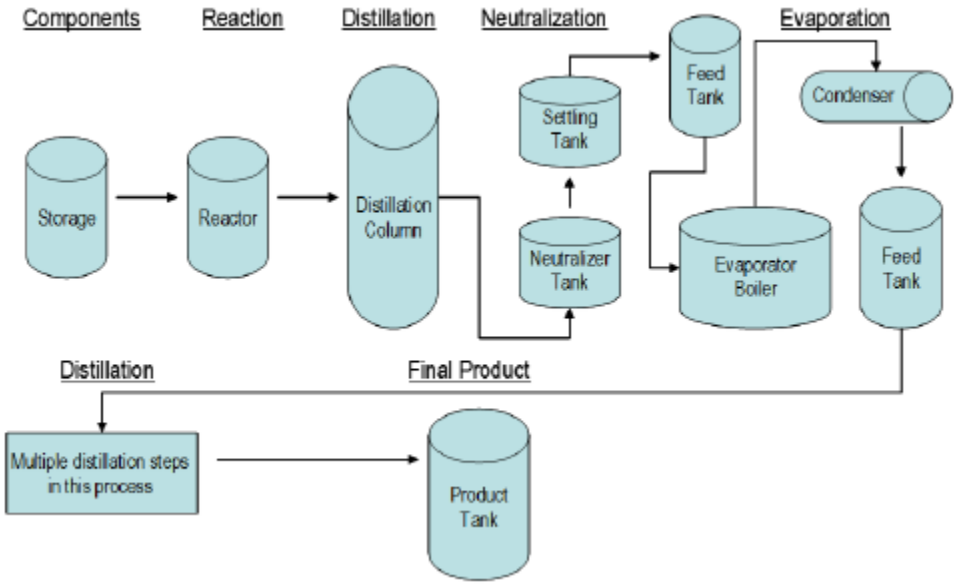
This appendix provides information and data found in preliminary data gathering for 1,4-dioxane.

## B.1 Process Information

Process-related information potentially relevant to the risk evaluation may include process diagrams, descriptions and equipment. Such information may inform potential release sources and worker exposure activities for consideration.

### B.1.1 Manufacture (Including Import)

The primary method for industrial production of 1,4-dioxane involves an acid-catalyzed conversion of ethylene glycol (mono-, di-, tri- and polyethylene glycol may be used) by ring closure in a closed system. The process is carried out at a temperature between 266 and 392°F (130 and 200°C) and a pressure between 0.25 and 1.1 atm (25 and 110 kPa). The synthesis step is performed in a heated vessel. The raw 1,4-dioxane product is then moved to a distillation column to start the purification process. Multiple steps are used to purify the 1,4-dioxane, including separation from water and volatile by-products by extractive distillation, heating with acids, salting out with NaCl, $CaCl_2$ or NaOH, and fine subsequent distillation (ECJRC, 2002). Figure_Apx B-1 (BASF, 2017).




**Figure_Apx B-1: General Process Flow Diagram for 1,4-Dioxane Manufacturing**
Source: EPA-HQ-OPPT-2016-0723-0012 (BASF, 2017).

Two other reactions can be used to make 1,4-dioxane, but they are primarily used to make substituted dioxanes and not known to be used for industrial 1,4-dioxane production (ECJRC, 2002).

### B.1.2 Processing and Distribution

#### B.1.2.1 Processing as a Reactant/Intermediate

1,4-Dioxane can be used as a chemical reactant in the production of pharmaceuticals, polyethylene terephthalate (PET) plastics, rubber, insecticides and pesticides, cement, deodorant fumigant, magnetic

tape and adhesives [EPA-HQ-OPPT-2017-0723-0003 (U.S. EPA, 2017b)]. Exact process operations involved in the use of 1,4-dioxane as a chemical reactant are dependent on the final product that is being synthesized. For the use of 1,4-dioxane as a chemical reactant, operations would typically involve unloading 1,4-dioxane from transport containers and feeding the 1,4-dioxane into a reaction vessel(s), where the 1,4-dioxane would react either fully or to a lesser extent. Following completion of the reaction, the produced substance may or may not be purified further, thus removing unreacted 1,4-dioxane (if any exists). Reacted 1,4-dioxane is assumed to be destroyed and is thus not expected to be released or cause potential worker exposures.

#### B.1.2.2 Processing – Non-Incorporative

1,4-Dioxane is used as a process solvent during the manufacturing of cellulose acetate, resins, waxes and fats [EPA-HQ-OPPT-2017-0723-0003 (U.S. EPA, 2017b)].

#### B.1.2.3 Repackaging

Typical repackaging operations involve transferring of chemicals into appropriately sized containers to meet customer demands/needs.

#### B.1.2.4 Recycling

1,4-Dioxane is used as a solvent in several applications. In this capacity, 1,4-dioxane can be regenerated and recycled for reuse.

### B.1.3 Uses

#### B.1.3.1 Processing Aids, Not Otherwise Listed

Processing aids are chemical substances used to improve the processing characteristics or the operation of process equipment or to alter or buffer the pH of the substance or mixture, when added to a process or to a substance or mixture to be processed. Processing agents do not become a part of the reaction product and are not intended to affect the function of a substance or article created (U.S. EPA, 2016c). 1,4-Dioxane is used in a number of industrial processes as a processing aid. These processes include wood pulping, extraction of animal and vegetable oils, textile processing, polymerization, pharmaceutical purification and etching of fluoropolymers [EPA-HQ-OPPT-2017-0723-0003; (U.S. EPA, 2017b); EPA-HQ-OPPT-2016-0723-0012 (BASF, 2017)]. Exact process operations involved in the use of 1,4-dioxane as a processing aid are dependent on the final product that is being synthesized.

#### B.1.3.1 Functional Fluids (Open and Closed Systems)

Functional fluids are liquid or gaseous chemical substances used for one or more operational properties (U.S. EPA, 2016c). 1,4-Dioxane is used in polyalkylene glycol lubricants, synthetic metalworking fluids, cutting and tapping fluids and hydraulic fluids [EPA-HQ-OPPT-2017-0723-0003 (U.S. EPA, 2017b)]. Exact operations involved in the use of 1,4-dioxane as a functional fluid are dependent on the final product.

#### B.1.3.2 Laboratory Chemicals

1,4-Dioxane is used in laboratories as a chemical reagent, reference material, stable reaction medium, liquid scintillation counting medium, spectroscopic and photometric measurement, cryoscopic solvent and histological preparation [EPA-HQ-OPPT-2017-0723-0003 (U.S. EPA, 2017b)]. Laboratory procedures are generally done within a fume hood, on a bench with local exhaust ventilation or under general ventilation.

#### B.1.3.3 Adhesives and Sealants

1,4-Dioxane is found in film cement and as a residual contaminant in two-component glues and adhesives [EPA-HQ-OPPT-2017-0723-0003 (U.S. EPA, 2017b)]. The application procedure depends on the type of adhesive and the type of substrate. After the adhesive is received by the user, it may be diluted or mixed prior to application. The formulation is then loaded into the application reservoir or apparatus and applied to the substrate via spray, roll, curtain or syringe or bead application. Application may be manual or automated. After application, the adhesive or sealant is allowed to dry, usually at ambient temperature, such that the solvent completely evaporates and a bond is formed between the substrates (OECD, 2015).

#### B.1.3.4 Other Uses

Other conditions of use where 1,4-dioxane may be formulated into a product or used as part of another process may include use in fuels and fuel additives [EPA-HQ-OPPT-2016-0723-0012 (BASF, 2017)], spray polyurethane foam and in printing and printing compositions [EPA-HQ-OPPT-2017-0723-0003 (U.S. EPA, 2017b)].

### B.1.4 Disposal

1,4-Dioxane is disposed of to a variety of environmental media: land, water and air. Land disposals include Class I underground injection, RCRA Subtitle C landfills and to other uncategorized land points. 1,4-Dioxane is sometimes discharged to water. Wastewater treatment may or may not precede these water releases. Additionally, 1,4-dioxane is also commonly incinerated (U.S. EPA, 2015c).

## B.2 Occupational Exposure Data

EPA presents below an example of occupational exposure-related information from the preliminary data gathering. EPA will consider this information and data in combination with other data and methods for use in the risk evaluation.

Table_Apx B 1 summarizes OSHA CEHD data by North American Industry Classification System (NAICS) code (OSHA, 2017a).

**Table_Apx B-1. Summary of Industry Sectors with 1,4-Dioxane Personal Monitoring Air Samples Obtained from OSHA Inspections Conducted Between 2002 and 2016**

| NAICS | NAICS Description |
|---|---|
| 315225 | Men's and Boys' Cut and Sew Work Clothing Manufacturing |
| 325199 | All Other Basic Organic Chemical Manufacturing |
| 334418 | Printed Circuit Assembly (Electronic Assembly) Manufacturing |
| 336399 | All Other Motor Vehicle Parts Manufacturing |
| 926150 | Regulation, Licensing, and Inspection of Miscellaneous Commercial Sectors |

# Appendix C ANALYSIS: ENVIRONMENTAL CONCENTRATION OF CONCERN (COC)

The concentrations of concern (COC) for aquatic species were calculated based on the environmental hazard data for 1,4-dioxane summarized in Section 2.4.1. The methods for calculating the COCs are are based on published EPA/OPPT methods (U.S. EPA, 2013a, 2012d). The acute and chronic COC for 1,4-dioxane for each endpoint are determined based on the lowest toxicity value in the dataset. For a particular environment (e.g., aquatic environment), the COC is based and on the most sensitive species in that environment.

After selecting the lowest toxicity value, an assessment factor (AF) is applied according to EPA/OPPT methods (U.S. EPA, 2013a, 2012d). The application of AFs provides a lower bound effect level that would likely encompass more sensitive species not specifically represented by the available experimental data. AFs are also account for differences in inter- and intra-species variability, as well as laboratory-to-field variability. These assessment factors are dependent upon the availability of datasets that can be used to characterize relative sensitivities across multiple species within a given taxa or species group, but are often standardized in risk assessments conducted under TSCA, since the data available for most industrial chemicals is limited. The acute COC for the aquatic plant endpoint is determined based on the lowest value in the dataset divided by an assessment factor (AF) of 4. For fish and aquatic invertebrates (e.g., daphnia) the acute COC values are divided by an AF of 5. For chronic COCs, an AF of 10 is used.

***Acute COC calculations***

The lowest acute toxicity value for aquatic organisms (i.e., most sensitive species) for 1,4-dioxane is from a 96-hour fish toxicity study where the $LC_{50}$ is >100 mg/L (Geiger et al., 1990). The lowest value was then divided by the assessment factor (AF) of 5 for aquatic invertebrates.

Lowest value for the 96-hour fish toxicity $LC_{50}$ (>100 mg/L) / AF of 5 = 20,000 µg/L or ppb.

***Chronic COC Calculations***

For the chronic COC, the lowest chronic toxicity value is from a chronic 32-day MATC fathead minnow study of > 145 mg/L (Brooke, 1987). This value was divided by an assessment factor of 10 then multiplied by 1,000 to convert from mg/L to µg/L or ppb.

Lowest value for 32-day fish MATC = 145 mg/L / 10 = 14.5 x 1000 = 14,500 µg/L or ppb.

***Summary***

The acute concentration of concern for 1,4-dioxane is based on the 96-hour toxicity value for fish of >100 mg/L (Geiger et al., 1990) and the chronic COC is based on a 32-day MATC fish toxicity value of 145 mg/L (Brooke, 1987). The acute and chronic COCs for 1,4-dioxane are 20,000 ppb and 14,500 ppb, respectively.

# Appendix D SUPPORTING TABLE FOR INDUSTRIAL AND COMMERCIAL ACTIVITIES AND USES CONCEPTUAL MODEL

As part of the Problem Formulation, EPA considered if each unique combination of exposure pathway, route, and receptor in the lifecycle of 1,4-dioxane would be further evaluated. All possible exposure scenarios for each condition of use were identified according to the COU in Table 2-3 and the conceptual model in Figure 2-2 and are presented in Table_Apx D-1. EPA used readily available fate, engineering, exposure and/or toxicity information to determine whether to conduct further analysis on each exposure scenario.

EPA has identified release/occupational exposure scenarios and mapped them to relevant conditions of use in the table below. As presented in the Release/Exposure Scenario column of this table, representative release/exposure scenarios each with 5-6 unique combinations of exposure pathway, route, and receptor will be further analyzed. EPA may further refine the mapping/grouping of industrial and commercial occupational exposure scenarios based on factors (e.g., process equipment and handling, magnitude of production volume used, and exposure/release sources) corresponding to conditions of use as additional information is identified during risk evaluation.

**Table_Apx D-1: Industrial and Commercial Occupational Exposure Scenarios for 1,4-Dioxane**

| Life Cycle Stage | Category | Subcategory | Release/ Exposure Scenario | Exposure Pathway | Exposure Route | Receptor | Further Evaluation? | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Manufacture | Domestic Manufacture or Import | Domestic Manufacture or Import | Manufacture of 1,4-dioxane via acid catalyzed conversion of ethylene glycol by ring closure<br><br>Repackaging of import containers | Liquid Contact | Dermal | Workers | Yes | Workers are expected to routinely handle liquids containing 1,4-dioxane. |
| Manufacture | Domestic Manufacture or Import | Domestic Manufacture or Import | | Vapor | Dermal | Workers | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of magnitude lower than via inhalation and will not be further analyzed. |
| Manufacture | Domestic Manufacture or Import | Domestic Manufacture or Import | | Vapor | Inhalation | Workers | Yes | Due to high volatility (VP = 40 mmHg) at room temperature, inhalation exposure from vapor should be further evaluated. |
| Manufacture | Domestic Manufacture or Import | Domestic Manufacture or Import | | Liquid Contact | Dermal | ONU (Occupational Non-User) | No | Dermal exposure is expected to be primarily to workers directly involved in handling the chemical. |
| Manufacture | Domestic Manufacture or Import | Domestic Manufacture or Import | | Vapor | Dermal | ONU | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of magnitude lower than via inhalation and will not be further analyzed. |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Manufacture | Domestic Manufacture or Import | Domestic Manufacture or Import | | Vapor | Inhalation | ONU | Yes | Due to high volatility (VP = 40 mmHg) at room temperature, inhalation exposure from vapor should be further evaluated. |
| Manufacture | Domestic Manufacture or Import | Domestic Manufacture or Import | | Mist | Dermal/Inhalation/Oral | Workers, ONU | No | Mist generation is not expected. |
| Processing | Processing as a Reactant | Pharmaceutical Intermediate<br><br>Polymerization catalyst | Pharmaceutical product manufacture<br><br>Polymer manufacture | Liquid Contact | Dermal | Workers | Yes | Workers are expected to routinely handle liquids containing 1,4-dioxane. |
| Processing | Processing as a Reactant | | | Vapor | Dermal | Workers | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of magnitude lower than via inhalation and will not be further analyzed. |
| Processing | Processing as a Reactant | | | Vapor | Inhalation | Workers | Yes | Due to high volatility at room temperature, inhalation exposure from vapor should be further evaluated. However, potential for exposure may be low in scenarios where 1,4-dioxane is consumed as a chemical intermediate or used as a catalyst. |
| Processing | Processing as a Reactant | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in handling the chemical. |
| Processing | Processing as a Reactant | | | Vapor | Dermal | ONU | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of magnitude lower than via inhalation and will not be further analyzed. |
| Processing | Processing as a Reactant | | | Vapor | Inhalation | ONU | Yes | Due to high volatility at room temperature, inhalation exposure from vapor should be further evaluated. However, potential for exposure may be low in scenarios where 1,4-dioxane is consumed as a chemical intermediate or used as a catalyst. |
| Processing | Processing as a Reactant | | | Mist | Dermal/Inhalation/Oral | Workers, ONU | No | Mist generation is not expected. |
| Processing | Non- | Pharmaceutical and medicine | Pharmaceutical product | Liquid Contact | Dermal | Workers | Yes | Workers are expected to routinely handle liquids containing 1,4-dioxane. |
| Processing | | | | Vapor | Dermal | Workers | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | incorporative | manufacturing (process solvent)<br><br>Basic organic chemical manufacturing (process solvent)<br><br>Bulk to packages, then distribute | manufacture<br><br>Basic organic chemical manufacture<br><br>Repackaging to large and small containers | | | | | magnitude lower than via inhalation and will not be further analyzed. |
| Processing | | | | Vapor | Inhalation | Workers | Yes | Due to high volatility at room temperature, inhalation exposure from vapor should be further evaluated. |
| Processing | Repackaging | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in handling the chemical. |
| Processing | | | | Vapor | Dermal | ONU | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of magnitude lower than via inhalation and will not be further analyzed. |
| Processing | | | | Vapor | Inhalation | ONU | Yes | Due to high volatility at room temperature, inhalation exposure from vapor should be further evaluated. |
| Processing | | | | Mist | Dermal/Inhalation/Oral | Workers, ONU | No | Mist generation is not expected. |
| Processing | Recycling | Recycling | Recycling of process solvents containing 1,4-dioxane | Liquid Contact | Dermal | Workers | Yes | Workers are expected to routinely handle liquids containing 1,4-dioxane. |
| Processing | Recycling | Recycling | | Vapor | Dermal | Workers | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of magnitude lower than via inhalation and will not be further analyzed. |
| Processing | Recycling | Recycling | | Vapor | Inhalation | Workers | Yes | Due to high volatility at room temperature, inhalation exposure from vapor should be further evaluated. |
| Processing | Recycling | Recycling | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in handling the chemical. |
| Processing | Recycling | Recycling | | Vapor | Dermal | ONU | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of magnitude lower than via inhalation and will not be further analyzed. |
| Processing | Recycling | Recycling | | Vapor | Inhalation | ONU | Yes | Due to high volatility at room temperature, inhalation exposure from vapor should be further evaluated. |
| Processing | Recycling | Recycling | | Mist | Dermal/Inhalation/Oral | Workers, ONU | Yes | EPA requires additional information on industry practices for recycling waste solvents containing 1,4-dioxane to |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | | determine if exposures to mists are possible. |
| Distribution in commerce | Distribution | Distribution | Distribution of bulk shipment of 1,4-dioxane | Liquid Contact, Vapor, Mist | Dermal/Inhalation/Oral | Workers, ONU | Yes | EPA will further analyze activities resulting in exposures associated with distribution in commerce (e.g. loading, unloading) throughout the various lifecycle stages and conditions of use (e.g. manufacturing, processing, industrial use) rather than as a single distribution scenario. |
| Industrial use | Intermediate Use<br><br>Processing aids, not otherwise listed | Agricultural chemical intermediate<br><br>Plasticizer intermediate<br><br>Catalysts and reagents for anhydrous acid reactions, brominations and sulfonations<br><br>Polymerization catalyst | Agricultural product manufacture<br><br>Plasticizer manufacture<br><br>Anhydrous acid, bromination and sulfonation reaction chemical manufacture<br><br>Polymer Manufacture | Liquid Contact | Dermal | Workers | Yes | Workers are expected to routinely handle liquids containing 1,4-dioxane. |
| Industrial use | | | | Vapor | Dermal | Workers | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of magnitude lower than via inhalation and will not be further analyzed. |
| Industrial use | | | | Vapor | Inhalation | Workers | Yes | Due to high volatility at room temperature, inhalation exposure from vapor should be further evaluated. However, potential for exposure may be low in scenarios where 1,4-dioxane is consumed as a chemical intermediate or used as a catalyst. |
| Industrial use | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in handling the chemical. |
| Industrial use | | | | Vapor | Dermal | ONU | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of magnitude lower than via inhalation and will not be further analyzed. |
| Industrial use | | | | Vapor | Inhalation | ONU | Yes | Due to high volatility at room temperature, inhalation exposure from vapor should be further evaluated. However, potential for exposure may be low in scenarios where 1,4-dioxane is consumed as a chemical intermediate or used as a catalyst. |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Industrial use | | | | Mist | Dermal/Inhalation/Oral | Workers, ONU | No | Mist generation is not expected. |
| Industrial use | Processing aids, not otherwise listed | Wood pulping<br><br>Extraction of animal and vegetable oils<br><br>Wetting and dispersing agent in textile processing | Wood pulping<br><br>Extraction of animal and vegetable oils<br><br>Textile processing | Liquid Contact | Dermal | Workers | Yes | Workers are expected to routinely handle liquids containing 1,4-dioxane. |
| Industrial use | Processing aids, not otherwise listed | | | Vapor | Dermal | Workers | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of magnitude lower than via inhalation and will not be further analyzed. |
| Industrial use | Processing aids, not otherwise listed | | | Vapor | Inhalation | Workers | Yes | Due to high volatility at room temperature, inhalation exposure from vapor should be further evaluated. |
| Industrial use | Processing aids, not otherwise listed | | | Liquid Contact | Dermal | ONU | Yes | Dermal exposure is expected to be primarily to workers directly involved in handling the chemical. |
| Industrial use | Processing aids, not otherwise listed | | | Vapor | Dermal | ONU | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of magnitude lower than via inhalation and will not be further analyzed. |
| Industrial use | Processing aids, not otherwise listed | | | Vapor | Inhalation | ONU | Yes | Due to high volatility at room temperature, inhalation exposure from vapor should be further evaluated. |
| Industrial use | Processing aids, not otherwise listed | | | Mist | Dermal/Inhalation/Oral | Workers, ONU | Yes | Mist generation may occur during these processes. |
| Industrial use | Processing aids, not otherwise listed | Purification of pharmaceuticals | Pharmaceutical product manufacture | Liquid Contact | Dermal | Workers | Yes | Workers are expected to routinely handle liquids containing 1,4-dioxane. |
| Industrial use | Processing aids, not otherwise listed | | | Vapor | Dermal | Workers | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of magnitude lower than via inhalation and will not be further analyzed. |
| Industrial use | Processing aids, not | | | Vapor | Inhalation | Workers | Yes | Due to high volatility at room temperature, inhalation exposure from vapor should be further evaluated. |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | otherwise listed | | | | | | | |
| Industrial use | Processing aids, not otherwise listed | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in handling the chemical. |
| Industrial use | Processing aids, not otherwise listed | | | Vapor | Dermal | ONU | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of magnitude lower than via inhalation and will not be further analyzed. |
| Industrial use | Processing aids, not otherwise listed | | | Vapor | Inhalation | ONU | Yes | Due to high volatility at room temperature, inhalation exposure from vapor should be further evaluated. |
| Industrial use | Processing aids, not otherwise listed | | | Mist | Dermal/Inhalation/Oral | Workers, ONU | No | Mist generation is not expected. |
| Industrial use | Processing aids, not otherwise listed | Etching of fluoropolymers | Etching of fluoropolymers | Liquid Contact | Dermal | Workers | Yes | Workers are expected to routinely handle liquids containing 1,4-dioxane. |
| Industrial use | Processing aids, not otherwise listed | | | Vapor | Dermal | Workers | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of magnitude lower than via inhalation and will not be further analyzed. |
| Industrial use | Processing aids, not otherwise listed | | | Vapor | Inhalation | Workers | Yes | Due to high volatility at room temperature, inhalation exposure from vapor should be further evaluated. |
| Industrial use | Processing aids, not otherwise listed | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in handling the chemical. |
| Industrial use | Processing aids, not otherwise listed | | | Vapor | Dermal | ONU | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of magnitude lower than via inhalation and will not be further analyzed. |
| Industrial use | Processing aids, not otherwise listed | | | Vapor | Inhalation | ONU | Yes | Due to high volatility at room temperature, inhalation exposure from vapor should be further evaluated. |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Industrial use | Processing aids, not otherwise listed | | | Mist | Dermal/Inhalation/Oral | Workers, ONU | Yes | Mist generation may occur during these processes. |
| Industrial use | Functional fluids (closed/open system) | Polyalkylene glycol lubricant<br><br>Cutting and Tapping Fluid<br><br>Synthetic metalworking fluid<br><br>Hydraulic fluid | Use of lubricants<br><br>Use of metalworking fluids<br><br>Servicing hydraulic equipment and charging hydraulic fluids in original equipment manufacture | Liquid Contact | Dermal | Workers | Yes | Workers are expected to routinely handle liquids containing 1,4-dioxane. |
| Industrial use | Functional fluids (closed/open system) | | | Vapor | Dermal | Workers | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of magnitude lower than via inhalation and will not be further analyzed. |
| Industrial use | Functional fluids (closed/open system) | | | Vapor | Inhalation | Workers | Yes | Due to high volatility at room temperature, inhalation exposure from vapor should be further evaluated. |
| Industrial use | Functional fluids (closed/open system) | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in handling the chemical. |
| Industrial use | Functional fluids (closed/open system) | | | Vapor | Dermal | ONU | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of magnitude lower than via inhalation and will not be further analyzed. |
| Industrial use | Functional fluids (closed/open system) | | | Vapor | Inhalation | ONU | Yes | Due to high volatility at room temperature, inhalation exposure from vapor should be further evaluated. |
| Industrial use | Functional fluids (closed/open system) | | | Mist | Dermal/Inhalation/Oral | Workers, ONU | Yes | Mist exposure can occur during open system uses and potentially while charging and servicing equipment with hydraulic fluid. |
| Industrial use, potential commercial use | Laboratory chemicals | Chemical reagent<br><br>Reference material<br><br>Spectroscopic and photometric | Laboratory chemical use | Liquid Contact | Dermal | Workers | Yes | Workers are expected to routinely handle liquids containing 1,4-dioxane. |
| Industrial use, potential commercial use | Laboratory chemicals | | | Vapor | Dermal | Workers | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of magnitude lower than via inhalation and will not be further analyzed. |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Industrial use, potential commercial use | Laboratory chemicals | measurement<br><br>Liquid scintillation and counting medium<br><br>Stable reaction medium<br><br>Cryoscopic solvent for molecular mass determinations<br><br>Preparation of histological sections for microscopic examination | | Vapor | Inhalation | Workers | Yes | Due to high volatility at room temperature, inhalation exposure from vapor should be further evaluated. |
| Industrial use, potential commercial use | Laboratory chemicals | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in handling the chemical. |
| Industrial use, potential commercial use | Laboratory chemicals | | | Vapor | Dermal | ONU | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of magnitude lower than via inhalation and will not be further analyzed. |
| Industrial use, potential commercial use | Laboratory chemicals | | | Vapor | Inhalation | ONU | Yes | Due to high volatility at room temperature, inhalation exposure from vapor should be further evaluated. |
| Industrial use, potential commercial use | Laboratory chemicals | | | Mist | Dermal/Inhalation/Oral | Workers, ONU | No | Mist generation is not expected. |
| Industrial use, potential commercial use | Adhesives and sealants<br><br>Other Uses | Film cement | Industrial and commercial small brush application | Liquid Contact | Dermal | Workers | Yes | Workers are expected to routinely handle liquids containing 1,4-dioxane. |
| Industrial use, potential commercial use | | | | Vapor | Dermal | Workers | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of magnitude lower than via inhalation and will not be further analyzed. |
| Industrial use, potential commercial use | | | | Vapor | Inhalation | Workers | Yes | Due to high volatility at room temperature, inhalation exposure from vapor should be further evaluated. |
| Industrial use, potential commercial use | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in handling the chemical. |
| Industrial use, potential commercial use | | | | Vapor | Dermal | ONU | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of magnitude lower than via inhalation and will not be further analyzed. |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Industrial use, potential commercial use | | | | Vapor | Inhalation | ONU | Yes | Due to high volatility at room temperature, inhalation exposure from vapor should be further evaluated. |
| Industrial use, potential commercial use | | | | Mist | Dermal/Inhalation/Oral | Workers, ONU | No | Mist generation is not expected. |
| Industrial use, potential commercial use | Other Uses | Spray polyurethane foam<br><br>Printing and printing compounds | Application of spray polyurethane foam through a nozzle<br><br>Use of Printing Inks | Liquid Contact | Dermal | Workers | Yes | Workers are expected to routinely handle liquids containing 1,4-dioxane. |
| Industrial use, potential commercial use | | | | Vapor | Dermal | Workers | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of magnitude lower than via inhalation and will not be further analyzed. |
| Industrial use, potential commercial use | | | | Vapor | Inhalation | Workers | Yes | Due to high volatility at room temperature, inhalation exposure from vapor should be further evaluated. |
| Industrial use, potential commercial use | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in handling the chemical. |
| Industrial use, potential commercial use | | | | Vapor | Dermal | ONU | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of magnitude lower than via inhalation and will not be further analyzed. |
| Industrial use, potential commercial use | | | | Vapor | Inhalation | ONU | Yes | Due to high volatility at room temperature, inhalation exposure from vapor should be further evaluated. |
| Industrial use, potential commercial use | | | | Mist | Dermal/Inhalation/Oral | Workers, ONU | Yes | Mist generation may occur during these processes. |
| Manufacture, processing, use, Disposal | Emissions to air<br><br>Wastewater | Air<br><br>Industrial pre-treatment<br><br>Industrial | Worker Handling of wastes | Liquid Contact | Dermal | Workers | Yes | Workers are expected to routinely handle liquids containing 1,4-dioxane. |
| Manufacture, processing, use, Disposal | | | | Vapor | Dermal | Workers | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Solid wastes and liquid wastes | wastewater treatment<br><br>Publicly owned treatment works (POTW)<br><br>Underground Injection<br><br>Municipal landfill<br><br>Hazardous landfill | | | | | | magnitude lower than via inhalation and will not be further analyzed. |
| Manufacture, processing, use, Disposal | | | | Vapor | Inhalation | Workers | Yes | Due to high volatility at room temperature, inhalation exposure from vapor should be further evaluated. |
| Manufacture, processing, use, Disposal | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in handling the chemical. |
| Manufacture, processing, use, Disposal | | | | Vapor | Dermal | ONU | No | The absorption of 1,4-dioxane vapor via skin is expected to be orders of magnitude lower than via inhalation and will not be further analyzed. |
| Manufacture, processing, use, Disposal | | | | Vapor | Inhalation | ONU | Yes | Due to high volatility at room temperature, inhalation exposure from vapor should be further evaluated. |
| Manufacture, processing, use, Disposal | | | | Mist | Dermal/Inhalation/Oral | Workers, ONU | No | Mist generation is not expected. |

# Appendix E SUPPORTING TABLE FOR ENVIRONMENTAL RELEASES AND WASTES CONCEPTUAL MODEL

All possible exposure scenarios for each condition of use were identified according to the COU in Table 2-3 and the environmental releases conceptual model in Figure 2-3 and are presented in Table_Apx E-1. EPA used readily available fate, exposure and/or toxicity information to determine whether to conduct further analysis on each exposure scenario.

EPA has identified release/environmental exposure scenarios and mapped them to relevant conditions of use in the table below. EPA may further refine the mapping/grouping of exposure scenarios based on factors corresponding to conditions of use as additional information is identified during risk evaluation.

**Table_Apx E-1: Environmental Releases and Wastes Exposure Scenarios for 1,4-Dioxane**

| Lifecycle Stage | Use Category | Release | Exposure Pathway | Exposure Route | Receptor | Further Evaluation? | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|
| Manufacturing and Processing | TBD | Industrial wastewater treatment operations | Water | N/A | Aquatic Species | No | Conservative screening indicates low potential for risk to aquatic organisms. |
| Manufacturing and Processing | TBD | Industrial wastewater treatment operations | Water, Air | N/A | Terrestrial Species | No | Ingestion of water and inhalation of air are not expected to be primary exposure routes for terrestrial organisms (see OPP tool). |
| Manufacturing and Processing | TBD | Industrial wastewater treatment operations | Sediment | N/A | Terrestrial Species | No | 1,4-Dioxane has low sorption to soil, sludge, and sediment and will instead stay in the associated aqueous phases. |
| Manufacturing and Processing | TBD | Industrial wastewater treatment operations | Sediment | | Aquatic Species | No | |
| Manufacturing and Processing | TBD | Industrial wastewater treatment operations | Biosolids disposed to soil, migration to groundwater | N/A | Terrestrial Species | No | 1,4 dioxane is not expected to remain in soil for long periods of time due to migration to groundwater and volatilization from soil. |
| Manufacturing and Processing | TBD | Industrial pre-treatment, then transfer to Publicly Owned Treatment Works (POTW) | Water | N/A | Aquatic Species | No | Conservative screening indicates low potential for risk to aquatic organisms. |
| Manufacturing and Processing | TBD | Industrial pre-treatment, then transfer to Publicly | Water, Air | N/A | Terrestrial Species | No | Ingestion of water and inhalation of air are not expected to be primary exposure routes for terrestrial organisms (see OPP tool). |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | Owned Treatment Works (POTW) | | | | | |
| Manufacturing and Processing | TBD | Industrial pre-treatment, then transfer to Publicly Owned Treatment Works (POTW) | Sediment | N/A | Terrestrial Species | No | 1,4-Dioxane has low sorption to soil, sludge, and sediment and will instead stay in the associated aqueous phases. |
| Manufacturing and Processing | TBD | Industrial pre-treatment, then transfer to Publicly Owned Treatment Works (POTW) | Sediment | | Aquatic Species | No | |
| Manufacturing and Processing | TBD | Industrial pre-treatment, then transfer to Publicly Owned Treatment Works (POTW) | Biosolids disposed to soil, migration to groundwater | N/A | Terrestrial Species | No | 1,4 dioxane is not expected to remain in soil for long periods of time due to migration to groundwater and volatilization from soil. |
| Disposal | TBD | Municipal landfill, Hazardous Landfill, and other land disposal | Soil | N/A | Terrestrial Species | No | 2015 TRI data indicates 3 sites reporting 13,422 lbs to landfill. However, 1,4-dioxane has low sorption to soil. |

# Appendix F INCLUSION AND EXCLUSION CRITERIA FOR FULL TEXT SCREENING

Appendix F contains the eligibility criteria for various data streams informing the TSCA risk evaluation: environmental fate; engineering and occupational exposure; exposure to the general population and consumers; and human health hazard. The criteria are applied to the *on-topic* references that were identified following title and abstract screening of the comprehensive search results published on June 22, 2017.

Systematic reviews typically describe the study eligibility criteria in the form of PECO statements or a modified framework. PECO stands for **P**opulation, **E**xposure, **C**omparator and **O**utcome and the approach is used to formulate explicit and detailed criteria about those characteristics in the publication that should be present in order to be eligible for inclusion in the review. EPA/OPPT adopted the PECO approach to guide the inclusion/exclusion decisions during full text screening.

Inclusion and exclusion criteria were also used during the title and abstract screening, and documentation about the criteria can be found in the *Strategy for Conducting Literature Searches* document published in June 2017 along with each of the TSCA Scope documents. The list of *on-topic* references resulting from the title and abstract screening is undergoing full text screening using the criteria in the PECO statements. The overall objective of the screening process is to select the most relevant evidence for the TSCA risk evaluation. As a general rule, EPA is excluding non-English data/information sources and will translate on a case by case basis.

The inclusion and exclusion criteria for ecotoxicological data have been documented in the ECOTOX SOPs. The criteria can be found at https://cfpub.epa.gov/ecotox/help.cfm?helptabs=tab4) and in the *Strategy for Conducting Literature Searches* document published along with each of the TSCA Scope documents.

Since full text screening commenced right after the publication of the TSCA Scope document, the criteria were set to be broad to capture relevant information that would support the initial scope. Thus, the inclusion and exclusion criteria for full text screening do not reflect the refinements to the conceptual model and analysis plan resulting from problem formulation. As part of the iterative process, EPA is in the process of refining the results of the full text screening to incorporate the changes in information/data needs to support the revised scope.

These refinements will include changes to the inclusion and exclusion criteria discussed in this appendix to better reflect the revised scope of the risk evaluation and will likely reduce the number of data/information sources that will undergo evaluation.

## F.1 Inclusion Criteria for the Data Sources Reporting Environmental Fate Data

EPA/OPPT developed a generic PESO statement to guide the full text screening of environmental fate data sources. PESO stands for Pathways and Processes, Exposure, Setting or Scenario, and Outcomes. Subsequent versions of the PESO statement may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the inclusion criteria in the PESO statement are eligible for inclusion, considered for evaluation, and

possibly included in the environmental fate assessment. On the other hand, data sources are excluded if they do not meet the criteria in the PESO statement.

During the development of conceptual models and consideration of the nexus between TSCA and other EPA regulations for 1,4-dioxane it was determined that no pathways for consumer or environmental exposure requiring environmental fate information would be further analyzed. As described in Section 2.5.2, EPA does not plan to evaluate exposure pathways to human receptors from consumer uses of 1,4-dioxane. As described in Section 2.5.3, there are no exposure pathways for general population or ecological receptors from environmental releases and waste streams associated with industrial and commercial activities for 1,4-dioxane that EPA plans to include and further analyze in the risk assessment.

For 1,4-dioxane no exposure pathways to human and ecological receptors from consumer products, environmental releases, or waste streams associated with industrial and commercial activities will be further analyzed in risk evaluation. In the absence of exposure pathways for further analysis, environmental fate data will not be evaluated further. Therefore, no PESO statement or fate data needs and associated processes, media and exposure pathways considered in the development of the environmental fate assessment for 1,4-dioxane will be presented.

## F.2 Inclusion Criteria for Data Sources Reporting Engineering and Occupational Exposure Data

EPA/OPPT developed a generic RESO statement to guide the full text screening of engineering and occupational exposure literature (Table_Apx F-1). RESO stands for Receptors, Exposure, Setting or Scenario, and Outcomes. Subsequent versions of the RESO statement may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the inclusion criteria specified in the RESO statement will be eligible for inclusion, considered for evaluation, and possibly included in the environmental release and occupational exposure assessments, while those that do not meet these criteria will be excluded.

The RESO statement should be used along with the engineering and occupational exposure data needs table (Table_Apx F-2) when screening the literature.

Since full text screening commenced right after the publication of the TSCA Scope document, the criteria for engineering and occupational exposure data were set to be broad to capture relevant information that would support the risk evaluation. Thus, the inclusion and exclusion criteria for full text screening do not reflect the refinements to the conceptual model and analysis plan resulting from problem formulation. As part of the iterative process, EPA is in the process of refining the results of the full text screening to incorporate the changes in information/data needs to support the risk evaluation.

**Table_Apx F-1: Inclusion Criteria for Data Sources Reporting Engineering and Occupational Exposure Data**

| RESO Element | Evidence |
|---|---|
| **Receptors** | • **Humans:**<br>Workers, including occupational non-users<br><br>Please refer to the conceptual models for more information about the human receptors included in the TSCA risk evaluation. |
| **Exposure** | • Worker exposure and relevant environmental releases of the chemical substance of interest<br><br>o Dermal and inhalation exposure routes (as indicated in the conceptual model)<br>o Surface water (as indicated in the conceptual model)<br><br>Please refer to the conceptual models for more information about the routes and media/pathways included in the TSCA risk evaluation. |
| **Setting or Scenario** | • Any occupational setting or scenario resulting in worker exposure and relevant environmental releases (includes all manufacturing, processing, use, disposal indicated in Table_Apx F-2 below. |
| **Outcomes** | • Quantitative estimates* of worker exposures and of relevant environmental releases from occupational settings<br>• General information and data related and relevant to the occupational estimates* |

* Metrics (e.g., mg/kg/day or $mg/m^3$ for worker exposures, kg/site/day for releases) are determined by toxicologists for worker exposures and by exposure assessors for releases; also, the Engineering Data Needs (Table_Apx F-2) provides a list of related and relevant general information.
TSCA=Toxic Substances Control Act

**Table_Apx F-2: Engineering, Environmental Release and Occupational Data Necessary to Develop the Environmental Release and Occupational Exposure Assessments**

| Objective Determined during Scoping | Type of Data |
|---|---|
| General Engineering Assessment (may apply for either or both Occupational Exposures and / or Environmental Releases) | 1. Description of the life cycle of the chemical(s) of interest, from manufacture to end-of-life (e.g., each manufacturing, processing, or use step), and material flow between the industrial and commercial life cycle stages. {Tags: Life cycle description, Life cycle diagram}[a]<br>2. The total annual U.S. volume (lb/yr or kg/yr) of the chemical(s) of interest manufactured, imported, processed, and used; and the share of total annual manufacturing and import volume that is processed or used in each life cycle step. {Tags: Production volume, Import volume, Use volume, Percent PV} [a]<br>3. Description of processes, equipment, unit operations, and material flows and frequencies (lb/site-day or kg/site-day and days/yr; lb/site-batch and batches/yr) of the chemical(s) of interest during each industrial/ commercial life cycle step. Note: if available, include weight fractions of the chemicals (s) of interest and material flows of all associated primary chemicals (especially water). {Tags: Process description, Process material flow rate, Annual operating days, Annual batches, Weight fractions (for each of above, manufacture, import, processing, use)} [a]<br>4. Basic chemical properties relevant for assessing exposures and releases, e.g., molecular weight, normal boiling point, melting point, physical forms, and room temperature vapor pressure. {Tags: Molecular weight, Boiling point, Melting point, Physical form, Vapor pressure, Water solubility} [a]<br>5. Number of sites that manufacture, process, or use the chemical(s) of interest for each industrial/ commercial life cycle step and site locations. {Tags: Numbers of sites (manufacture, import, processing, use), Site locations} [a] |
| Occupational Exposures | 6. Description of worker activities with exposure potential during the manufacture, processing, or use of the chemical(s) of interest in each industrial/commercial life cycle stage. {Tags: Worker activities (manufacture, import, processing, use)} [a]<br>7. Potential routes of exposure (e.g., inhalation, dermal). {Tags: Routes of exposure (manufacture, import, processing, use)} [a]<br>8. Physical form of the chemical(s) of interest for each exposure route (e.g., liquid, vapor, mist) and activity. {Tags: Physical form during worker activities (manufacture, import, processing, use)} [a]<br>9. Breathing zone (personal sample) measurements of occupational exposures to the chemical(s) of interest, measured as time-weighted averages (TWAs), short-term exposures, or peak exposures in each occupational life cycle stage (or in a workplace scenario similar to an occupational life cycle stage). {Tags: PBZ measurements (manufacture, import, processing, use)} [a]<br>10. Area or stationary measurements of airborne concentrations of the chemical(s) of interest in each occupational setting and life cycle stage (or in a workplace scenario similar to the life cycle stage of interest). {Tags: Area measurements (manufacture, import, processing, use)} [a]<br>11. For solids, bulk and dust particle size characterization data. {Tags: PSD measurements (manufacture, import, processing, use)} [a]<br>12. Dermal exposure data. {Tags: Dermal measurements (manufacture, import, processing, use)}<br>13. Data needs associated with mathematical modeling (will be determined on a case-by-case basis). {Tags: Worker exposure modeling data needs (manufacture, import, processing, use)} [a]<br>14. Exposure duration (hr/day). {Tags: Worker exposure durations (manufacture, import, processing, use)} [a]<br>15. Exposure frequency (days/yr). {Tags: Worker exposure frequencies (manufacture, import, processing, use)} [a]<br>16. Number of workers who potentially handle or have exposure to the chemical(s) of interest in each occupational life cycle stage. {Tags: Numbers of workers exposed (manufacture, import, processing, use)} [a]<br>17. Personal protective equipment (PPE) types employed by the industries within scope. {Tags: Worker PPE (manufacture, import, processing, use)} [a]<br>18. Engineering controls employed to reduce occupational exposures in each occupational life cycle stage (or in a workplace scenario similar to the life cycle stage of interest), and associated data or estimates of exposure reductions. {Tags: Engineering controls (manufacture, import, processing, use), Engineering control effectiveness data} [a] |

| Objective Determined during Scoping | Type of Data |
|---|---|
| Environmental Releases | 19. Description of relevant sources of potential environmental releases, including cleaning of residues from process equipment and transport containers, involved during the manufacture, processing, or use of the chemical(s) of interest in each life cycle stage. {Tags: Release sources (manufacture, import, processing, use)} [a]<br>20. Estimated mass (lb or kg) of the chemical(s) of interest released from industrial and commercial sites to relevant environmental media (water) and treatment and disposal methods (POTW), including releases per site and aggregated over all sites (annual release rates, daily release rates) {Tags: Release rates (manufacture, import, processing, use)} [a]<br>21. Relevant release or emission factors. {Tags: Emission factors (manufacture, import, processing, use)} [a]<br>22. Number of release days per year. {Tags: Release frequencies (manufacture, import, processing, use)} [a]<br>23. Data needs associated with mathematical modeling (will be determined on a case-by-case basis). {Tags: Release modeling data needs (manufacture, import, processing, use)} [a]<br>24. Waste treatment methods and pollution control devices employed by the industries within scope and associated data on release/emission reductions. {Tags: Treatment/ emission controls (manufacture, import, processing, use), Treatment/ emission controls removal/ effectiveness data} [a] |

**Notes:**

[a] These are the tags included in the full text screening form. The screener makes a selection from these specific tags, which describe more specific types of data or information.

**Abbreviations:**

hr=Hour
kg=Kilogram(s)
lb=Pound(s)
yr=Year
PV=Particle volume
PBZ=
POTW=Publicly owned treatment works
PPE=Personal projection equipment
PSD=Particle size distribution
TWA=Time-weighted average

## F.3 Inclusion Criteria for Data Sources Reporting Environmental and General Population Exposure

EPA/OPPT developed a generic PECO statement to guide the full text screening of environmental and general population exposure data sources. PECO stands for Population, Exposure, Comparator and Outcome and the approach is used to formulate explicit and detailed criteria about those characteristics in the publication that should be present to be eligible for inclusion in the review. Subsequent versions of the PECO statement may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Exposure pathways to human and ecological receptors from environmental releases associated with industrial and commercial activities will not be further analyzed in risk evaluation (see Section 2.5.3.2 and Section 2.5.3.3). In the absence of exposure pathways for further analysis, data related to environmental and general population exposure will not be further analyzed.

# F.4 Inclusion Criteria for Data Sources Reporting Human Health Hazards

**Table_Apx F-3: Inclusion and Exclusion Criteria for Data Sources Reporting Human Health Hazards Related to 1,4-Dioxane Exposure[a]**

| PECO Element | Evidence Stream | Papers/Features Included | Papers/Features Excluded |
|---|---|---|---|
| **Population** | *Human* | • Any population<br>• All lifestages<br>• Study designs:<br>  ○ Controlled exposure, cohort, case-control, cross-sectional, case-crossover, case studies, and case series for all endpoints | |
| | *Animal* | • All non-human whole-organism mammalian species<br>• All lifestages | • Non-mammalian species |
| | *Mechanistic* | • Human or animal cells, tissues, or biochemical reactions (e.g., ligand binding assays) with *in vitro* exposure regimens; bioinformatics pathways of disease analysis; or high throughput screening data. | |
| **Exposure** | *Human* | • Exposure based on administered dose or concentration of 1,4-dioxane, biomonitoring data (e.g., urine, blood or other specimens), environmental or occupational-setting monitoring data (e.g., air, water levels), job title or residence<br>• Primary metabolites of interest (e.g., HTTA) as identified in biomonitoring studies<br>• All routes of exposure<br>• Any number of exposure groups<br>• Quantitative, semi-quantitative or qualitative estimates of exposure<br>• Exposures to multiple chemicals/mixtures only if 1,4-dioxane or related metabolites were independently measured and analyzed | • Multiple chemical/mixture exposures with no independent measurement of or exposure to 1,4-dioxane (or related metabolite) |
| | *Animal* | • A minimum of 2 quantitative dose or concentration levels of 1,4-dioxane plus a negative control group [a]<br>• Acute, subchronic, chronic exposure from oral, dermal, inhalation routes<br>• Exposure to 1,4-dioxane only (no chemical mixtures) | • Only 1 quantitative dose or concentration level in addition to the control [a]<br>• Route of exposure ***not*** by inhalation, oral or dermal type (e.g., intraperitoneal, injection)<br>• No duration of exposure stated<br>• Exposure to 1,4-dioxane in a chemical mixture |
| | *Mechanistic* | • Exposure based on concentrations of the neat material of 1,4-dioxane<br>• A minimum of 2 dose or concentration levels tested plus a control group [a] | • Only 1 quantitative dose or concentration level in addition to the control [a]<br>• Exposure to 1,4-dioxane in a chemical mixture |
| **Comparator** | *Human* | • A comparison population [not exposed, exposed to lower levels, exposed below detection] for all endpoints | • No comparison population for all endpoints |
| | *Animal* | • Negative controls that are vehicle-only treatment and/or no treatment | • Negative controls ***other than*** vehicle-only treatment or no treatment |
| | *Mechanistic* | • Exposed to vehicle-only treatment and/or no treatment<br>• ***For genotoxicity studies only***, studies using positive controls | • Negative controls ***other than*** vehicle-only treatment or no treatment<br>• ***For genotoxicity studies only***, a lack of positive controls |
| **Outcome** | *Human and Animal* | • Endpoints described in the 1,4-dioxane scope document [b]:<br>  ○ Cancer<br>  ○ Liver toxicity | |

| PECO Element | Evidence Stream | Papers/Features Included | Papers/Features Excluded |
|---|---|---|---|
| | | ○ Kidney toxicity<br>○ Neurotoxicity<br>○ Irritation<br>○ Acute Toxicity/Poisoning<br>• Other endpoints [c] | |
| | *Mechanistic* | • All mechanistic data that may inform the following health outcomes:<br>○ Cancer<br>○ Genotoxicity<br>○ Neurological/Behavior<br>○ Renal<br>○ Hepatic<br>○ Irritation<br>○ Acute Toxicity/Poisoning<br>○ ADME/PBPK | • Data related to other mechanisms of toxicity [a] |
| **General Considerations** | | **Papers/Features Included** | **Papers/Features Excluded** |
| | | • Written in English [d]<br>• Reports a primary source or meta-analysis [a]<br>• Full-text available<br>• Reports both 1,4-dioxane exposure ***and*** a health outcome (or mechanism of action) | • Not written in English [d]<br>• Reports a secondary source (e.g., review papers) [a]<br>• No full-text available (e.g., only a study description/abstract, out-of-print text)<br>• Reports a 1,4-dioxane-related exposure ***or*** a health outcome, but not both (e.g. incidence, prevalence report) |

[a] Some of the studies that are excluded based on the PECO statement may be considered later during the systematic review process. For 1,4-dioxane, EPA will evaluate studies related to susceptibility after other data are reviewed. Finally, EPA may also review other data as needed (e.g., animal studies using one concentration, review papers).

[b] EPA will review key and supporting studies in the IRIS assessment that were considered in the dose-response assessment for non-cancer and cancer endpoints as well as studies published after the IRIS assessment.

[c] EPA may screen for hazards other than those listed in the scope document if they were identified in the updated literature search that accompanied the scope document.

[d] EPA may translate studies as needed.

## F.5 List Of Retracted Papers

The following reference was retracted by the journal:

HERO ID: 3538089 (1,4-dioxane; HBCD)
Kreipke, CW; Rafols, JA; Reynolds, CA; Schafer, S; Marinica, A; Bedford, C; Fronczak, M; Kuhn, D; Armstead, WM. (2011). Clazosentan, a novel endothelin A antagonist, improves cerebral blood flow and behavior after traumatic brain injury. Neurol Res 33: 208-213.
http://dx.doi.org/10.1179/016164111X12881719352570

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Office of Chemical Safety and
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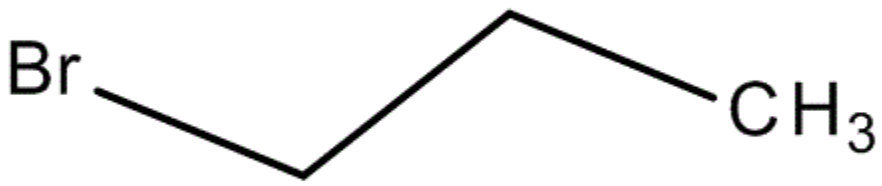
United States
Environmental Protection Agency

# Problem Formulation of the Risk Evaluation for 1-Bromopropane

# CASRN: 106-94-5




***May 2018***

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# ACKNOWLEDGEMENTS

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**Docket**

Supporting information can be found in public docket (Docket: EPA-HQ-OPPT-2016-0741).

**Disclaimer**

Reference herein to any specific commercial products, process or service by trade name, trademark, manufacturer or otherwise does not constitute or imply its endorsement, recommendation or favoring by the United States Government.

# ABBREVIATIONS

| | |
|---|---|
| °C | Degrees Celsius |
| ACGIH | American Conference of Government Industrial Hygienists |
| ACR | Acute-to-Chronic Ratio |
| atm | Atmosphere(s) |
| ATCM | Airborne Toxic Control Measure |
| ATSDR | Agency for Toxic Substances and Disease Registry |
| AF | Assessment Factor |
| BAF | Bioaccumulation Factor |
| BCF | Bioconcentration Factor |
| BMD | Benchmark Dose Modeling |
| 1-BP | 1-Bromopropane |
| CAA | Clean Air Act |
| CARB | California Air Resources Board |
| CASRN | Chemical Abstracts Service Registry Number |
| CBI | Confidential Business Information |
| CCL | Contaminant Candidate List |
| CDR | Chemical Data Reporting |
| CEHD | Chemical Exposure Health Data |
| CEM | Consumer Exposure Model |
| CFC | Chlorofluorocarbon |
| CFR | Code of Federal Regulations |
| ChV | Chronic Value (MATC) |
| COC | Concentration of Concern |
| COU | Conditions of Use |
| CSCL | Chemical Substances Control Law |
| CWA | Clean Water Act |
| DIY | Do It Yourself |
| DOE | Department of Energy |
| DNA | Deoxyribonucleic Acid |
| DRE | Destruction Removal Efficiencies |
| $EC_{50}$ | Effective Concentration with 50% immobilized test organisms |
| ECHA | European Chemicals Agency |
| EPA | Environmental Protection Agency |
| EPCRA | Emergency Planning and Community Right-to-Know Act |
| ESD | Emissions Scenario Document |
| g/L | Gram(s) per Liter |
| GS | Generic Scenario |
| HAP | Hazardous Air Pollutant |
| HCFC | Hydrochlorofluorocarbon |
| HHE | Health Hazard Evaluation |
| Hr | Hour |
| IMAP | Inventory Multi-Tiered Assessment and Prioritisation (Australia) |
| IRIS | Integrated Risk Information System |
| ISHA | Industrial Safety and Health Act |

| | |
|---|---|
| ISOR | Initial Statement of Reasons |
| IUR | Inhalation Unit Risk |
| kg | Kilogram(s) |
| kPa | Kilopascal(s) |
| L | Liter(s) |
| LOAEL | Lowest Observed Adverse Effect Level |
| lb | Pound(s) |
| $LC_{50}$ | Lethal Concentration of 50% test organisms |
| LOEC | Lowest Observed Effect Concentration |
| Log $K_{oc}$ | Logarithmic Soil Organic Carbon:Water Partitioning Coefficient |
| Log $K_{ow}$ | Logarithmic Octanol:Water Partition Coefficient |
| $m^3$ | Cubic Meter(s) |
| mg/L | Milligram(s) per Liter |
| mmHg | Millimeter(s) of Mercury |
| mPa·s | Millipascal(s)-Second |
| MACT | Maximum Achievable Control Technology |
| MATC | Maximum Acceptable Toxicant Concentration |
| MSWLFs | Municipal Solid Waste Landfills |
| NAAQS | National Ambient Air Quality Standards |
| NAICS | North American Industry Classification System |
| NEI | National Emissions Inventory |
| NESHAP | National Emission Standards for Hazardous Air Pollutants |
| NF/FF | Near Field/Far Field |
| NICNAS | National Industrial Chemicals Notification and Assessment Scheme (Australia) |
| NIOSH | National Institute for Occupational Safety and Health |
| NOAEL | No Observed Adverse Effect Level |
| NOEC | No Observed Effect Concentration |
| NTP | National Toxicology Program |
| OAQPS | Office of Air Quality Planning and Standards |
| OCSPP | Office of Chemical Safety and Pollution Prevention |
| OECD | Organisation for Economic Co-operation and Development |
| ONU | Occupational Non-User |
| OPPT | Office of Pollution Prevention and Toxics |
| OSHA | Occupational Safety and Health Administration |
| OTVD | Open Top Vapor Degreaser |
| PECO | Populations, Exposures, Comparisons, Outcomes |
| PESS | Potentially Exposed or Susceptible Subpopulations |
| PBPK | Physiologically Based Pharmacokinetic |
| PBZ | Personal Breathing Zone |
| PEL | Permissible Exposure Limit |
| PERC | Perchloroethylene |
| POD | Point of Departure |
| POTW | Publicly Owned Treatment Works |
| PPE | Personal Protective Equipment |
| ppm | Part(s) per Million |
| PSD | Particle Size Distribution |

| | |
|---|---|
| PV | Production Volume |
| QC | Quality Control |
| RCRA | Resource Conservation and Recovery Act |
| REACH | Registration, Evaluation, Authorisation and Restriction of Chemicals (European Union) |
| REL | Recommended Exposure Limit |
| SDS | Safety Data Sheet |
| SDWA | Safe Drinking Water Act |
| SNAP | Significant New Alternatives Policy |
| STP | Sewage Treatment Plant |
| SVHC | Substance of Very High Concern (European Union) |
| t ½ | Half-Life |
| TCE | Trichloroethylene |
| TLV | Threshold Limit Value |
| TRI | Toxics Release Inventory |
| TSCA | Toxic Substances Control Act |
| TWA | Time-Weighted Average |
| VP | Vapor Pressure |
| VOC | Volatile Organic Compound |
| U.S. | United States |
| WTP | Wastewater Treatment Plant |
| WWT | Wastewater Treatment |
| Yr | Year |

# EXECUTIVE SUMMARY

TSCA § 6(b)(4) requires the U.S. Environmental Protection Agency (U.S. EPA) to establish a risk evaluation process. In performing risk evaluations for existing chemicals, EPA is directed to "determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of costs or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator under the conditions of use." In December of 2016, EPA published a list of 10 chemical substances that are the subject of the Agency's initial chemical risk evaluations (81 FR 91927), as required by TSCA § 6(b)(2)(A). 1-Bromopropane (1-BP) was one of these chemicals.

TSCA § 6(b)(4)(D) requires that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use and potentially exposed or susceptible subpopulations that the Administrator expects to consider. In June, 2017, EPA published the Scope of the Risk Evaluation for 1-BP (Scope Document; EPA-HQ-OPPT-2016-0741-0049). As explained in the Scope Document, because there was insufficient time for EPA to provide an opportunity for comment on a draft of the scope, as EPA intends to do for future scope documents, EPA is publishing and taking public comment on a problem formulation document to refine the current scope, as an additional interim step prior to publication of the draft risk evaluation for 1-BP. Comments received on this problem formulation document will inform development of the draft risk evaluation.

This problem formulation document refines the conditions of use, exposures and hazards presented in the scope of the risk evaluation for 1-BP and presents refined conceptual models and analysis plans that describe how EPA expects to evaluate risk for 1-BP.

1-BP is primarily used as a solvent cleaner in vapor and immersion degreasing operations to clean optics, electronics and metals, but it has also been reported to be used as an alternative to ozone-depleting substances and chlorinated solvents, as a solvent vehicle in industries using spray adhesives such as foam cushion manufacturing and in the dry cleaning industry. Information from the 2016 Chemical Data Reporting (CDR) for 1-BP indicates the reported production volume is 25.9 million lbs/year (manufacture and import).

This document presents the potential exposures that may result from the conditions of use of 1-BP. Exposures to workers, consumers, and/or the general population may occur from industrial, commercial, consumer uses of 1-BP and industrial releases to air, water or land. Workers and occupational non-users (i.e., workers who do not directly handle the chemical but perform work in an area where the chemical is used) may be exposed to 1-BP during a variety of conditions of use such as manufacturing, processing, distribution, repackaging, spray adhesives, dry cleaning (including spot cleaning) and degreasing (vapor, cold cleaning, and aerosol). Consumers and bystanders may be exposed to 1-BP from various consumer uses such as aerosol and spray adhesives, aerosol spot removers and aerosol cleaning and degreasing products. For 1-BP, EPA considers workers, occupational non-users, consumers, bystanders, and certain other groups of individuals who may experience greater exposures than the general population due to proximity to conditions of use to be potentially exposed or susceptible subpopulations. Exposures to the general population may occur from industrial and/or commercial uses; industrial releases to air, water, or land; and other conditions of use. EPA will evaluate whether groups of individuals within the general population may be exposed via pathways that are distinct from the general population due to unique characteristics (e.g., life stage, behaviors, activities, or duration) that increase exposure and whether groups of individuals have heightened susceptibility, and should therefore be considered potentially exposed or susceptible subpopulations for purposes of the risk evaluation. EPA plans to further analyze inhalation exposures to vapors and mists for workers and occupational non-users (workers who do not

directly handle the chemical but perform work in an area where the chemical is present) and dermal exposures for skin contact with liquids in occluded situations for workers in the risk evaluation. EPA plans to further analyze inhalation exposures to vapors and mists for consumers and bystanders and dermal exposures for skin contact with liquids in the risk evaluation. For environmental release pathways, EPA does not plan to further analyze surface water exposure to aquatic invertebrates and aquatic plants in the risk evaluation.

1-BP has been the subject of numerous health hazard reviews including the Agency for Toxic Substances and Disease Registry's (ATSDR's) Toxicological Profile, and the National Institute for Occupational Safety and Health's (NIOSH's) Criteria Document, in addition to the 2016 Draft Risk Assessment (U.S. EPA, 2016b). Any existing assessments will be a starting point as EPA conducts a systematic review of the literature, including new literature since the existing assessments, as available in *1-Bromopropane (CASRN 106-94-5) Bibliography: Supplemental File for the TSCA Scope Document*,) EPA-HQ-OPPT-2016-0741-0047). If additional hazard concerns are identified during the systematic review of the literature, these will also be considered. These hazards will be evaluated based on the specific exposure scenarios identified.

The revised conceptual models presented in this problem formulation identify conditions of use; exposure pathways (e.g., media); exposure routes (e.g., inhalation, dermal, oral); potentially exposed or susceptible subpopulations; and hazards EPA expects to consider in the risk evaluation. The initial conceptual models provided in the scope document were revised during problem formulation based on evaluation of reasonably available information for physical and chemical properties, fate, exposures, hazards, and conditions of use and based upon consideration of other statutory and regulatory authorities. In each problem formulation document for the first 10 chemical substances, EPA also refined the activities, hazards, and exposure pathways that will be included in and excluded from the risk evaluation.

EPA's overall objectives in the risk evaluation process are to conduct timely, relevant, high-quality, and scientifically credible risk evaluations within the statutory deadlines, and to evaluate the conditions of use that raise greatest potential for risk. 82 FR 33726, 33728 (July 20, 2017).

# 1 INTRODUCTION

This document presents for comment the problem formulation of the risk evaluation to be conducted for 1-Bromopropane (1-BP) under the Frank R. Lautenberg Chemical Safety for the 21st Century Act. The Frank R. Lautenberg Chemical Safety for the 21st Century Act amended the Toxic Substances Control Act (TSCA), the Nation's primary chemicals management law, on June 22, 2016. The new law includes statutory requirements and deadlines for actions related to conducting risk evaluations of existing chemicals.

In December of 2016, EPA published a list of 10 chemical substances that are the subject of the Agency's initial chemical risk evaluations (81 FR 91927), as required by TSCA § 6(b)(2)(A). These 10 chemical substances were drawn from the 2014 update of EPA's TSCA Work Plan for Chemical Assessments, a list of chemicals that EPA identified in 2012 and updated in 2014 (currently totaling 90 chemicals) for further assessment under TSCA. EPA's designation of the first 10 chemical substances constituted the initiation of the risk evaluation process for each of these chemical substances, pursuant to the requirements of TSCA § 6(b)(4).

TSCA § 6(b)(4)(D) requires that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use (COU) and potentially exposed or susceptible subpopulations (PESS) that the Administrator expects to consider, within 6 months after the initiation of a risk evaluation. The scope documents for all first 10 chemical substances were issued on June 22, 2017. The first 10 problem formulation documents are a refinement of what was presented in the first 10 scope documents. TSCA § 6(b)(4)(D) does not distinguish between scoping and problem formulation, and requires EPA to issue scope documents that include information about the chemical substance, including the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations that the Administrator expects to consider in the risk evaluation. In the future, EPA expects scoping and problem formulation to be completed prior to the issuance of scope documents and intends to issue scope documents that include problem formulation.

As explained in the scope document, because there was insufficient time for EPA to provide an opportunity for comment on a draft of the scope, as EPA intends to do for future scope documents, EPA is publishing and taking public comment on a problem formulation document to refine the current scope, as an additional interim step prior to publication of the draft risk evaluation for 1-BP. Comments received on this problem formulation document will inform development of the draft risk evaluation.

The Agency defines problem formulation as the analytical phase of the risk assessment in which "the purpose for the assessment is articulated, the problem is defined and a plan for analyzing and characterizing risk is determined" [see Section 2.2 of the Framework for Human Health Risk Assessment to Inform Decision Making; (U.S. EPA, 2014b)]. The outcome of problem formulation is a conceptual model(s) and an analysis plan. The conceptual model describes the linkages between stressors and adverse human health effects, including the stressor(s), exposure pathway(s), exposed life stage(s) and population(s), and endpoint(s) that will be addressed in the risk evaluation (U.S. EPA, 2014b). The analysis plan follows the development of the conceptual model(s) and is intended to describe the approach for conducting the risk evaluation, including its design, methods and key inputs and intended outputs as described in (U.S. EPA, 2014b). The problem formulation documents refine the initial conceptual models and analysis plans that were provided in the scope documents.

First, EPA has removed from the risk evaluation any activities and exposure pathways that EPA has concluded do not warrant inclusion in the risk evaluation. For example, for some activities that were

listed as "conditions of use" in the scope document, EPA has insufficient information following the further investigations during problem formulation to find they are circumstances under which the chemical is actually "intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of."

Second, EPA also identified certain exposure pathways that are under the jurisdiction of regulatory programs and associated analytical processes carried out under other EPA-administered environmental statutes – namely, the Safe Drinking Water Act (SDWA), the Clean Water Act (CWA), and the Resource Conservation and Recovery Act (RCRA) – and which EPA does not expect to include in the risk evaluation.

As a general matter, EPA believes that certain programs under other Federal environmental laws adequately assess and effectively manage the risks for the covered exposure pathways. To use Agency resources efficiently under the TSCA program, to avoid duplicating efforts taken pursuant to other Agency programs, to maximize scientific and analytical efforts, and to meet the three-year statutory deadline, EPA is planning to exercise its discretion under TSCA 6(b)(4)(D) to focus its analytical efforts on exposures that are likely to present the greatest concern and consequently merit a risk evaluation under TSCA, by excluding, on a case-by-case basis, certain exposure pathways that fall under the jurisdiction of other EPA-administered statutes.[1] EPA does not expect to include any such excluded pathways as further explained below in the risk evaluation. The provisions of various EPA-administered environmental statutes and their implementing regulations represent the judgment of Congress and the Administrator, respectively, as to the degree of health and environmental risk reduction that is sufficient under the various environmental statutes.

Third, EPA identified any conditions of use, hazards, or exposure pathways which were included in the scope document and that EPA expects to include in the risk evaluation but which EPA does not plan to further analyze in the risk evaluation. EPA expects to be able to reach conclusions about particular conditions of use, hazards or exposure pathways without further analysis and therefore plans to conduct no further analysis on those conditions of use, hazards or exposure pathways in order to focus the Agency's resources on more extensive or quantitative analyses. Each risk evaluation will be "fit-for-purpose," meaning not all conditions of use will warrant the same level of evaluation and the Agency may be able to reach some conclusions without comprehensive or quantitative risk evaluations. 82 FR 33726, 33734, 33739 (July 20, 2017).

EPA received comments on the published scope document for 1-BP and has considered the comments specific to 1-BP in this problem formulation document. EPA is soliciting public comment on this problem formulation document and when the draft risk evaluation is issued the Agency intends to respond to comments that are submitted. In its draft risk evaluation, EPA may revise the conclusions and approaches contained in this problem formulation, including the conditions of use and pathways covered and the conceptual models and analysis plans, based on comments received.

## 1.1 Regulatory History

EPA conducted a search of existing domestic and international laws, regulations and assessments pertaining to 1-BP. EPA compiled this summary from data available from federal, state, international

[1] As explained in the final rule for chemical risk evaluation procedures, "EPA may, on a case-by case basis, exclude certain activities that EPA has determined to be conditions of use in order to focus its analytical efforts on those exposures that are likely to present the greatest concern, and consequently merit an unreasonable risk determination [82 FR 33726 (July 20 2017)].

and other government sources, as cited in Appendix A. EPA evaluated and considered the impact of existing laws and regulations (e.g., regulations on landfill disposal, design, and operations) in the problem formulation step to determine what, if any further analysis might be necessary as part of the risk evaluation. Consideration of the nexus between these existing regulations and TSCA conditions of use may additionally be made as detailed/specific conditions of use and exposure scenarios are developed in conducting the analysis phase of the risk evaluation.

### *Federal Laws and Regulations*

1-BP is subject to federal statutes or regulations, other than TSCA, that are implemented by other offices within EPA and/or other federal agencies/departments. A summary of federal laws, regulations and implementing authorities is provided in Appendix A.1.

### *State Laws and Regulations*

1-BP is subject to state statutes or regulations implemented by state agencies or departments. A summary of state laws, regulations and implementing authorities is provided in Appendix A.2.

### *Laws and Regulations in Other Countries and International Treaties or Agreements*

1-BP is subject to statutes or regulations in countries other than the United States and/or international treaties and/or agreements. A summary of these laws, regulations, treaties and/or agreements is provided in Appendix A.3.

## 1.2 Assessment History

EPA has identified assessments conducted by other EPA Programs and other organizations (see Table 1-1). Depending on the source, these assessments may include information on conditions of use, hazards, exposures and potentially exposed or susceptible subpopulations. Table 1-1 shows the assessments that have been conducted. EPA found no additional assessments beyond those listed in the Scope Document (Scope Document; EPA-HQ-OPPT-2016-0741-0049).

In addition to using this information, EPA intends to conduct a full review of the relevant data and information collected in the initial comprehensive search (see *1-Bromopropane (CASRN 106-94-5) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0741-0048) using the literature search and screening strategies documented in the *Strategy for Conducting Literature Searches for 1-Bromopropane: Supplemental File for the TSCA Scope Document*, (EPA-HQ-OPPT-2016-0741-0048). This will ensure that EPA considers data and information that has been made available since these assessments were conducted.

**Table 1-1. Assessment History of 1-BP**

| Authoring Organization | Assessment |
|---|---|
| **EPA Assessments** | |
| Office of Chemical Safety and Pollution Prevention (OCSPP)/Office of Pollution Prevention and Toxics (OPPT) | TSCA work plan chemical risk assessment: Peer review draft 1-bromopropane: (n-Propyl bromide) spray adhesives, dry cleaning, and degreasing uses CASRN: 106-94-5 (2016b) [2016 Draft Risk Assessment (U.S. EPA, 2016b)] |

**Table 1-1. Assessment History of 1-BP**

| Authoring Organization | Assessment |
|---|---|
| Office of Air Quality Planning and Standards (OAQPS) | Draft notice to grant the petition to add 1-BP to the list of HAPs (https://www.regulations.gov/document?D=EPA-HQ-OAR-2014-0471-0062) |
| **Other U.S.-Based Organizations** | |
| National Institute for Occupational Safety and Health (NIOSH) | Criteria for a Recommended Standard: Occupational Exposure to 1-Bromopropane (2016) |
| Agency for Toxic Substances and Disease Registry (ATSDR) | Toxicological Profile for 1-Bromopropane (2017) |

## 1.3 Data and Information Collection

EPA/OPPT generally applies a systematic review process and workflow that includes: (1) data collection; (2) data evaluation; and (3) data integration of the scientific data used in risk evaluations developed under TSCA. Scientific analysis is often iterative in nature as new knowledge is obtained. Hence, EPA/OPPT expects that multiple refinements regarding data collection may occur during the process of risk evaluation. Additional information that may be considered and was not part of the initial comprehensive bibliographies will be documented in the Draft Risk Evaluation for 1-BP.

***Data Collection: Data Search***

EPA/OPPT conducted chemical-specific searches for data and information on: physical and chemical properties; environmental fate and transport; conditions of use information; environmental exposures, human exposures, including potentially exposed or susceptible subpopulations; ecological hazard, human health hazard, including potentially exposed or susceptible subpopulations.

EPA/OPPT designed its initial data search to be broad enough to capture a comprehensive set of sources containing information potentially relevant to the risk evaluation. For most disciplines, the search was not limited by date and was conducted on a wide range of data sources, including but not limited to: peer-reviewed literature and gray literature (e.g., publicly-available industry reports, trade association resources, government reports). For human health hazard, EPA/OPPT relied on the search strategies from recent assessments, such as the National Toxicology Program's (NTP) *Report on Carcinogens* (NTP, 2013), to identify relevant information published after the end date of the previous search to capture more recent literature. The *Strategy for Conducting Literature Searches for 1-Bromopropane: Supplemental File for the TSCA Scope Document,* (EPA-HQ-OPPT-2016-0741-0048) provides details about the data sources and search terms that were used in the literature search.

***Data Collection: Data Screening***

Following the data search, references were screened and categorized using selection criteria outlined in the *Strategy for Conducting Literature Searches for 1-Bromopropane: Supplemental File for the TSCA Scope Document*, (EPA-HQ-OPPT-2016-0741-0048). Titles and abstracts were screened against the

criteria as a first step with the goal of identifying a smaller subset of the relevant data to move into the subsequent data extraction and data evaluation steps. Prior to full-text review, EPA/OPPT anticipates refinements to the search and screening strategies, as informed by an evaluation of the performance of the initial title/abstract screening and categorization process.

The categorization scheme (or tagging structure) used for data screening varies by scientific discipline (i.e., physical and chemical properties; environmental fate and transport; chemical use/conditions of use information; human and environmental exposures, including potentially exposed or susceptible subpopulations identified by virtue of greater exposure; human health hazard, including potentially exposed or susceptible subpopulations identified by virtue of greater susceptibility; and ecological hazard. However, within each data set, there are two broad categories or data tags: (1) o*n-topic* references or (2) *off-topic* references. *On-topic* references are those that may contain data and/or information relevant to the risk evaluation. O*ff-topic* references are those that do not appear to contain data or information relevant to the risk evaluation. The supplemental document, *Strategy for Conducting Literature Searches for 1-Bromopropane: Supplemental File for the TSCA Scope Document*, (EPA-HQ-OPPT-2016-0741-0048) discusses the inclusion and exclusion criteria that EPA/OPPT used to categorize references as *on-topic* or *off-topic*.

Additional data screening using sub-categories (or sub-tags) was also performed to facilitate further sorting of data/information – for example, identifying references by source type (e.g., published peer-reviewed journal article, government report); data type (e.g., primary data, review article); human health hazard (e.g., liver toxicity, cancer, reproductive toxicity); or chemical-specific and use-specific data or information. These sub-categories are described in the supplemental document, *Strategy for Conducting Literature Searches for 1-Bromopropane: Supplemental File for the TSCA Scope Document*, (EPA-HQ-OPPT-2016-0741-0048) and will be used to organize the different streams of data during the stages of data evaluation and data integration steps of systematic review.

Results of the initial search and categorization can be found in the *1-Bromopropane (CASRN 106-94-5) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0741-0047). This document provides a comprehensive list (bibliography) of the sources of data identified by the initial search and the initial categorization for *on-topic* and *off-topic* references. Because systematic review is an iterative process, EPA/OPPT expects that some references may move from the *on-topic* to the *off-topic* categories, and vice versa. Moreover, targeted supplemental searches may also be conducted to address specific needs for the analysis phase (e.g., to locate specific data needed for modeling); hence, additional *on-topic* references not initially identified in the initial search may be identified as the systematic review process proceeds.

## 1.4 Data Screening During Problem Formulation

EPA/OPPT is in the process of completing the full text screening of the on-topic references identified in the *1-Bromopropane (CASRN 106-94-5) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0741-0047). The screening process at the full-text level is described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018). Appendix F provides the inclusion and exclusion criteria applied at the full text screening. The eligibility criteria are guided by the analytical considerations in the revised conceptual models and analysis plans, as discussed in the problem formulation document. Thus, it is expected that the number of data/information sources entering evaluation is reduced to those that are relevant to address the technical approach and issues described in the analysis plan of this document.

Following the screening process, the quality of the included data/information sources will be assessed using the evaluation strategies that are described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018).

# 2 PROBLEM FORMULATION

As required by TSCA, the scope of the risk evaluation identifies the conditions of use, hazards, exposures and potentially exposed or susceptible subpopulations that the Administrator expects to consider. To communicate and visually convey the relationships between these components, EPA included in the scope document (Scope Document; EPA-HQ-OPPT-2016-0741-0049) a life cycle diagram and conceptual models that describe the actual or potential relationships between 1-BP and human and ecological receptors. During the problem formulation, EPA revised the conceptual models based on further data gathering and analysis as presented in this Problem Formulation document. An updated analysis plan is also included which identifies, to the extent feasible, the approaches and methods that EPA may use to assess exposures, effects (hazards) and risks under the conditions of use of 1-BP.

## 2.1 Physical and Chemical Properties

Physical-chemical properties influence the environmental behavior and the toxic properties of a chemical, thereby informing the potential conditions of use, exposure pathways and routes and hazards that EPA intends to consider. For scope development, EPA considered the measured or estimated physical-chemical properties set forth in Table 2-1 and EPA found no additional information during problem formulation that would change these values.

**Table 2-1. Physical and Chemical Properties of 1-BP**

| Property | Value [a] | References |
|---|---|---|
| Molecular formula | $C_3H_7Br$ | O'Neil (2013) |
| Molecular weight | 122.99 | O'Neil (2013) |
| Physical form | Colorless liquid; sweet hydrocarbon odor | O'Neil (2013) |
| Melting point | -110°C | O'Neil (2013) |
| Boiling point | 71°C at 760 mmHg | O'Neil (2013) |
| Density | 1.353 g/cm$^3$ at 20°C | O'Neil (2013) |
| Vapor pressure | 146.26 mmHg (19.5 kPa) at 20°C | Boublík et al. (1984) |
| Vapor density | 4.25 (relative to air) | Patty et al. (1963) |
| Water solubility | 2.450 g/L at 20°C | Yalkowsky et al. (2010) |

**Table 2-1. Physical and Chemical Properties of 1-BP**

| | | |
|---|---|---|
| Octanol/water partition coefficient (Log $K_{ow}$) | 2.10 | Hansch (1995) |
| Henry's Law constant | $7.3x10^{-3}$ atm-$m^3$/mole (estimated) | U.S. EPA (2012b) |
| Flash point | 22°C | O'Neil (2013) |
| Autoflammability | 490°C | NFPA (2010) |
| Viscosity | 5.241 mPa·s at 20°C | Haynes and Lide (2010) |
| Refractive index | 1.4341 | O'Neil (2013) |
| Dielectric constant | 8.09 at 20°C | Haynes and Lide (2010) |

[a] Measured unless otherwise noted.

## 2.2 Conditions of Use

TSCA § 3(4) defines the conditions of use as ''the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of.''

### 2.2.1 Data and Information Sources

In the scope documents, EPA identified, based on reasonably available information, the conditions of use for the subject chemicals. EPA searched a number of available data sources (e.g., *Use and Market Profile for 1-Bromopropane;* EPA-HQ-OPPT-2016-0741-0050). Based on this search, EPA published a preliminary list of information and sources related to chemical conditions of use (see *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: 1-Bromopropane*, EPA-HQ-OPPT-2016-0741-0003) prior to a February 2017 public meeting on scoping efforts for risk evaluation convened to solicit comment and input from the public. EPA also convened meetings with companies, industry groups, chemical users and other stakeholders to aid in identifying conditions of use and verifying conditions of use identified by EPA. The information and input received from the public and stakeholder meetings was incorporated into the problem formulation document to the extent appropriate. Thus, EPA believes the manufacture, processing, distribution, use and disposal activities identified in these documents constitute the intended, known, or reasonably foreseeable activities associated with the subject chemicals, based on reasonably available information.

### 2.2.2 Identification of Conditions of Use

To determine the current conditions of use of 1-BP and inversely, activities that do not qualify as conditions of use, EPA conducted extensive research and outreach. This included EPA's review of published literature and online databases including the most recent data available from EPA's Chemical Data Reporting program (CDR) and Safety Data Sheets (SDSs). EPA also conducted online research by reviewing company websites of potential manufacturers, importers, distributors, retailers, or other users of 1-BP and queried government and commercial trade databases. EPA also received comments on the Scope of the Risk Evaluation for 1-BP (Scope Document; EPA-HQ-OPPT-2016-0741-0049) that were

used to determine the conditions of use. Some of the comments received were more relevant to the risk evaluation process. In addition, EPA convened meetings with companies, industry groups, chemical users, states, environmental groups, and other stakeholders to aid in identifying conditions of use and verifying conditions of use identified by EPA. Those meetings included a February 14, 2017 public meeting with such entities and an October 25, 2017 site visit to CRC Industries (EPA-HQ-OPPT-2016-0741).

EPA has removed from the risk evaluation any activities that EPA has concluded do not constitute conditions of use – for example, because EPA has insufficient information to find certain activities are circumstances under which the chemical is actually "intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of." EPA has also identified any conditions of use that EPA does not expect to include in the risk evaluation. As explained in the final rule for Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act, TSCA section 6(b)(4)(D) requires EPA to identify "the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations the Administrator expects to consider in a risk evaluation," suggesting that EPA may exclude certain activities that EPA has determined to be conditions of use on a case-by-case basis (82 FR 33736, 33729; July 20, 2017). For example, EPA may exclude conditions of use that the Agency has sufficient basis to conclude would present only de minimis exposures or otherwise insignificant risks (such as use in a closed system that effectively precludes exposure or use as an intermediate).

The activities that EPA no longer believes are conditions of use or that were otherwise excluded during problem formulation are described in Section 2.2.2.1. The conditions of use included in the scope of the risk evaluation are summarized in Section 2.2.2.2.

#### 2.2.2.1 Categories and Subcategories Determined Not to be Conditions of Use During Problem Formulation

EPA has conducted public outreach and literature searches to collect information about 1-BP's conditions of use and has reviewed reasonably available information obtained or possessed by EPA concerning activities associated with 1-BP. As a result of that analysis during problem formulation, EPA determined there is insufficient information to support a finding that certain activities which were listed as conditions of use in the Scope Document (Scope Document; EPA-HQ-OPPT-2016-0741-0049) for 1-BP actually constitute "circumstances…under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of." Consequently, EPA intends to exclude these activities not considered conditions of use from the scope of the evaluation. These activities are shown in Table 2-2, and consist of agricultural non-pesticidal industrial/commercial/consumer use and the consumer use of: adhesives (except as an adhesive accelerant for arts and crafts), engine degreasing, and brake cleaning.

Based on information available to EPA, EPA determined that 1-BP is not used in agricultural products (non-pesticidal), only in the processing of such products.

A review of the use of 1-BP as a solvent in adhesives, engine degreasers, and in brake cleaners showed that these uses of 1-BP are not consumer uses, except as an adhesive accelerant in arts and crafts. In all other uses of 1-BP as an adhesive, 1-BP-containing adhesives are sold through wholesale channels for commercial and industrial uses, and usually in amounts larger than consumers could use. 1-BP has never been advertised (or used) as a consumer brake cleaner or engine degreaser. Instead, 1-BP has been advertised and used as a specialized general duty industrial or commercial degreaser. 1-BP is sometimes used by industrial and commercial users to degrease engines when these users want a nonflammable

degreaser, or are concerned about disposal of chlorinated solvents in the waste. In practice, this is only a consideration for industrial and commercial users, and not for consumers. Some industrial and commercial users use 1-BP as a general degreaser because chlorinated solvents are listed hazardous wastes under RCRA, whereas 1-BP is not, and therefore waste containing 1-BP may not be hazardous depending on the characteristics of the overall waste stream.

Also, consumers will avoid the use of 1-BP as an engine degreaser or brake cleaner because 1-BP is expensive. In general, heavy duty degreasers containing 1-BP are twice the cost of other heavy duty degreasers and five times the cost of other available consumer brake cleaners.

**Table 2-2. Categories and Subcategories Determined Not to be Conditions of Use During Problem Formulation**

| Life Cycle Stage | Category | Subcategory | References |
|---|---|---|---|
| Industrial/Commercial/ Consumer Use | Agricultural products (non pesticidal) | Miscellaneous agricultural products | U.S. EPA (2016a) |
| Consumer Use | Adhesives and Sealants | Adhesive chemicals – spray adhesive for foam cushion manufacturing and other uses | U.S. EPA (2016b); Public Comment, EPA-HQ-OPPT-2016-0741-0016 |
| | Other Uses | Automotive care products – engine degreaser, brake cleaner | Use Document, EPA-HQ-OPPT-2016-0741-0003 |

#### 2.2.2.2 Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation

EPA has conducted public outreach and literature searches to collect information about 1-BP's conditions of use and has reviewed reasonably available information obtained or possessed by EPA concerning activities associated with 1-BP. Based on this research and outreach, other than the category and subcategory described above in Section 2.2.2.1. EPA does not have reason to believe that any conditions of use identified in the 1-BP scope should be excluded from risk evaluation. Therefore, all of the remaining conditions of use for 1-BP will be included in the risk evaluation.

EPA currently believes that few dry cleaners use 1-BP as a dry cleaning solvent. In the 2016 Draft Risk Assessment (U.S. EPA, 2016b), EPA estimated that about 267 (1.1% of all) dry cleaning establishments used 1-BP. Recent (March 2017) public comments (EPA-HQ-OPPT-2016-0741-0016) on the 1-BP Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal of 1-BP (EPA-HQ-OPPT-2016-0741-0003) suggest than only 23 machines used 1-BP in 2016, only about 30,000 pounds of 1-BP would be used in dry cleaning machines in 2017, and that almost no dry cleaning machines would use 1-BP by 2020. However, the use of 1-BP in the dry cleaning industry remains a reasonably foreseen condition of use. EPA is currently evaluating tetrachloroethylene (perc) under TSCA, and if EPA were to restrict the use of perc in dry cleaning, many dry cleaners might use 1-BP in their machines absent regulatory restrictions from doing so. For many dry cleaners, it is less expensive to convert perc machines to use 1-BP than it is to purchase new machines that use alternative solvents. This is especially true because many dry cleaners are small, capital-constrained, family-owned and operated businesses. Most use of 1-BP in dry cleaning has been from converted machines; very few machines designed to use 1-BP as a solvent have been sold. In addition, based on monitoring data and

the low ACGIH TLV-TWA, EPA expects that the use of 1-BP in dry cleaning results in unreasonable risks to workers, as presented in the 2016 Draft Risk Assessment (U.S. EPA, 2016b).

Table 2-3 summarizes each life cycle stage and the corresponding categories and subcategories of conditions of use for 1-BP that EPA expects to consider in the risk evaluation. Using the 2016 CDR, EPA identified industrial processing or use activities, industrial function categories and commercial and consumer use product categories. EPA identified the subcategories by supplementing CDR data with other published literature and information obtained through stakeholder consultations. For risk evaluations, EPA intends to consider each life cycle stage (and corresponding use categories and subcategories) and assess relevant potential sources of release and human exposure associated with that life cycle stage. In addition, activities related to distribution (e.g., loading and unloading) will be considered throughout the life cycle rather than using a single distribution scenario.

Beyond the uses identified in the Scope Document (Scope Document; EPA-HQ-OPPT-2016-0741-0049), EPA has received no additional information identifying confirming additional current conditions of use for 1-BP from public comment and stakeholder meetings.

**Table 2-3. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation**

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| Manufacture | Domestic manufacture | Domestic manufacture | U.S. EPA (2016a) |
| | Import | Import | U.S. EPA (2016a) |
| Processing | Processing as a reactant | Intermediate in all other basic inorganic chemical manufacturing, all other basic organic chemical manufacturing, and pesticide, fertilizer and other agricultural chemical manufacturing | U.S. EPA (2016a) |

**Table 2-3. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation**

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| Processing | Processing - incorporating into formulation, mixture or reaction product | Solvents for cleaning or degreasing in manufacturing of:<br>- all other chemical product and preparation<br>- computer and electronic product<br>- electrical equipment, appliance and component<br>- soap, cleaning compound and toilet preparation<br>- services | U.S. EPA (2016a) |
| | Processing - incorporating into articles | Solvents (which become part of product formulation or mixture) in construction | U.S. EPA (2016a); Public Comment, EPA-HQ-OPPT-2016-0741-0017 |
| | Repackaging | Solvent for cleaning or degreasing in all other basic organic chemical manufacturing | U.S. EPA (2016a) |
| | Recycling | Recycling | U.S. EPA (2016a); Use Document, EPA-HQ-OPPT-2016-0741-0003 |
| Distribution in commerce | Distribution | Distribution | U.S. EPA (2016a); Use Document, EPA-HQ-OPPT-2016-0741-0003 |

**Table 2-3. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation**

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| Industrial/ commercial/ use | Solvent (for cleaning or degreasing) | Batch vapor degreaser (e.g., open-top, closed-loop) | U.S. EPA (2016b); Public Comment, EPA-HQ-OPPT-2016-0741-0014; Public Comment, EPA-HQ-OPPT-2016-0741-0015; Public Comment, EPA-HQ-OPPT-2016-0741-0016 |
| | | In-line vapor degreaser (e.g., conveyorized, web cleaner) | Kanegsberg and Kanegsberg (2011); Public Comment, EPA-HQ-OPPT-2016-0741-0014; Public Comment, EPA-HQ-OPPT-2016-0741-0016 |
| | | Cold cleaner | U.S. EPA (2016b); Public Comment, EPA-HQ-OPPT-2016-0741-0016 |
| | | Aerosol spray degreaser/cleaner | U.S. EPA (2016b); Public Comment, EPA-HQ-OPPT-2016-0741-0016; Public Comment, EPA-HQ-OPPT-2016-0741-0018; Public Comment, EPA-HQ-OPPT-2016-0741-0020 |
| | Adhesives and sealants | Adhesive chemicals - spray adhesive for foam cushion manufacturing and other uses | U.S. EPA (2016b); Public Comment, EPA-HQ-OPPT-2016-0741-0016 |

**Table 2-3. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation**

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| Industrial/ commercial/use (continued) | Cleaning and furniture care products | Dry cleaning solvent | U.S. EPA (2016b); Public Comment, EPA-HQ-OPPT-2016-0741-0005; Public Comment, EPA-HQ-OPPT-2016-0741-0016 |
| | | Spot cleaner, stain remover | U.S. EPA (2016b); Public Comment, EPA-HQ-OPPT-2016-0741-0016; Public Comment, EPA-HQ-OPPT-2016-0741-0022 |
| | | Liquid cleaner (e.g., coin and scissor cleaner) | Use Document, EPA-HQ-OPPT-2016-0741-0003 |
| | | Liquid spray/aerosol cleaner | Use Document, EPA-HQ-OPPT-2016-0741-0003 |
| | Other uses | Arts, crafts and hobby materials - adhesive accelerant | U.S. EPA (2016b) |
| | | Automotive care products - engine degreaser, brake cleaner | Use Document, EPA-HQ-OPPT-2016-0741-0003 |
| | | Anti-adhesive agents - mold cleaning and release product | U.S. EPA (2016b); Public Comment, EPA-HQ-OPPT-2016-0741-0014; Public Comment, EPA-HQ-OPPT-2016-0741-0015; Public Comment, EPA-HQ-OPPT-2016-0741-0016; Public Comment, EPA-HQ-OPPT-2016-0741-0018 |
| | | Building/construction materials not covered elsewhere - insulation | Use Document, EPA-HQ-OPPT-2016-0741-0003; Public Comment, EPA-HQ-OPPT-2016-0741-0027 |

**Table 2-3. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation**

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| Industrial/ commercial/use (continued) | Other uses | Electronic and electronic products and metal products | U.S. EPA (2016a); Public Comment, EPA-HQ-OPPT-2016-0741-0016; Public Comment, EPA-HQ-OPPT-2016-0741-0024 |
| | | Functional fluids (closed systems) - refrigerant | Use Document, EPA-HQ-OPPT-2016-0741-0003 |
| | | Functional fluids (open system) - cutting oils | Use Document, EPA-HQ-OPPT-2016-0741-0003; Public Comment, EPA-HQ-OPPT-2016-0741-0014 |
| | | Other - asphalt extraction | Use Document, EPA-HQ-OPPT-2016-0741-0003; Public Comment, EPA-HQ-OPPT-2016-0741-0016 |
| | | Temperature Indicator – Laboratory chemicals | Use Document, EPA-HQ-OPPT-2016-0741-0003 |
| | | Temperature Indicator – Coatings | Use Document, EPA-HQ-OPPT-2016-0741-0003; Public Comment, EPA-HQ-OPPT-2016-0741-0014; Public Comment, EPA-HQ-OPPT-2016-0741-0016 |
| Consumer uses | Solvent (for cleaning or degreasing) | Aerosol spray degreaser/cleaner | U.S. EPA (2016b); |
| | Cleaning and furniture care products | Spot cleaner, stain remover | U.S. EPA (2016b); Public Comment, EPA-HQ-OPPT-2016-0741-0022 |
| | | Liquid cleaner (e.g., coin and scissor cleaner) | Use Document, EPA-HQ-OPPT-2016-0741-0003 |
| | | Liquid spray/aerosol cleaner | Use Document, EPA-HQ-OPPT-2016-0741-0003 |
| | Other uses | Arts, crafts and hobby materials - adhesive accelerant | U.S. EPA (2016b) |

**Table 2-3. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation**

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| | | Automotive care products – refrigerant flush | U.S. EPA (2016b) |
| | | Anti-adhesive agents - mold cleaning and release product | U.S. EPA (2016b) |
| | | Building/construction materials not covered elsewhere - insulation | Use Document, EPA-HQ-OPPT-2016-0741-0003; Public Comment, EPA-HQ-OPPT-2016-0741-0027 |
| Disposal (Manufacturing, Processing, Use) | Disposal | Municipal waste incinerator<br>Off-site transfer | 2016 TRI Data (updated October 2017) U.S. EPA (2017c) |
| | | Municipal waste incinerator | |
| | | Off-site waste transfer | |

[a]These categories of conditions of use appear in the Life Cycle Diagram, reflect CDR codes, and broadly represent conditions of use of 1-BP in industrial and/or commercial settings.
[b]These subcategories reflect more specific uses of 1-BP.

Although EPA indicated in the 1-BP Scope Document (Scope Document; EPA-HQ-OPPT-2016-0741-0049) that EPA did not expect to evaluate the uses assessed in the 2016 Draft Risk Assessment (U.S. EPA, 2016b) in the 1-BP risk evaluation, EPA has decided to evaluate these conditions of use in the risk evaluation as described in this problem formulation. EPA is including these conditions of use so that they are part of EPA's determination of whether 1-BP presents an unreasonable risk "under the conditions of use," TSCA 6(b)(4)(A). EPA has concluded that the Agency's assessment of the potential risks from this widely used chemical will be more robust if the potential risks from these conditions of use are evaluated by applying standards and guidance under amended TSCA. In particular, this includes ensuring the evaluation is consistent with the scientific standards in Section 26 of TSCA, the Procedures for Chemical Risk Evaluation under the Amended Toxic Substances Control Act (40 CFR Part 702) and EPA's supplemental document, *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018). EPA also expects to consider other available hazard and exposure data to ensure that all reasonably available information is taken into consideration.

#### 2.2.2.3 Overview of Conditions of Use and Life Cycle Diagram

The life cycle diagram provided in Figure 2-1 depicts the conditions of use that are considered within the scope of the risk evaluation during various life cycle stages including manufacturing, processing, distribution, use (industrial, commercial, and consumer; when distinguishable), and disposal. Additions or changes to the conditions of use based on additional information gathered or analyzed during problem

formulation were described in Sections 2.2.2.1 and 2.2.2.2. The activities that EPA determined are out of scope during problem formulation are not included in the life cycle diagram. The information is grouped according to Chemical Data Reporting (CDR) processing codes and use categories (including functional use codes for industrial uses and product categories for industrial, commercial and consumer uses), in combination with other data sources (e.g., published literature and consultation with stakeholders), to provide an overview of conditions of use. EPA notes that some subcategories of use may be grouped under multiple CDR categories.

Use categories include the following: "industrial use" means use at a site at which one or more chemicals or mixtures are manufactured (including imported) or processed. "Commercial use" means the use of a chemical or a mixture containing a chemical (including as part of an article) in a commercial enterprise providing saleable goods or services. "Consumer use" means the use of a chemical or a mixture containing a chemical (including as part of an article, such as furniture or clothing) when sold to or made available to consumers for their use (U.S. EPA, 2016a).

Based on market information from other sources, EPA expects degreasing and spray adhesive to be the primary uses of 1-BP; however, the exact use volumes associated with these categories are claimed CBI in the 2016 CDR (U.S. EPA, 2016a). EPA will evaluate activities resulting in exposures associated with distribution in commerce (e.g. loading, unloading) throughout the various lifecycle stages and conditions of use (e.g. manufacturing, processing, industrial use, consumer use, disposal) rather as a single distribution scenario. EPA expects that some commercial products containing 1-BP are also available for purchase by consumers, such that many products are used in both commercial and consumer applications/scenarios.

To understand conditions of use relative to one another and associated potential exposures under those conditions of use, the life cycle diagram includes the production volume associated with each stage of the life cycle, as reported in the 2016 CDR reporting (U.S. EPA, 2016a), when the volume was not claimed confidential business information (CBI). The 2016 CDR reporting data for 1-BP are provided in Table 2-4 for 1-BP from EPA's CDR database (U.S. EPA, 2016a). This information has not changed from that provided in the Scope Document (EPA-HQ-OPPT-2016-0741-0049).

**Table 2-4. Production Volume of 1-BP in CDR Reporting Period (2012 to 2015) [a]**

| Reporting Year | 2012 | 2013 | 2014 | 2015 |
|---|---|---|---|---|
| Total Aggregate Production Volume (lbs) | 18,800,000 | 24,000,000 | 18,500,000 | 25,900,000 |

[a] The CDR data for the 2016 reporting period is available via ChemView (https://java.epa.gov/chemview) (U.S. EPA, 2016a). Because of an ongoing CBI substantiation process required by amended TSCA, the CDR data available in the Scope Document (EPA-HQ-OPPT-2016-0741-0049) is more specific than currently in ChemView.

According to data collected in EPA's 2016 Chemical Data Reporting (CDR) Rule, 25.9 million pounds of 1-BP were produced or imported in the United States in 2015 (U.S. EPA, 2016a). Data reported indicate that there are two manufacturers and six importers of 1-BP in the United States. Additional companies manufacturing or importing 1-BP are claimed as CBI.

Total production volume (manufacture plus import) of 1-BP has increased from 2012 to 2015, as can be seen in Table 2-4 (U.S. EPA, 2016a). 1-BP's use has increased because it has been an alternative to ozone-depleting substances and chlorinated solvents. Import volumes for 1-BP reported to the 2016

CDR are between 10 million and 25 million pounds per year (U.S. EPA, 2016a). In past years, import data from 1-BP were claimed as CBI, but import data from other sources indicate that import volumes of brominated derivatives of acyclic hydrocarbons (which includes 1-BP as well as other chemicals) were 10.9 million pounds in 2007, which dropped to 10.3 million pounds in 2011 (NTP, 2013).

Descriptions of the industrial, commercial and consumer use categories identified from the 2016 CDR and included in the life cycle diagram are summarized below (U.S. EPA, 2016a). The descriptions provide a brief overview of the use category; Appendix B contains more detailed descriptions (e.g., process descriptions, worker activities, process flow diagrams, equipment illustrations) for each manufacture, processing, distribution, use and disposal category. The descriptions provided below are primarily based on the corresponding industrial function category and/or commercial and consumer product category descriptions from the 2016 CDR and can be found in EPA's Instructions for Reporting 2016 TSCA Chemical Data Reporting (U.S. EPA, 2016a).

The "***Solvents for Cleaning and Degreasing***" category encompasses chemical substances used to dissolve oils, greases and similar materials from a variety of substrates, including metal surfaces, glassware and textile. This category includes the use of 1-BP in vapor degreasing, cold cleaning and in industrial and commercial aerosol degreasing products.

The "***Adhesives and Sealants***" category encompasses chemical substances contained in adhesive and sealant products used to fasten other materials together. EPA anticipates that a subcategory within the Adhesives and Sealants category is the use of 1-BP as a solvent in spray adhesive for foam cushion manufacturing. This category also covers uses of 1-BP in other adhesive products.

The "***Cleaning and Furniture Care Products***" category encompasses chemical substances contained in products that are used to remove dirt, grease, stains and foreign matter from furniture and furnishings, or to cleanse, sanitize, bleach, scour, polish, protect or improve the appearance of surfaces. This category includes a wide variety of 1-BP uses, including, but not limited to, the use of 1-BP as dry cleaning solvent, in spot cleaning formulations and in aerosol and non-aerosol type cleaners.

Figure 2-1 depicts the life cycle diagram of 1-BP from manufacture to the point of disposal. Activities related to distribution (e.g., loading, unloading) will be considered throughout the 1-BP life cycle, rather than using a single distribution scenario.

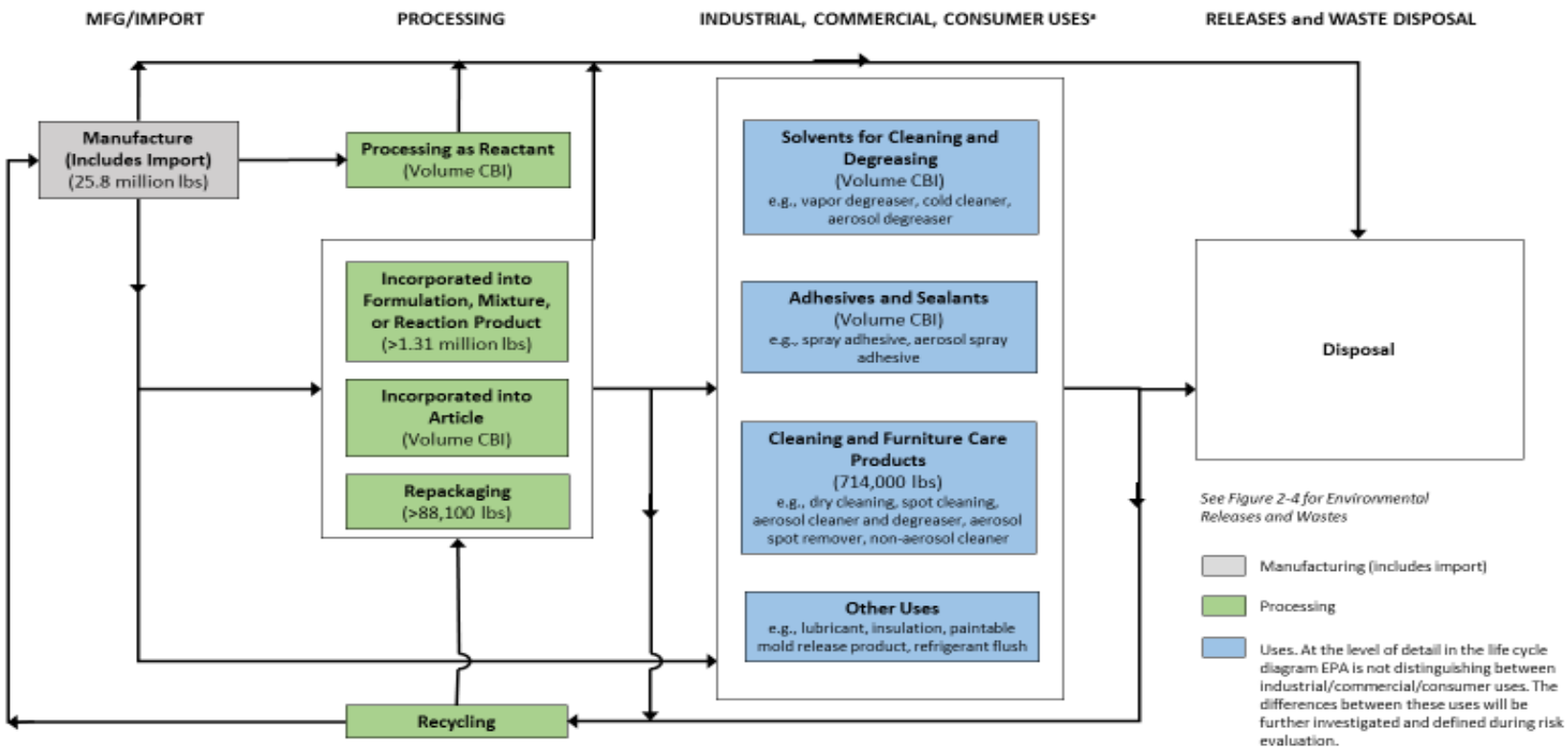


**Figure 2-1. 1-BP Life Cycle Diagram**

The life cycle diagram depicts the conditions of use that are within the scope of the risk evaluation during various life cycle stages including manufacturing, processing, use (industrial, commercial, consumer), distribution and disposal. The production volumes shown are for reporting year 2015 from the 2016 CDR reporting period (U.S. EPA, 2016a). EPA will evaluate activities resulting in exposures associated with distribution in commerce (e.g. loading, unloading) throughout the various lifecycle stages and conditions of use (e.g. manufacturing, processing, industrial use, consumer use, disposal) rather as a single distribution scenario.

[a] See Table 2-3 for additional uses not mentioned specifically in this diagram.

## 2.3 Exposures

For TSCA exposure assessments, EPA expects to evaluate exposures and releases to the environment resulting from the conditions of use applicable to 1-BP. Post-release pathways and routes will be described to characterize the relationship or connection between the conditions of use for 1-BP and the exposure to human receptors, including potentially exposed or susceptible subpopulations and ecological receptors. EPA will take into account, where relevant, the duration, intensity (concentration), frequency and number of exposures in characterizing exposures to 1-BP.

### 2.3.1 Fate and Transport

Environmental fate includes both transport and transformation processes. Environmental transport is the movement of the chemical within and between environmental media. Transformation occurs through the degradation or reaction of the chemical with other species in the environment. Hence, knowledge of the environmental fate of the chemical informs the determination of the specific exposure pathways and potential human and environmental receptors EPA expects to consider in the risk evaluation. Table 2-5 provides environmental fate data that EPA identified and considered in developing the scope for 1-BP. This information has not changed from that provided in the Scope Document (EPA-HQ-OPPT-2016-0741-0049).

Fate data including volatilization during wastewater treatment, volatilization from lakes and rivers, biodegradation rates, and organic carbon:water partition coefficient (log $K_{OC}$) were used when considering changes to the conceptual models. Model results and basic principles were used to support the fate data used in problem formulation while the literature review is currently underway through the systematic review process.

EPI Suite™ (U.S. EPA, 2012b) modules were used to predict volatilization of 1-BP from wastewater treatment plants, lakes, and rivers and to confirm the data showing moderate to rapid biodegradation. The EPI Suite™ module that estimates chemical removal in sewage treatment plants ("STP" module) was run using default settings to evaluate the potential for 1-BP to volatilize to air or adsorb to sludge during wastewater treatment. The STP module estimates that 73% of 1-BP in wastewater will be removed by volatilization while 1% of 1-BP will be removed by adsorption.

The EPI Suite™ module that estimates volatilization from lakes and rivers ("Volatilization" module) was run using default settings to evaluate the volatilization half-life of 1-BP in surface water. The parameters required for volatilization (evaporation) rate of an organic chemical from the water body are water depth, wind and current velocity of the river or lake. The volatilization module estimates that the half-life of 1-BP in a model river will be 1.2 hours and the half-life in a model lake will be 4.4 days.

The EPI Suite™ module that predicts biodegradation rates ("BIOWIN" module) was run using default settings to estimate biodegradation rates of 1-BP under aerobic conditions. Three of the models built into the BIOWIN module (BIOWIN 2, 5 and 6) estimate that 1-BP will not rapidly biodegrade in aerobic environments, while a fourth (BIOWIN 1) estimates that 1-BP will rapidly biodegrade in aerobic environments. These results support the biodegradation data presented in the 1-BP Scope Document (EPA-HQ-OPPT-2016-0741-0049), which demonstrate a range of biodegradation rates under aerobic conditions. The model that estimates anaerobic biodegradation (BIOWIN 7) predicts that 1-BP will rapidly biodegrade under anaerobic conditions. Further, previous assessments of 1-BP found that biodegradation occurred over a range of rates from slow to rapid [Toxicological Profile for 1-Bromopropane; (ATSDR, 2017)].

The log $K_{OC}$ reported in the 1-BP scope document was predicted using EPI Suite™. That value (1.6) is supported by the basic principles of environmental chemistry which states that the $K_{OC}$ is typically within one order of magnitude (one log unit) of the octanol:water partition coefficient ($K_{OW}$). Indeed, the log $K_{OW}$ reported for 1-BP in the Scope Document (EPA-HQ-OPPT-2016-0741-0049) was 2.1, which is within the expected range. Further, the $K_{OC}$ could be approximately one order of magnitude larger than predicted by EPI Suite™ before sorption would be expected to significantly impact the mobility of 1-BP in groundwater. No measured $K_{OC}$ values were found.

**Table 2-5. Environmental Fate Characteristics of 1-BP**

| Property or Endpoint | Value [a] | References |
|---|---|---|
| Direct photodegradation | Not expected to undergo direct photolysis | U.S. EPA (2016b) |
| Indirect photodegradation | 9-12 days (estimated for atmospheric degradation) | U.S. EPA (2016b) |
| Hydrolysis half-life | 26 days | U.S. EPA (2016b) |
| Biodegradation | 70% in 28 days (OECD 301C)<br>19.2% in 28 days (OECD 301D) | U.S. EPA (2016b) |
| Bioconcentration factor (BCF) | 11 (estimated) | U.S. EPA (2012b) |
| Bioaccumulation factor (BAF) | 12 (estimated) | U.S. EPA (2016b) |
| Organic carbon:water partition coefficient (Log $K_{oc}$) | 1.6 (estimated) | U.S. EPA (2016b) |

[a] Measured unless otherwise noted

1-BP is a water soluble, volatile liquid and mobile in soil. Adsorption to soils is not expected; therefore, 1-BP can migrate through soil to ground water. 1-BP is degraded by sunlight and reactants when released to the atmosphere with a half-life of 9-12 days. Based on this estimated half-life in air, long-range transport via the atmosphere is possible. Volatilization and microbial degradation influence the fate of 1-BP when released to water, sediment or soil. Biotic and abiotic degradation rates ranging from days to months have been reported.

Biotic and abiotic degradation studies have not shown this substance to be persistent (overall environmental half-life of <2 months). No measured bioconcentration studies for 1-BP are available. An estimated BCF of 11 and an estimated BAF of 12 suggest that bioconcentration and bioaccumulation potential in aquatic organisms is low (BCF and BAF <1,000).

### 2.3.2 Releases to the Environment

Releases to the environment from conditions of use (e.g., industrial and commercial processes, commercial or consumer uses resulting in down-the-drain releases) are one component of potential exposure and may be derived from reported data that are obtained through direct measurement, calculations based on empirical data and/or assumptions and models.

1-BP is expected to be released to air during manufacturing, processing, distribution and use due to its high volatility (vapor pressure of 146.26 mmHg at 20°C). 1-BP is also expected to be released to other environmental media through waste disposal (e.g., disposal of spent solvent, rags, wipe materials, and transport containers).

A source of information that EPA expects to consider in evaluating exposure are data reported under the Toxics Release Inventory (TRI) program. Under the Emergency Planning and Community Right-to-Know Act (EPCRA) Section 313 rule, 1-BP is a TRI-reportable chemical beginning with the 2016 calendar year with the first reporting forms from facilities were submitted on July 1, 2017 and on each following year. During problem formulation, EPA analyzed the TRI data reported for 2016 and examined the reported treatment and disposal methods employed to determine the level of confidence that a release would result from certain types of disposal to land (e.g., Resource Conservation and Recovery Act or RCRA Subtitle C hazardous waste landfills, Subtitle D municipal landfills, and Class I underground injection wells) and incineration.

#### 2.3.2.1 Disposal of Wastes containing 1-BP

Industrial wastewater containing 1-BP may be subject to state or local regulations or permit limits. Solid wastes containing 1-BP may be regulated as a hazardous waste under the RCRA waste code D001 (ignitable liquids, 40 CFR 261.21). These wastes would be either incinerated in a hazardous waste incinerator or disposed to a hazardous waste landfill. Consumer wastes containing 1-BP may be disposed with general municipal wastes, which may be incinerated or landfilled. Depending on the incinerator destruction efficiency, the incineration of 1-BP may result in subsequent releases to air. Landfilling wastes containing 1-BP may result in subsequent fugitive emissions to air or migration to groundwater. 1-BP migration to groundwater from RCRA Subtitle C landfills or RCRA Subtitle D municipal landfills regulated by the state / local jurisdictions to groundwater will likely be mitigated by landfill design (double liner, leachate capture for RCRA Subtitle C landfills and single liner for RCRA Subtitle D municipal landfills) and requirements to adsorb liquids onto solid adsorbent and containerize prior to disposal.

***2016 TRI Data***

A key source of information that EPA expects to consider in the risk evaluation in evaluating releases to the environment are data reported under the TRI program. EPA published a final rule on November 23, 2015 (80 FR 72906) to add 1-BP to the TRI chemical list, as 1-BP meets the Emergency Planning and Community Right-to-Know Act (EPCRA) Section 313(d)(2)(B) statutory listing criteria. Under this rule, 1-BP is reportable beginning with the 2016 calendar year with the first reporting forms from facilities submitted on July 1, 2017.

Table 2-6 summarizes TRI release data for 1-BP. For the 2016 reporting year, 55 out of an estimated 140 facilities filed TRI reporting forms containing release and waste management data for 1-BP. The estimated number of facilities expected to report was derived from the Economic Analysis Report of 1-BP (https://www.regulations.gov/document?D=EPA-HQ-TRI-2015-0011-0011).[2] The difference in estimated versus actual reporting facilities could be due to several factors such as, 1) facilities could be moving away from using 1-BP; 2) some facilities may not yet be aware of the reporting requirements since this is the first year of reporting; 3) facilities could be below the threshold for reporting. Facilities

[2] Note: This estimated values of 140 facilities was derived from the Economic Analysis Report of 1-BP (https://www.regulations.gov/document?D=EPA-HQ-TRI-2015-0011-0011. Potential reporting for facilities was compiled using available US facility data and other resources such as NAICS codes, Japanese PRTR data on 1-BP, and from proxy chemical models.

are required to report if they manufacture (including import) or process more than 25,000 pounds of 1-BP, or if they otherwise use more than 10,000 pounds of 1-BP.

**Table 2-6. Summary of 2016 TRI Releases for 1-BP (CASRN 106-94-5)**

| Waste Type | Conceptual Model Release Category | TRI Category | Volume from TRI (lbs) | Number of Reporting Sites from TRI | % of Total Production-Related Waste Managed |
|---|---|---|---|---|---|
| Wastewater or Liquid Wastes | Industrial Pre-Treatment (indirect discharge) | POTW | 0 | 0 | 0% |
| | Industrial WWT (indirect discharge) | Off-site WWT (non-POTW) | 0 | 0 | 0% |
| | Industrial WWT (direct discharge) | Water | 5 | 1 | <0.001% |
| | Underground Injection | Class I Underground Injection | 10 | 1 | <0.001% |
| Solid Wastes and Liquid Wastes | Hazardous and Municipal Waste Landfills | RCRA Subtitle C Landfills | 57,617 | 1 | 3.7% |
| | | Other Landfills | 90,273 | 3 | 5.8% |
| | Waste Treatment and Management Methods | Off-site Incineration | 61,301 | 10 | 3.9% |
| | | Energy Recovery | 325,752 | 15 | 20.9% |
| | | Other Treatment and Management Methods | 20,892 | 5 | 1.3% |
| | | Transfer to Storage-Only Facility | 3,307 | 1 | <0.001% |
| | | Transfer to Waste Broker | 750 | 1 | <0.001% |
| | | Recycling | 322,097 | 11 | 20.6% |
| | | On-site Waste Treatment Methods[a] | 53,550 | 2 | 3.4% |
| Emissions to Air | Emissions to Air | Fugitive Air | 394,469 | 43 | 25.3% |
| | | Stack Air | 232,191 | 26 | 14.9% |
| Total Production Related Waste Managed | | | 1,562,213 | 55 | |
| Total One-Time Release Waste | | | 0 | 0 | 0% |
| Total Waste Managed | | | 1,562,213 | 55 | |

[a] Because sites such as treatment, storage, and disposal facilities (TSDFs) are required to report to TRI if they meet reporting thresholds, the total volumes for these categories may include volumes that were reported as transferred off-site for waste treatment purposes by other facilities, such as for off-site incineration.

***Releases to Air***

Table 2-6 shows air as a primary medium of environmental release. These releases include both fugitive air emissions and point source (stack) air emissions. Fugitive air emissions (totaling 394,469 pounds from 2016 TRI data) are emissions that do not occur through a confined air stream, which may include equipment leaks, releases from building ventilation systems, and evaporative losses from surface impoundments and spills. Point source (stack) air emissions (totaling 232,191 pounds from TRI 2016 data) are releases to air that occur through confined air streams, such as stacks, ducts or pipes.

***Releases to Water***

In the 2016 TRI, only 1 facility out of 55 reported releases to water. This facility reported 5 lbs of direct surface water discharge; assuming the release occurred over a single day, the surface water concentration in reported receiving waters is well below the COC based on EPA's preliminary calculations. No facility reported any amounts of 1-BP sent to Publicly Owned Treatment Works (POTWs).

***Releases to Land***

Table 2-6 shows TRI reports approximately 58,000 pounds of disposal to a single RCRA Subtitle C landfill. EPA will not further analyze releases to hazardous waste landfills because these types of landfill mitigate exposure to the wastes. TRI also reports approximately 90,000 pounds of 1-BP transferred to other off-site landfills. Further review of TRI data indicated that all reported transfers "other off-site landfills" were to facilities permitted to manage RCRA regulated waste.

***Releases of Solid and Liquid Wastes to Incineration/Energy Recovery***

***On-site***

On-site waste treatment (including incineration) and energy recovery total 275,917 lbs, which is approximately 18% of the total production waste managed. Air emissions resulting from these operations are already included in the TRI reports and will be used in the analysis of air releases.

***Off-site***

In Table 2-6, off-site transfers for incineration and energy recovery total 164,686 lbs, almost 10% of the total production waste managed.

***Recycling***

Table 2-6 shows 1-BP recycling amounts totaling 322,097 lbs in 2016, approximately 21 percent of the total production waste managed. This estimate includes all quantities of 1-BP recycled on-site and off-site, as reported in Section 8 of the Form R. EPA expects recycling to involve recovery of waste solvents containing 1-BP for re-use (e.g., using distillation, evaporation). Currently, EPA is not aware of the presence of 1-BP in recycled articles.

### 2.3.3 Presence in the Environment and Biota

Monitoring studies or a collection of relevant and reliable monitoring studies provide(s) information that can be used in an exposure assessment. Monitoring studies that measure environmental concentrations or concentrations of chemical substances in biota provide evidence of exposure.

Environmental monitoring data were not identified in the 2016 Draft Risk Assessment (U.S. EPA, 2016b); however, any environmental monitoring data that may result from the updated literature search will be considered. Biomonitoring data were identified in the 2016 Draft Risk Assessment (U.S. EPA,

2016b). Several human and laboratory animal studies have investigated the utility of both urine and serum bromide ion levels, as well as urinary metabolites, as biomarkers of human exposure to 1-BP.

### 2.3.4 Environmental Exposures

The manufacturing, processing, use and disposal of 1-BP can result in releases to the environment. In this section, EPA presents exposures to aquatic and terrestrial organisms. The predominance of these exposures will be via the air pathway as releases to water are very low as described in Section 2.3.2.

***Aquatic Environmental Exposures***

EPA used the reported releases from EPA's Toxics Release Inventory (TRI) to predict surface water concentrations near reported facilities for this Problem Formulation. To examine whether near-facility surface water concentrations could approach 1-BP's aquatic concentrations of concern, EPA employed a first-tier approach, using readily-available modeling tools and data, as well as conservative assumptions. EPA's Exposure and Fate Assessment Screening Tool (E-FAST 2014) was used to estimate site-specific surface water concentrations based on estimated loadings of 1-BP into receiving water bodies as reported to TRI. E-FAST 2014 incorporates stream dilution using stream flow information contained within the model. E-FAST also incorporates wastewater treatment removal efficiencies. Wastewater treatment removal was assumed to be 0% for this exercise, as reported loadings/releases are assumed to account for any treatment. As days of release and operation are not reported, EPA assumed a range of possible release days (i.e., 1, 20, and 100 days/year). Refer to the E-FAST 2014 Documentation Manual for equations used in the model to estimate surface water concentrations (U.S. EPA, 2007).

Estimated surface water concentrations from all E-FAST 2014 runs ranged from 0.08 to 77.9 µg/L, with all values below the aquatic chronic concentration of concern by a factor of 3 – 3,038. For further details of this estimation approach, see Appendix C.

***Terrestrial Environmental Exposures***

EPA does not plan to further analyze terrestrial exposures, due to low expected toxicity (see Section 2.4.1) and low expected exposure based on the physical/chemical properties (e.g., high vapor pressure; see Section 2.1).

### 2.3.5 Human Exposures

In this section, EPA presents occupational, consumer, and general population exposures. Subpopulations, including potentially exposed and susceptible subpopulations within these exposure categories, are also presented.

#### 2.3.5.1 Occupational Exposures

Exposure pathways and exposure routes are listed below for worker activities under the various conditions of use (industrial or commercial) described in Section 2.3. In addition, exposures to occupational non-users (ONU), who do not directly handle the chemical but perform work in an area where the chemical is present are listed. Engineering controls and/or personal protective equipment may affect the occupational exposure levels.

In the 2016 Draft Risk Assessment (U.S. EPA, 2016b), EPA evaluated inhalation exposures to 1-BP for occupational use in spray adhesives, dry cleaning (including spot cleaning) and degreasing (vapor, cold cleaning and aerosol), which will be considered in the 1-BP risk evaluation. As described in Section 2.2, all the conditions of use identified which results in occupational exposures will be considered during the risk evaluation.

***Worker Activities***

Workers and occupational non-users may be exposed to 1-BP when performing activities associated with the conditions of use described in Section 2.2. Work activities with potential for exposure may include, but are not limited to:

- Unloading and transferring 1-BP to and from storage containers and to process vessels;
- Handling, transporting and disposing waste containing 1-BP;
- Handling and transporting 1-BP during distribution in commerce;
- Using 1-BP in process equipment (e.g., vapor degreasing machine);
- Cleaning and maintaining equipment;
- Sampling chemicals, formulations or products containing 1-BP for quality control (QC);
- Applying formulations and products containing 1-BP onto substrates (e.g., spray applying adhesive containing 1-BP onto furniture pieces);
- Performing other work activities in or near areas where 1-BP is used.

***Inhalation***

Based on these occupational exposure scenarios, EPA expects inhalation of vapor to be the primary route of exposure for workers and occupational non-users. Where mist generation is expected (e.g. spray application), EPA will also analyze inhalation exposure to mist for workers and ONU.

The Occupational Safety and Health Administration (OSHA) has not set permissible exposure limits (PELs) and the NIOSH has not recommended worker exposure limits (RELs) for 1-BP; however, NIOSH recently proposed a REL of 0.3 ppm (Criteria for a Recommended Standard: Occupational Exposure to 1-Bromopropane (2016); 81 FR 7122, February 10, 2016). A revised document was released for comment in January of 2017. The American Conference of Governmental Industrial Hygienists (ACGIH) has recommended a Threshold Limit Value (TLV) of 0.1 ppm 8-hour time-weighted average (TWA) 1-BP for workers (ACGIH, 2015).

***Oral***

Worker exposure via the oral route is not expected. Exposure may occur through mists that deposit in the upper respiratory tract however, based on physical chemical properties, mists of 1-BP will likely be rapidly absorbed in the respiratory tract or evaporate and will be considered as an inhalation exposure.

***Dermal***

For conditions of use where workers may come into contact with liquids containing 1-BP, EPA estimates the skin contact time to be less than 2 minutes due to rapid volatilization. The estimated evaporation time is based on vapor generation rate of 1-BP at ambient conditions as calculated using the EPA/OPPT Penetration Model. 1-BP is an organic chemical with vapor pressure of 111 mmHg at 20°C. At the typical skin surface temperature of 32°C, the vapor pressure is estimated to be 186 mmHg (Frasch et al., 2014). The Penetration Model estimates the release of a chemical from an open, exposed liquid surface in an indoor environment. Evaporation time can then be calculated from the vapor generation rate, and the exposure load from EPA/OPPT 2-Hand Dermal Contact with Liquid Model or the EPA/OPPT 2-Hand Dermal Immersion in Liquid Model (2.1 to 10.3 mg/cm$^2$), and skin surface area of two hands (1,070 cm$^2$) from EPA/OPPT models (U.S. EPA, 2013a). Therefore, dermal exposure to 1-BP based on a single finite exposure event is likely negligible.

EPA also expects the dermal absorbed fraction to be low (0.16 percent – see discussion under Dermal section of Section 2.3.5.2). However, there is potential for increased dermal penetration for uses where occluded exposure, repeated contact, or dermal immersion may occur. For occupational non-users, dermal exposure to liquid is generally not expected as they do not directly handle 1-BP.

***Key Data***

Key data that inform occupational exposure assessment include: the OSHA Chemical Exposure Health Data (CEHD) and NIOSH Health Hazard Evaluation (HHE) program data. OSHA data are workplace monitoring data from OSHA inspections. OSHA sampling data can be obtained through the CEHD at https://www.osha.gov/opengov/healthsamples.html. Table_Apx B-1 and Table_Apx B-2 summarize the exposure scenarios and industry sectors where 1-BP personal and area monitoring data are available from OSHA inspections conducted between 2013 and 2016.

### 2.3.5.2 Consumer Exposures

1-BP can be found in consumer products and/or commercial products that are readily available for public purchase at common retailers (Sections 3 and 4 of *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: 1-Bromopropane,* EPA-HQ-OPPT-2016-0741-0003) and can therefore result in exposures to consumers and bystanders [non-product users that are incidentally exposed to the product or article, (U.S. EPA, 2017b)].

The previous 2016 Draft Risk Assessment (U.S. EPA, 2016b) characterized inhalation exposures to 1-BP from the following uses:

1. Aerosol spray adhesives
2. Aerosol spot removers
3. Aerosol cleaners and degreasers (including engine degreasing, brake cleaning and electronics cleaning)

During Problem Formulation, further review of consumer products and consumer uses was performed, and is discussed in Section 2.2.2. It was concluded that there is no consumer use of 1-BP for engine degreasers, brake cleaning, or aerosol spray adhesives (except as an adhesive accelerant in arts and crafts applications). Although 1-BP is sometimes used by industrial and commercial users to degrease engines when these users want a nonflammable degreaser, it is not expected to be used by consumers for the purposes of engine degreasing or brake cleaning.

Based on information summarized in Section 2.2.2, additional consumer uses that will be further analyzed include:

- Solvents (for cleaning or degreasing)
  - Aerosol spray degreaser/cleaner
- Cleaning and Furniture Care Products
  - Spot cleaner, stain remover
  - Liquid cleaner (e.g., coin and scissor cleaner)
  - Liquid spray/aerosol cleaner
- Other uses
  - Arts, crafts and hobby materials – adhesive accelerant
  - Automotive care products – refrigerant flush

- Anti-adhesive agents – mold cleaning and release product
- Building and construction materials not covered elsewhere – insulation

Use patterns and habits and practices may vary depending on the use and user. There may be higher end users (e.g., DIY) who purchase consumer products, and use these products more frequently. Examples may be small shops or businesses (e.g., art shops that routinely use a spray adhesive, small garages that frequently use degreasers) where the frequency of use is higher or where users or hobbyists may use products more than once per day on a regular basis. This may lead to chronic exposure whereas typical consumer exposures are expected to be acute in nature based on the identified consumer products/uses. Use of articles, such as insulation, may lead to exposures that occur over longer periods of time. Use patterns for the consumer products identified will be considered using available information on magnitude, frequency and duration of exposures.

***Inhalation***

Based on the physical-chemical properties of 1-BP and the conditions of use, inhalation is expected to be the primary route of exposure for consumer users of 1-BP containing products. The magnitude of exposure will depend upon the concentration of 1-BP in products, use patterns (including frequency, duration, amount of product used, room of use) and application methods. Several product types and scenarios were evaluated in the 2016 Draft Risk Assessment (U.S. EPA, 2016b), including spray adhesives, spray degreasers (engine cleaning and electronics cleaning), and aerosol spot removers. Information regarding use patterns and application methods will be used to build exposure scenarios. Any products which are spray applied will result in some level of inhalation exposure to the consumer user and also to a bystander in the room of use. Products used in the liquid form are also likely to result in some level of inhalation exposure to the consumer given the high vapor pressure of 1-BP. Consumer exposures are expected to be acute in nature, however, there may be a subset of consumers who use products on a frequent or regular basis resulting in sub-chronic or chronic exposures. Based on the potential for spray application of some products containing 1-BP, exposures to mists are also expected. The exposures to consumers and bystanders through mists may deposit in the upper respiratory tract and EPA assumes these are absorbed via inhalation.

Acute inhalation exposures to consumers (such as residential users) and bystanders (those who may not be actively engaged in the use of the product, but may be in the room of use) in residential settings were also assessed for the consumer uses identified in the 2016 Draft Risk Assessment (U.S. EPA, 2016b).

***Oral***

EPA does not plan to further analyze exposure to consumers via ingestion of 1-BP. Ingestion is not expected to be a primary route of exposure. Based on the vapor pressure, 1-BP will exist as a vapor/mist during use. A fraction of 1-BP may be available for absorption in the respiratory tract however ingestion of 1-BP is anticipated to be low since 1-BP is expected to be absorbed in the lung quickly and not have appreciable ability to travel up the mucosal elevator and be swallowed.

***Dermal***

There is the potential for dermal exposure from consumer uses of 1-BP. Dermal exposure may occur via vapor/mist deposition onto skin or via direct liquid contact during use, particularly in occluded scenarios. As described in the NIOSH Skin Notation Profile for 1-BP (NIOSH, 2017), *in vitro* dermal penetration of 0.16% of the applied dose (13.5 mg/cm$^2$) was measured following transient exposure in a non-occluded environment to simulate splash scenarios; therefore, losses due to evaporation were approximately 500-fold greater than the dermal absorption flux. However, measurements of skin

penetration were one to two orders or magnitude higher in occluded environments where evaporation losses were not considered (transient 10 minute exposures, or 'infinite' 3 hour exposures). Based on this information, dermal exposure in non-occluded scenarios will be a less significant route of exposure when compared to occluded scenarios, however there may be exceptions such as situations of transient or infinite exposures (e.g., vapor trapped against skin by gloves or continued contact with a wet rag) or where there is greater potential for dermal penetration due to longer durations of exposure.

Whereas users may be exposed dermally during use of consumer products depending on the specific use, it is not expected that bystanders would be dermally exposed to 1-BP.

***Exposures from Disposal***

EPA does not expect exposure to consumers from disposal of consumer products. It is anticipated that most products will be disposed of in original containers, particularly those products that are purchased as aerosol cans. Liquid products may be recaptured in an alternate container following use (refrigerant flush or coin cleaning).

#### 2.3.5.3 General Population Exposures

Wastewater/liquid wastes, solid wastes or air emissions of 1-BP could result in potential pathways for oral, dermal or inhalation exposure to the general population.

***Inhalation***

Emissions to air from industrial manufacturing, processing and use are expected. TRI data in Table 2-6 show air as a primary medium of environmental release. These releases include both fugitive air emissions and point source (stack) air emissions. Based on the relatively long hydroxy radical oxidation half-life (t ½ 14 days) emissions to ambient air could results in exposures to near facility human receptors and the general population. Inhalation is expected to be the primary route of exposure for the general population and near facility populations.

Inhalation of 1-BP may also occur in indoor settings as a result of co-location with dry cleaning facilities that use 1-BP.

***Oral***

Recent TRI reporting indicated 0 pounds released to POTWs and 5 pounds released directly to water in 2016. EPA pretreatment regulations for industrial users discharging wastewater to POTWs are expected to limit the discharge of 1-BP to POTWs and ultimately to surface water (see Section 2.3.4). Waste disposal practices and 1-BP's rapid volatilization from water are expected to mitigate drinking water exposure potential and there is no data of 1-BP found in US drinking water.

Although incidental hand-to-mouth ingestion of soil may occur, adsorption to soils is not expected since 1-BP is volatile and mobile in soil (see Section 2.3.1); therefore, ingestion of soil and contaminated drinking water are not expected.

***Dermal***

Based on the physical and chemical properties of 1-BP (relatively high volatility), low expected dermal absorption, and expected media concentrations (see Section 2.3.4), dermal exposure to 1-BP via surface water or soil is not expected to be a significant route of exposure.

#### 2.3.5.4 Potentially Exposed or Susceptible Subpopulations

TSCA requires the determination of whether a chemical substance presents an unreasonable risk to "a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation" by EPA. TSCA § 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." General population is "the total of individuals inhabiting an area or making up a whole group" and refers here to the U.S. general population (U.S. EPA, 2011).

As part of the Problem Formulation, EPA identified potentially exposed and susceptible subpopulations for further analysis during the development and refinement of the life cycle, conceptual models, exposure scenarios, and analysis plan. In this section, EPA addresses the potentially exposed or susceptible subpopulations identified as relevant based on greater exposure. EPA will address the subpopulations identified as relevant based on greater susceptibility in the hazard section.

EPA identifies the following as potentially exposed or susceptible subpopulations that EPA expects to consider in the risk evaluation due to their *greater exposure*:

- Workers and occupational non-users.
- Consumers and bystanders associated with consumer use. 1-BP has been identified in products available to consumers; however, only some individuals within the general population may use these products. Therefore, those who do use these products are a potentially exposed or susceptible subpopulation due to greater exposure.
- Other groups of individuals within the general population who may experience greater exposures due to their proximity to conditions of use identified in Section 2.2 that result in releases to the environment and subsequent exposures (e.g., individuals who live or work near manufacturing, processing, use or disposal sites).

In developing exposure scenarios, EPA will analyze available data to ascertain whether some human receptor groups may be exposed via exposure pathways that may be distinct to a particular subpopulation or lifestage and whether some human receptor groups may have higher exposure via identified pathways of exposure due to unique characteristics (e.g., activities, duration or location of exposure) when compared with the general population (U.S. EPA, 2006a).

In summary, in the risk evaluation for 1-BP, EPA plans to analyze the following potentially exposed groups of human receptors: workers, occupational non-users, consumers, bystanders associated with consumer use, and other groups of individuals within the general population who may experience greater exposure. EPA may also identify additional potentially exposed or susceptible subpopulations that will be considered based on greater exposure.

## 2.4 Hazards (Effects)

For scoping, EPA conducted comprehensive searches for data on hazards of 1-BP, as described in *Strategy for Conducting Literature Searches for 1-Bromopropane: Supplemental File for the TSCA Scope Document*, (EPA-HQ-OPPT-2016-0741-0048). Based on initial screening, EPA plans to analyze the hazards of 1-BP identified in the scope document (EPA-HQ-OPPT-2016-0741-0049). However, when conducting the risk evaluation, the relevance of each hazard within the context of a specific

exposure scenario will be judged for appropriateness. For example, hazards that occur as a result of chronic exposures may not be applicable for acute exposure scenarios. This means that it is unlikely that every identified hazard will be analyzed for every exposure scenario.

### 2.4.1 Environmental Hazards

Environmental hazard data identified for 1-BP are studies described in the robust summaries in the ECHA Database (ECHA, 2015) and the Ecological Hazard Literature Search Results in the 1-Bromopropane (CASRN 106-94-5) Bibliography: *Supplemental File for the TSCA Scope Document*, (U.S. EPA, 2017a). Only the *on-topic* references listed in the Ecological Hazard Literature Search Results were considered as potentially relevant data/information sources for the risk evaluation. Inclusion criteria were used to screen the results of the ECOTOX literature search (as explained in the *Strategy for Conducting Literature Searches for 1-Bromopropane: Supplemental File for the TSCA Scope Document*, (EPA-HQ-OPPT-2016-0741-0048). Data from the screened literature are summarized below (Table 2-7). EPA expects to review these data/information sources during risk evaluation using the data quality review evaluation metrics and the rating criteria described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018).

#### *Toxicity to Sediment and Terrestrial Organisms*

During data screening, there were no available sediment, soil, nor avian toxicity studies found in the scientific literature for 1-BP. The toxicity of 1-BP is expected to be low based on the lack of on-topic environmental hazard data for 1-BP to sediment and terrestrial organisms in the published literature and the physical/chemical/fate properties (relatively high volatility (Henry's Law constant of $7.3X10^{-3}$ atm-$m^3$/mole), high water solubility (2.4 g/L), and low log $K_{oc}$ (1.6) suggesting that 1-BP will only be present at low concentrations in these environmental compartments.

#### *Toxicity to Aquatic Organisms*

During problem formulation, EPA identified aquatic (aqueous-only) data reported in the literature to assess the aquatic hazard of 1-BP. The 96-hour $LC_{50}$ value for 1-BP with fish ranged from 24.3 to 67.3 mg/L. The acute aquatic invertebrate $EC_{50}$ for 1-BP was 99.3 mg/L. The $EC_{50}$ for the algae toxicity test was 52.4 mg/L (biomass) and 72.3 mg/L (growth rate). The NOEC for the algae toxicity test was 12.4 mg/L.

#### *Toxicity to Microorganisms*

The $EC_{50}$ and NOEC for micro-organisms toxicity study for a 5-minute time period was 270 mg/L and 100 mg/L, respectively.

**Table 2-7. Ecological Hazard Characterization of 1-Bromopropane**

| Duration | Test organism | Endpoint | Hazard value* | Units | Effect Endpoint | Citation |
|---|---|---|---|---|---|---|
| Acute | Fish | $LC_{50}$ | 24.3 - 67.3 | mg/L | Mortality | ECHA (2015);Geiger et al. (1988) |
| | Aquatic invertebrates | $EC_{50}$ | 99.3 | mg/L | Immobilization | ECHA (2015) |
| | Algae | $EC_{50}$ | 52.4 / 72.3 | mg/L | Biomass / growth rate | ECHA (2015) |
| | Microorganism | $EC_{50}$ | 270 | mg/L | Respiration | ECHA (2015) |
| | Acute COC | | 4.86 | mg/L | | |
| Chronic | Fish | ChV | 2.43 | mg/L | Acute to chronic ratio of 10 | ECHA (2015) |
| | Aquatic invertebrates | ChV | 9.93 | mg/L | Acute to chronic ratio of 10 | ECHA (2015) |
| | Algae | NOEC | 12.4 | mg/L | Growth rate | ECHA (2015) |
| | Microorganism | NOEC | 100 | mg/L | Respiration | ECHA (2015) |
| | Chronic COC | | 0.24 | mg/L | | |

* Values in the tables are presented as reported by the study authors

***Concentrations of Concern***

The screening-level acute and chronic concentrations of concern (COCs) for 1-BP were derived based on the lowest or most toxic ecological toxicity values (e.g., L/$EC_{50}$). The information below describes how the acute and chronic COC's were calculated for environmental toxicity of 1-BP using assessment factors. The application of assessment factors is based on established EPA/OPPT methods (U.S. EPA, 2013b, 2012c) and were used in this Problem Formulation to calculate lower bound effect levels (referred to as the concentration of concern; COC) that would likely encompass more sensitive species not specifically represented by the available experimental data. Also, assessment factors are included in the COC calculation to account for differences in inter- and intra-species variability, as well as laboratory-to-field variability. It should be noted that these assessment factors are dependent upon the availability of datasets that can be used to characterize relative sensitivities across multiple species within a given taxa or species group, but are often standardized in risk evaluations conducted under TSCA, due to limited data availability.

The acute COC is derived by dividing the fish 96-hr $LC_{50}$ of 24.3 mg/L (the lowest acute value in the dataset) by an assessment factor (AF) of 5:

- Lowest value for the 96-hr fish $LC_{50}$ (24.3 mg/L) / AF of 5 = 4.86 mg/L or 4,860 µg/L.

The acute COC of 4,860 µg/L, derived from experimental fish endpoint, is used as a conservative hazard level in this problem formulation for 1-BP.

Since there are no long-term chronic studies for 1-BP, the fish 96-hr $LC_{50}$ of 24.3 mg/L (the lowest acute value in the dataset) is divided by an acute-to-chronic ratio (ACR) of 10 to obtain a chronic value (ChV) for fish. The fish ChV is then divided by an assessment factor of 10 to obtain a chronic COC:

- Lowest value for the fish 96-hr $LC_{50}$ (24.3 mg/L) / 10 (ACR) / AF of 10 = 0.243 mg/L or 243 µg/L.

The chronic COC of 243 µg/L, derived from experimental fish endpoint, is used as the lower bound hazard level in this problem formulation for 1-BP.

The derived acute COC (4,860 ppb) and chronic COC (243 ppb) are based on environmental toxicity endpoint values (e.g., $LC_{50}$) from ECHA. Full study reports associated with these COCs were not available and will not be available in the future. In addition, the data represent the lowest bound of all 1-BP data available, so it represents the most conservative hazard value.

### 2.4.2 Human Health Hazards

1-BP does not have an existing EPA IRIS Assessment; however, EPA has previously reviewed data/information on health effects endpoints, identified hazards and conducted dose-response analysis in the 2016 Draft Risk Assessment (U.S. EPA, 2016b); these hazard identification and dose-response analyses on 1-BP have been recently peer reviewed (EPA-HQ-OPPT-2015-0805-0028). EPA expects to use these previous analyses as a starting point for identifying key and supporting studies to inform the human health hazard assessment, including dose-response analyses. The relevant studies will be evaluated using the data quality criteria in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018). In addition, EPA intends to review studies published after the 2016 Draft Risk Assessment (U.S. EPA, 2016b) [see (*1-Bromopropane (CASRN 106-94-5) Bibliography: Supplemental File for the TSCA Scope Document* EPA-HQ-OPPT-2016-0741-0047], using the approaches and/or methods described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018) to ensure that EPA is considering information that has been made available since the 2016 Draft Risk Assessment (U.S. EPA, 2016b) was conducted. Based on reasonably available information, the following sections describe the hazards EPA expects to further analyze.

#### 2.4.2.1 Non-Cancer Hazards

For the 2016 Draft Risk Assessment (U.S. EPA, 2016b) on 1-BP, EPA evaluated studies for the following non-cancer hazards: acute toxicity (acute lethality at high concentrations only), blood toxicity, immunotoxicity, cardiovascular toxicity, liver toxicity, kidney toxicity, reproductive toxicity, developmental toxicity, and neurotoxicity. A comprehensive summary of all endpoints considered can be found in the 2016 Draft Risk Assessment. Five health hazards were used for quantitative risk characterization and will be evaluated using our systematic review approach. These hazards include:

***Liver Toxicity***

Reported effects include liver histopathology (e.g., hepatocellular vacuolation, swelling, degeneration and necrosis), increased liver weight and clinical chemistry changes indicative of hepatotoxicity [2016 Draft Risk Assessment (U.S. EPA, 2016b)].

***Kidney Toxicity***

Laboratory animal studies have provided evidence of kidney toxicity following 1-BP exposure. Reported kidney effects include increased organ weight, histopathology (pelvic mineralization, tubular

casts) and associated clinical chemistry changes (e.g., increased blood urea nitrogen) [2016 Draft Risk Assessment (U.S. EPA, 2016b)]. Other kidney endpoints include increased incidence of pelvic mineralization in male and female rats from a subchronic duration inhalation study.

***Reproductive/Developmental Toxicity***

A two-generation reproduction study in rats reported a variety of adverse effects on male and female reproductive parameters (U.S. EPA, 2016b; WIL Research, 2001), including significant increases in the number of implantation sites, decreases in mating indices, increased estrous cycle length, increased numbers of females with evidence of mating without delivery, decreased absolute prostate and epididymal weights, decreased sperm motility and decreased mating and fertility indices. These findings are supported by similar reports of reproductive toxicity from other laboratory studies with rats and mice, including spermatogenic effects (decreased sperm count, altered sperm morphology and decreased sperm motility), organ weight changes in males (decreased epididymis, prostate and seminal vesicle weights), estrous cycle alterations and decreased numbers of antral follicles in females.

Developmental effects of 1-BP exposure have been evaluated on the basis of standard prenatal developmental toxicity studies, and a two-generation reproductive toxicity study in rats exposed via inhalation. Evidence for 1-BP-induced developmental toxicity includes dose-related adverse effects on live litter size, postnatal survival, pup body weight, brain weight and skeletal development.

***Neurotoxicity***

Data from studies in humans and animals demonstrate that the nervous system is a sensitive target of 1-BP exposure. Both the central and peripheral nervous systems are affected. Most inhalation studies using concentrations ≥1,000 ppm reported ataxia progressing to severely altered gait, hindlimb weakness to loss of hindlimb control, convulsions and death [2016 Draft Risk Assessment (U.S. EPA, 2016b)]. Other effects include neuropathological changes such as peripheral nerve degeneration, myelin sheath abnormalities and spinal cord axonal swelling. Brain pathology has also been reported in several studies, including white and gray matter vacuolization, degeneration of Purkinje cells in the cerebellum and decreased noradrenergic but not serotonergic axonal density in frontal cortex and amygdala. Decreased brain weight has been reported in adult and developmental studies. In a two-generation study, decreased brain weight in F1-generation males was reported.

Human studies (case-control studies, industrial surveys and case reports) corroborate that the nervous system is a sensitive target of 1-BP exposure in humans. Clinical signs of neurotoxicity (including headache, dizziness, weakness, numbness in lower extremities, ataxia, paresthesias and changes in mood) and motor and sensory impairments were noted in the case reports of workers occupationally exposed to 1-BP for 2 weeks to 3 years, and in industrial surveys ranging from 2 weeks to 9 years [2016 Draft Risk Assessment (U.S. EPA, 2016b)].

#### 2.4.2.2 Mutagenicity/Genotoxicity and Cancer Hazards

There is some evidence for mutagenicity and deoxyribonucleic acid (DNA) binding associated with exposure to 1-BP in vitro, but the results are not conclusive as to whether and to what extent such effects may occur in mammals in vivo. In vitro mammalian cell assays showed increased mutation frequency, and DNA damage was significantly increased in human leukocytes; however, tests conducted in vivo were mostly negative, including assays for dominant lethal mutations and micronuclei induction. An evaluation of leukocytes in workers exposed to 1-BP showed no definitive evidence of DNA damage. Positive results have been observed in several genotoxicity tests using known or postulated metabolites of 1-BP.

The National Toxicology Program's (NTP) *Report on Carcinogens* (NTP, 2013) concludes 1-BP is "reasonably anticipated to be a human carcinogen. In the 2016 Draft Risk Assessment (U.S. EPA, 2016b) on 1-BP, EPA evaluated cancer hazards from studies in laboratory animals and humans following chronic [≥10% of a lifetime (U.S. EPA, 2011)] inhalation exposures. Repeated exposures (e.g., ≥5 consecutive days) are anticipated during chronic exposure. 1-BP has been shown to be a multi-target carcinogen in rats and mice. The exact mechanism/mode of action of 1-BP carcinogenesis is not clearly understood, however, the weight-of-evidence analysis for the cancer endpoint is inconclusive but does not rule out a probable mutagenic mode of action for 1-BP carcinogenesis. In the 2016 Draft Risk Assessment (U.S. EPA, 2016b), EPA derived an inhalation unit risk (IUR) based on lung tumors in female mice. This health hazard was used for quantitative risk characterization and will be evaluated using our systematic review approach.

#### 2.4.2.3 Potentially Exposed or Susceptible Subpopulations

TSCA requires that the determination of whether a chemical substance presents an unreasonable risk include consideration of unreasonable risk to "a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation" by EPA. TSCA § 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." In developing the hazard assessment, EPA will evaluate available data to ascertain whether some human receptor groups may have greater susceptibility than the general population to the chemical's hazard(s).

## 2.5 Conceptual Models

EPA risk assessment guidance (U.S. EPA, 2014b, 1998), defines Problem Formulation as the part of the risk assessment framework that identifies the major factors to be considered in the assessment. It draws from the regulatory, decision-making and policy context of the assessment and informs the assessment's technical approach.

A conceptual model describes the actual or predicted relationships between the chemical substance and receptors, either human or environmental. These conceptual models are integrated depictions of the conditions of use, exposures (pathways and routes), hazards and receptors. The initial conceptual models describing the scope of the assessment for 1-BP (Scope Document, EPA-HQ-OPPT-2016-0741-0049), which was published in June 2017, have been refined during problem formulation. The changes to the conceptual models in this Problem Formulation are described along with the rationales.

In this section, EPA outlines those pathways that will and will not be further analyzed in the TSCA risk evaluation and the underlying rationale for these decisions.

EPA determined as part of problem formulation that it is not necessary to conduct further analysis on certain exposure pathways that were identified in the 1-BP scope document and that remain in the risk evaluation. Each risk evaluation will be "fit-for-purpose," meaning not all conditions of use will warrant the same level of evaluation and the Agency may be able to reach some conclusions without extensive or quantitative risk evaluations.  82 FR 33726, 33734, 33739 (July 20, 2017).

As part of this problem formulation, EPA also identified exposure pathways under regulatory programs of other environmental statutes, administered by EPA, which adequately assess and effectively manage

exposures and for which long-standing regulatory and analytical processes already exist, i.e., the Safe Drinking Water Act (SDWA), the Clean Water Act (CWA) and the Resource Conservation and Recovery Act (RCRA). EPA worked closely with the offices within EPA that administer and implement the regulatory programs under these statutes. In some cases, EPA has determined that chemicals present in various media pathways (i.e., water, land) fall under the jurisdiction of existing regulatory programs and associated analytical processes carried out under other EPA-administered statutes and have been assessed and effectively managed under those programs. EPA believes that the TSCA risk evaluation should generally focus on those exposure pathways associated with TSCA conditions of use that are not adequately assessed and effectively managed under the regulatory regimes discussed above because these pathways are likely to represent the greatest areas of risk concern. As a result, EPA does not expect to include in the risk evaluation certain exposure pathways identified in the 1-BP scope document.

### 2.5.1 Conceptual Model for Industrial and Commercial Activities and Uses: Potential Exposures and Hazards

The revised conceptual model (Figure 2-2) illustrates the expected exposure pathways to workers and occupational non-users from industrial and commercial activities and uses of 1-BP that EPA expects to include in the risk evaluation. For most activities and uses, EPA anticipates that workers and occupational non-users may be exposed to 1-BP via inhalation and dermal routes, with inhalation of vapor/mist being the most likely exposure route. In addition to the pathways illustrated in the figure, EPA will evaluate activities resulting in exposures associated with distribution in commerce (e.g. loading, unloading) throughout the various lifecycle stages and conditions of use (e.g. manufacturing, processing, industrial use, commercial use, disposal) rather than a single distribution scenario.

As discussed in Section 2.2.2.1, EPA will not assess the commercial use of 1-BP in non-pesticidal agricultural products during risk evaluation. Based on information available to EPA, EPA determined that 1-BP is not used in agricultural products (non-pesticidal), only in the processing of such products.

#### *Inhalation*

EPA expects to analyze inhalation exposure to workers during manufacturing, processing, use and disposal of 1-BP for all uses identified in the scope (except use in non-pesticidal agricultural products). The analysis will include worker exposure to vapor from open sources, and exposure to mist during activities and uses where mist generation is expected (e.g. spray application of 1-BP).

Where inhalation exposure is expected, EPA will also analyze inhalation exposure to vapor and mists for occupational non-users.

#### *Dermal*

For most industrial and commercial activities, EPA does not plan to further analyze dermal contact with liquid because 1-BP readily evaporates from the skin. Based on the vapor generation rate of 1-BP at ambient conditions as calculated using the EPA/OPPT Penetration Model, the contact time with skin is expected to be less than 2 minutes. Further, the fraction absorbed was measured to be small (0.16%) by NIOSH (https://www.cdc.gov/niosh/docket/review/docket057a/pdfs/057-arevisedctd-1-bpcriteriadocument_030716_corrected.pdf). This exposure pathway and route will not be further analyzed for manufacturing, processing, and several uses, e.g. insulation materials, asphalt extraction, temperature indicator.

Certain conditions of use, such as maintenance of industrial degreasing tanks or commercial dry cleaning machines, can present a potential for occluded exposure (e.g. where 1-BP is trapped within a worker's gloves) or repeated dermal contacts. EPA plans to further analyze exposures to a subset of workers where occluded/repeated contact or immersion exposure are likely.

Occupational non-users are not directly handling 1-BP; therefore, skin contact with liquid 1-BP is not expected for occupational non-users and EPA does not expect to further analyze this pathway in the risk evaluation.

***Businesses Co-located with Dry Cleaners***

For businesses co-located with dry cleaners, inhalation is expected to be the primary route of exposure. EPA does not plan to further analyze dermal and oral exposure to indoor vapor for co-located businesses. The potential for incidental ingestion of vapor is expected to be low, since 1-BP is absorbed quickly in the lung and does not have appreciable ability to travel up the mucosal elevator to be swallowed.

***Waste Handling, Treatment and Disposal***

Figure 2-2 shows that waste handling, treatment and disposal is expected to lead to the same pathways as other industrial and commercial activities and uses. The path leading from the "Waste Handling, Treatment and Disposal" box to the "Hazards Potentially Associated with Acute and/or Chronic Exposures See Section 2.4.2" box was re-routed to accurately reflect the expected exposure pathways, routes, and receptors associated with these conditions of use of 1-BP.

For each condition of use identified in Table 2-3, a determination was made as to whether or not each unique combination of exposure pathway, route, and receptor will be further analyzed in the risk evaluation. The results of that analysis along with the supporting rationale are presented in Appendix D.

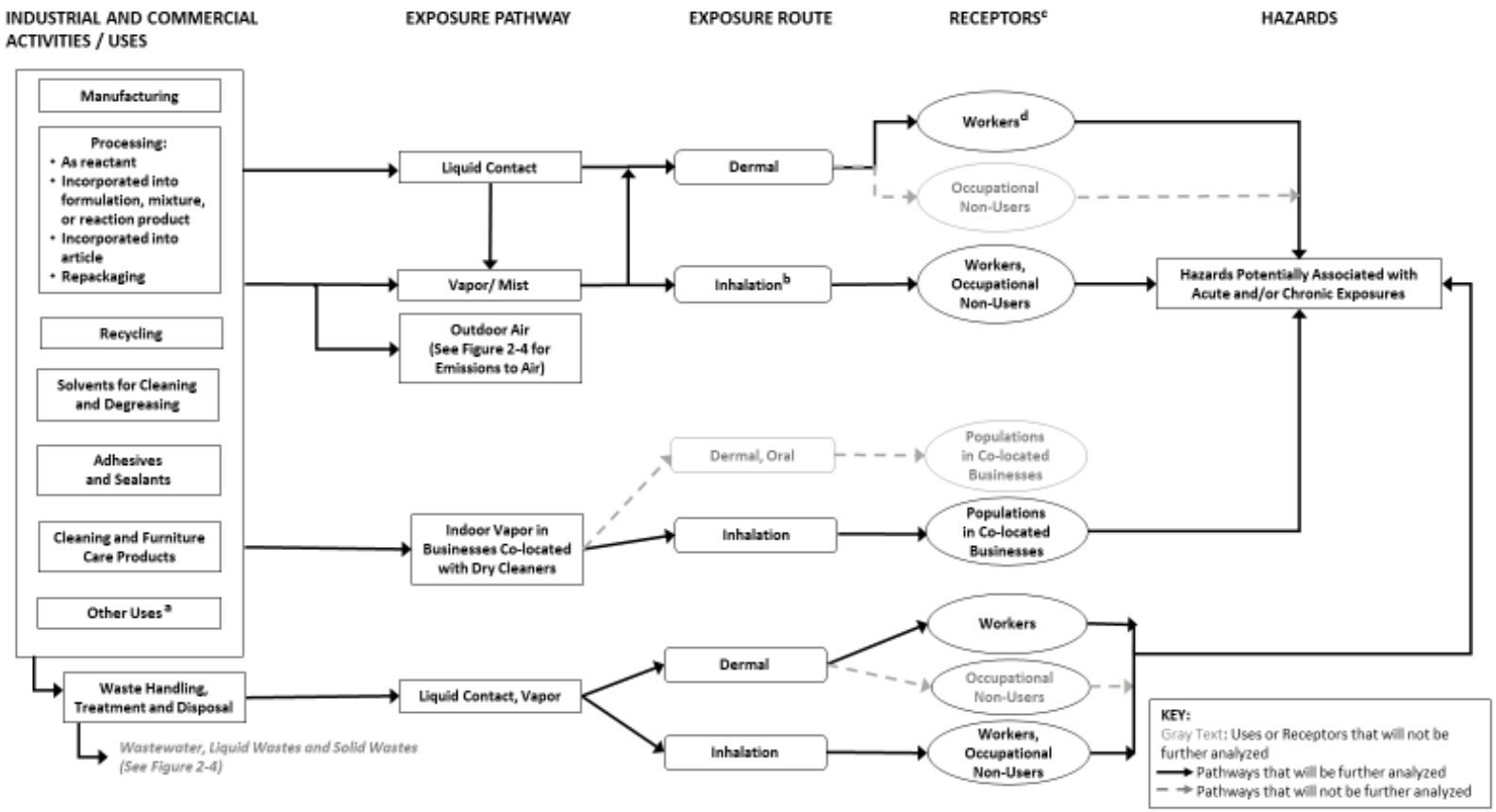


**Figure 2-2. 1-BP Conceptual Model for Industrial and Commercial Activities and Uses: Potential Exposures and Hazards**

The conceptual model presents the exposure pathways, exposure routes and hazards to human receptors from industrial and commercial activities and uses of 1-BP.

[a]Some products are used in both commercial and consumer applications. Additional uses of 1-BP are included in Table 2-3.
[b] Exposure may occur through mists that deposit in the upper respiratory tract, however based on physical chemical properties, mists of 1-BP will likely be rapidly absorbed in the respiratory tract or evaporate and will be considered as an inhalation exposure.
[c]Receptors include potentially exposed or susceptible subpopulations.
[d] When data and information are available to support the analysis, EPA also considers the effect that engineering controls and/or personal protective equipment have on occupational exposure levels.

### 2.5.2 Conceptual Model for Consumer Activities and Uses: Potential Exposures and Hazards

The revised conceptual model (Figure 2-3) illustrates the expected exposure pathways to human receptors from consumer uses of 1-BP that EPA expects to include in the risk evaluation. EPA expects that the primary route of exposure for consumers will be via inhalation. There may also be dermal exposure from skin contact with liquids in occluded scenarios, such as the use of a rag that has been soaked in a product containing 1-BP. For bystanders, the primary route of exposure is expected to be inhalation. Oral exposure from mists that deposit in the upper respiratory tract and are swallowed or from incidental ingestion of 1-BP residue on hand/body is not expected to be a significant route of exposure given the physical-chemical properties of 1-BP. It should be noted that some consumers may purchase and use products primarily intended for commercial use.

EPA has reviewed the uses described in the 2016 Draft Risk Assessment (U.S. EPA, 2016b) including aerosol spray degreaser/cleaners, use in adhesives and spot cleaners and has concluded that there is no consumer use of 1-BP for engine degreasers, brake cleaning, or aerosol spray adhesives (except as an adhesive accelerant in arts and crafts applications). EPA intends to continue to evaluate the uses identified in the 2016 Draft Risk Assessment (U.S. EPA, 2016b) as aerosol spray degreaser/cleaner and spot cleaners. EPA will further evaluate additional uses identified in problem formulation including: stain remover, adhesive accelerant, automotive care products, anti-adhesive agents, liquid cleaners, and building and construction materials.

***Inhalation***

Based on the physical-chemical properties of 1-BP and the conditions of use, inhalation exposures to 1-BP in the vapor phase from use of consumer products is expected and will be further analyzed for consumers and bystanders. This is expected to be the primary route of exposure.

***Oral***

EPA does not expect to further analyze exposure to consumers via ingestion of 1-BP. Ingestion is not expected to be a primary route of exposure. Based on the vapor pressure, 1-BP is likely to exist as a vapor during use. A fraction of 1-BP may be available for absorption in the respiratory tract however ingestion of 1-BP is anticipated to be low since 1-BP is expected to be absorbed in the lung quickly and not have appreciable ability to travel up the mucosal elevator and be swallowed.

***Dermal***

Based on the physical-chemical properties and high evaporative losses compared to dermal absorption as described in Section 2.3.5.2, non-occluded dermal exposures are not expected to be the primary route of exposure for consumers, although dermal exposures will contribute to the overall exposure. Some products may be purchased and used as a liquid. For these uses, consumers may have dermal contact from occluded exposures such as holding a rag soaked in liquid 1–BP where limited evaporation rates and penetration may be expected to be higher in these scenarios. EPA does not expect to further analyze dermal exposure to 1-BP vapor, however EPA does expect to further analyze direct dermal contact with liquid 1-BP for consumers during the risk evaluation phase.

Whereas users may be exposed dermally during use of consumer products, particularly in occluded scenarios, bystanders would generally not be expected to be dermally exposed to 1-BP in occluded or non-occluded scenarios, therefore dermal exposure to bystanders will not be further analyzed.

***Disposal***

EPA does not expect to further analyze exposure to consumers from disposal of consumer products. It is anticipated that most products will be disposed of in original containers, particularly those products that are purchased as aerosol cans. Liquid products may be recaptured in an alternate container following use (e.g., refrigerant flush or coin cleaning).

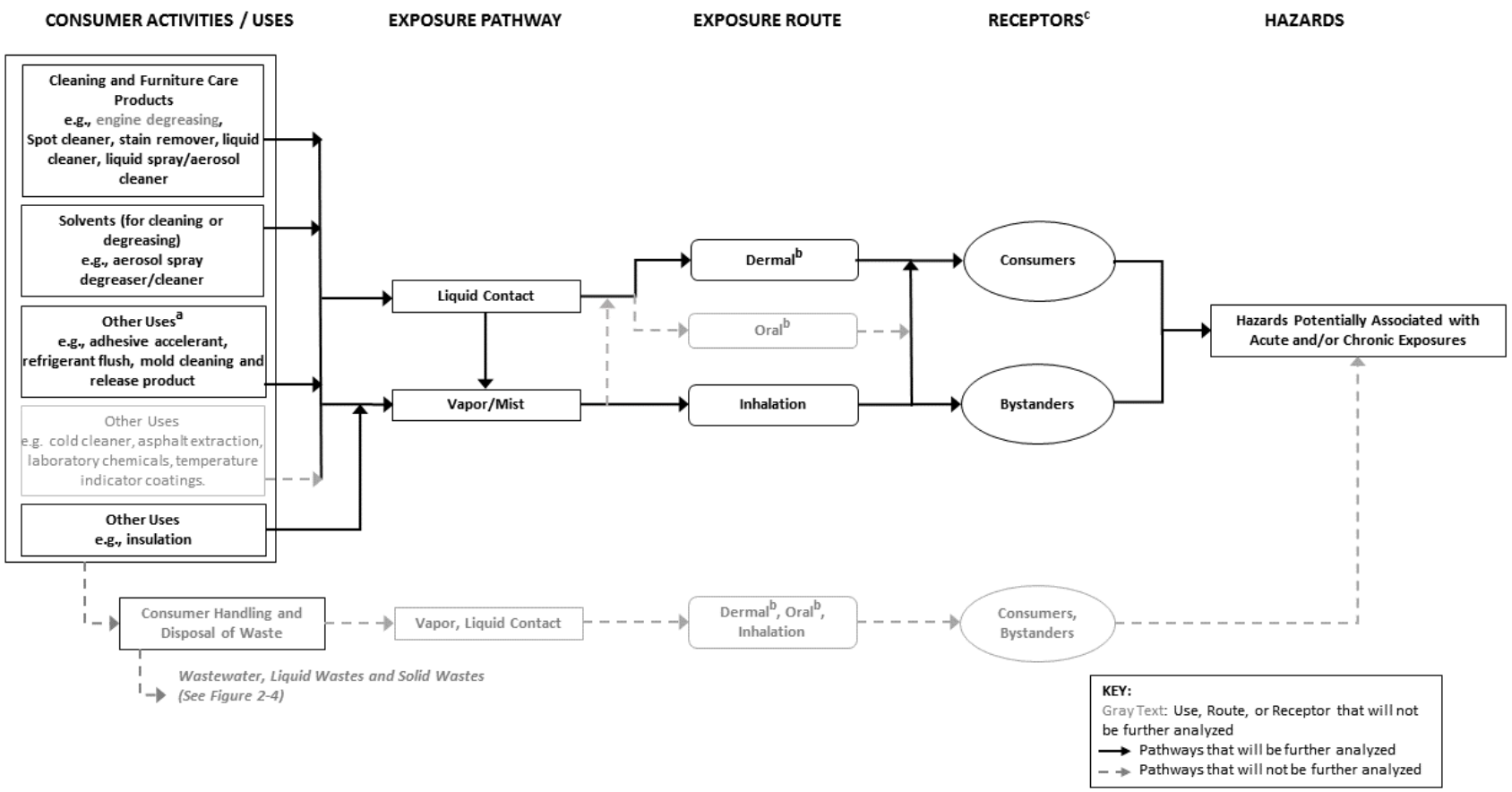


**Figure 2-3. 1-BP Conceptual Model for Consumer Activities and Uses: Potential Exposures and Hazards**

The conceptual model presents the exposure pathways, exposure routes and hazards to human receptors from consumer activities and uses of 1-BP.

[a]Some products are used in both commercial and consumer applications. Additional uses of 1-BP are included in Table 2-3.
[b] Dermal exposure may occur through skin contact with liquids; ingestion is anticipated to be low since 1-BP is expected to be absorbed in the lung quickly and not have appreciable ability to travel up the mucosal elevator and be swallowed.
[c]Receptors include potentially exposed or susceptible subpopulations.

### 2.5.3 Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards

The revised conceptual model (Figure 2-4) illustrates the expected exposure pathways to ecological receptors from environmental releases and waste streams associated with industrial and commercial activities for 1-BP that EPA expects to include in the risk evaluation. The pathways that EPA expects to include and analyze further in the risk evaluation is described in Section 2.5.3.1 and shown in the conceptual model. The pathways that EPA expects to include but not further analyze in risk evaluation are described in Section 2.5.3.2 and the pathways that EPA does not expect to include in risk evaluation are described in Section 2.5.3.3.

#### 2.5.3.1 Pathways That EPA Expects to Include and Further Analyze in the Risk Evaluation

***Air Pathways***

EPA expects to further analyze air emissions resulting in the general population. Emissions to air from industrial manufacturing, processing and use are expected. Based on the relatively long hydroxy radical oxidation half-life ($t_{½}$ = 14 days) emissions to ambient air could travel far enough from the release point to reach both near facility human receptors and the general population. Inhalation is expected to be the primary route of exposure for the general population and near facility populations.

During problem formulation, EPA reviewed TRI data for on-site releases to air from fugitive and point sources; these data will be used in EPA's release analysis during risk evaluation. The data also includes any air release resulting from on-site waste treatment and energy recovery.

For off-site transfer of wastes, EPA will further analyze the Destruction Removal Efficiencies (DRE's) occurring from incineration/energy recovery processes at off-site facilities, as well as the resulting air emissions. It is possible that some of these air emissions are already accounted for in the TRI data (in the on-site releases) if the off-site facility is also a TRI reporter (e.g. a TSDF facility).

These pathways include:

- The general populations living near industrial and commercial facilities using 1-BP that are exposed via inhalation of outdoor air.
- The populations co-located with dry cleaners are expected to be exposed to 1-BP via the inhalation route (recommended for assessment in peer review).
- Releases from Manufacturing, Processing, Use, Recycling to Air: land disposal, non-hazardous waste incineration and emissions to air can be expected. In the atmosphere, 1-BP is expected to occur primarily in the vapor phase and may undergo long-range transport. The 2016 TRI data reported onsite recycling and transfers to offsite for recycling.
- Releases to Air from Disposal and Recycling: TRI reports a total of 115,222 pounds of off-site releases after transfer (90,273 pounds of transfers to other landfills for disposal (3 facilities), 20,892 pounds of unknown transfers for disposal (6 facilities), 3307 pounds of transfer for disposal to a storage only facility, and 750 pounds of transfer for disposal to a waste broker.

#### 2.5.3.2 Pathways That EPA Expects to Include in the Risk Evaluation But Not Further Analyze

***Air Pathways***

EPA will not further analyze inhalation exposures for ecological terrestrial species in this risk evaluation due to the physical/chemical properties associated with 1-BP (high vapor pressure; see Section 2.1) and the low expected toxicity (see Section 2.4.1), and since their inhalation exposures are expected to be short and/or of sporadic frequency due to their mobile behavior.

***Water Pathways***

As described in Section 2.3.5.3, there is no data of 1-BP found in US drinking water. Recent TRI reporting indicated 0 pounds released to POTWs and 5 pounds released directly to water in 2016. In addition, 1-BP is slightly soluble in water and its rapid volatilization from water are expected to mitigate exposure potential from drinking water supplied from public water systems. Therefore, EPA does not plan to further analyze drinking water pathways in the risk evaluation for 1-BP under TSCA.

EPA does not expect to further analyze releases to wastewater or surface water. As discussed in Section 2.1, 1-BP is volatile and has a relatively high Henry's law constant. 1-BP is somewhat biodegradable and is not expected to sorb to solids in wastewater. EPA's STP WTP model predicts 73% removal of 1-BP by volatilization in activated sludge treatment and 1% partitioning to biosolids. 1-BP discharged in wastewater treatment plant effluent to the aquatic environment would be subject to volatilization and biodegradation thereby reducing aquatic exposure. Although 1-BP is not a priority pollutant, EPA pretreatment regulations for industrial users discharging wastewater to POTWs for treatment prohibit the discharge of flammable substances and substances that could generate toxic vapors to POTWs. These restrictions are expected to limit the discharge of 1-BP to POTWs and ultimately to surface water. Recent TRI reporting indicated 0 pounds released to POTWs and 5 pounds released directly to water in 2016 further indicating that general population and environmental exposure via direct releases to surface waters or releases of 1-BP by POTWs is not a pathway for further exposure analysis.

In addition, EPA does not expect to further analyze hazard to aquatic organisms exposed to 1-BP in surface water. Based on 1-BP surface water concentrations estimated using TRI 2016 releases to water, EFAST modeling and the acute fish toxicity $EC_{50}$ value 24.3 mg/L, the concentration of concern is not expected to be exceeded. For three different conservative scenarios (1, 20, and 100 days per year), the screening-level surface water concentrations were well below levels of concern for aquatic species. In addition, 1-BP is expected to be volatile from surface water based on the estimated Henry's Law Constant, mitigating exposure to aquatic life. Thus, EPA does not expect to further analyze ecological aquatic species in the risk evaluation. This conclusion is supported by the ecological risk classification derived for 1-BP by Environment and Climate Change Canada which identified a low ecological hazard and exposure for 1-BP (https://www.ec.gc.ca/ese-ees/A96E2E98-2A04-40C8-9EDC-08A6DFF235F7/CMP3%20ERC_EN.pdf). (ECCC, 2016)

***Biosolids, Sediment and Soil Pathways***

EPA does not expect to further analyze releases to biosolids, sediment or soils. Based on the log $K_{oc}$ of 1.6, 1-BP is not expected to adsorb strongly to sediment or soil. If present in biosolids, 1-BP would be expected to associate with the aqueous component and volatilize to air as the biosolids are applied to soil and allowed to dry. Due to its water solubility and low sorption, some 1-BP associated with land applied sludge could migrate with water towards groundwater, however, volatilization and biodegradation may attenuate migration. Therefore, based on the characteristics of environmental fate and industrial release

information, exposure to the general population and aquatic biota via surface water, drinking water, and sediment is expected to be low. In addition, EPA does not plan to further analyze hazard to aquatic organisms exposed to 1-BP in sediment or soil environments. Based on the log $K_{oc}$ of 1.6 and high water solubility (2.45 g/L), 1-BP is not expected to significantly partition to sediments or soils. Given low releases to water and low concentrations in the water column, low concentrations in sediments would also be expected. 1-BP released to soil is not expected to be a viable pathway of exposure for terrestrial species as 1-BP released to surface soil is expected to volatilize rapidly due to high vapor pressure (146 mmHg at 25 ºC). Thus, EPA does not expect to further analyze sediment and soil ecological species in the risk evaluation.

#### 2.5.3.3 Pathways That EPA Does Not Expect to Include in the Risk Evaluation

Exposures to receptors (i.e., general population, terrestrial species) may occur from industrial and/or commercial uses; industrial releases to air, water or land; and other conditions of use. As described in Section 2.5, EPA does not expect to include in the risk evaluation pathways under programs of other environmental statutes, administered by EPA, which adequately assess and effectively manage exposures and for which long-standing regulatory and analytical processes already exist. These pathways are described below.

***Disposal Pathways***

1-BP is regulated as a hazardous waste, waste code D001 (ignitable liquids, 40CFR 261.21). The general RCRA standard in section 3004(a) for the technical (regulatory) criteria that govern the management (treatment, storage, and disposal) of hazardous waste (i.e., Subtitle C) are those "necessary to protect human health and the environment," RCRA 3004(a). The regulatory criteria for identifying "characteristic" hazardous wastes and for "listing" a waste as hazardous also relate solely to the potential risks to human health or the environment. 40 C.F.R. §§ 261.11, 261.21-261.24. RCRA statutory criteria for identifying hazardous wastes require EPA to "tak[e] into account toxicity, persistence, and degradability in nature, potential for accumulation in tissue, and other related factors such as flammability, corrosiveness, and other hazardous characteristics." Subtitle C controls cover not only hazardous wastes that are landfilled, but also hazardous wastes that are incinerated (subject to joint control under RCRA Subtitle C and the Clean Air Act (CAA) hazardous waste combustion MACT) or injected into UIC Class I hazardous waste wells (subject to joint control under Subtitle C and the Safe Drinking Water Act (SDWA)).

Emissions from hazardous waste incinerators will not be included in the risk evaluation. 40 CFR 264.345 specifies performance standards for hazardous waste incinerators. An incinerator burning hazardous waste must achieve a destruction and removal efficiency (DRE) of 99.99% for each principal organic hazardous constituent. Furthermore, RCRA provisions for site-specific risk assessments and the Hazardous Waste Combustor maximum achievable control technology (MACT) rule provisions for a Residual Risk and Technology Review together cover risks for RCRA hazardous wastes and CAA HAPs. Air emissions from municipal and industrial waste incineration and energy recovery units are regulated under the Clean Air Act. Incineration treatment of 1-BP would be subject to these regulations, as would 1-BP burned for energy recovery.

EPA does not expect to include on-site releases to land that go to underground injection in its risk evaluation. TRI reporting in 2016 only indicated 10 pounds released to underground injection to a Class I well and no releases to underground injection wells of Classes II-VI. Environmental disposal of 1-BP injected into Class I well types is managed and prevented from further environmental release by RCRA

and SDWA regulations. Therefore, disposal of 1-BP via underground injection is not likely to result in environmental and general population exposures.

EPA does not expect to include on-site releases to land that go to RCRA Subtitle C hazardous waste landfills in its risk evaluation. Based on 2016 reporting to TRI, there were 57,617 pounds of 1-BP disposal to an on-site RCRA Subtitle C landfill. Design standards for Subtitle C landfills require double liner, double leachate collection and removal systems, leak detection system, run on, runoff, and wind dispersal controls, and a construction quality assurance program. They are also subject to closure and post-closure care requirements including installing and maintaining a final cover, continuing operation of the leachate collection and removal system until leachate is no longer detected, maintaining and monitoring the leak detection and groundwater monitoring system. Bulk liquids may not be disposed in Subtitle C landfills. Subtitle C landfill operators are required to implement an analysis and testing program to ensure adequate knowledge of waste being managed, and to train personnel on routine and emergency operations at the facility. Hazardous waste being disposed in Subtitle C landfills must also meet RCRA waste treatment standards before disposal. Given these controls, general population exposure to 1-BP in groundwater from Subtitle C landfill leachate is not expected to be a significant pathway.

EPA does not expect to include on-site releases to land from RCRA Subtitle D municipal solid waste landfills (MSWLFs) or exposures of the general population (including susceptible populations) or terrestrial species from such releases in the TSCA evaluation. While permitted and managed by the individual states, municipal solid waste landfills (MSWLFs) are required by federal regulations to implement many of the same requirements as Subtitle C landfills. MSWLFs must have a liner system with leachate collection and conduct groundwater monitoring and corrective action when releases are detected. MSWLFs are also subject to closure and post-closure care requirements, as well as providing financial assurance for funding of any needed corrective actions. MSWLFs have also been designed to allow for the small amounts of hazardous waste generated by households and very small quantity waste generators (less than 100 kg per month). Bulk liquids, such as free solvent, may not be disposed of at MSWLFs.

EPA does not expect to include on-site releases to land from industrial non-hazardous and construction/demolition waste landfills. Industrial non-hazardous and construction/demolition waste landfills are primarily regulated under state regulatory programs. States must also implement limited federal regulatory requirements for siting, groundwater monitoring, and corrective action, and a prohibition on open dumping and disposal of bulk liquids. States may also establish additional requirement such as for liners, post-closure and financial assurance, but are not required to do so. Therefore, EPA does not expect to include this pathway in the risk evaluation.

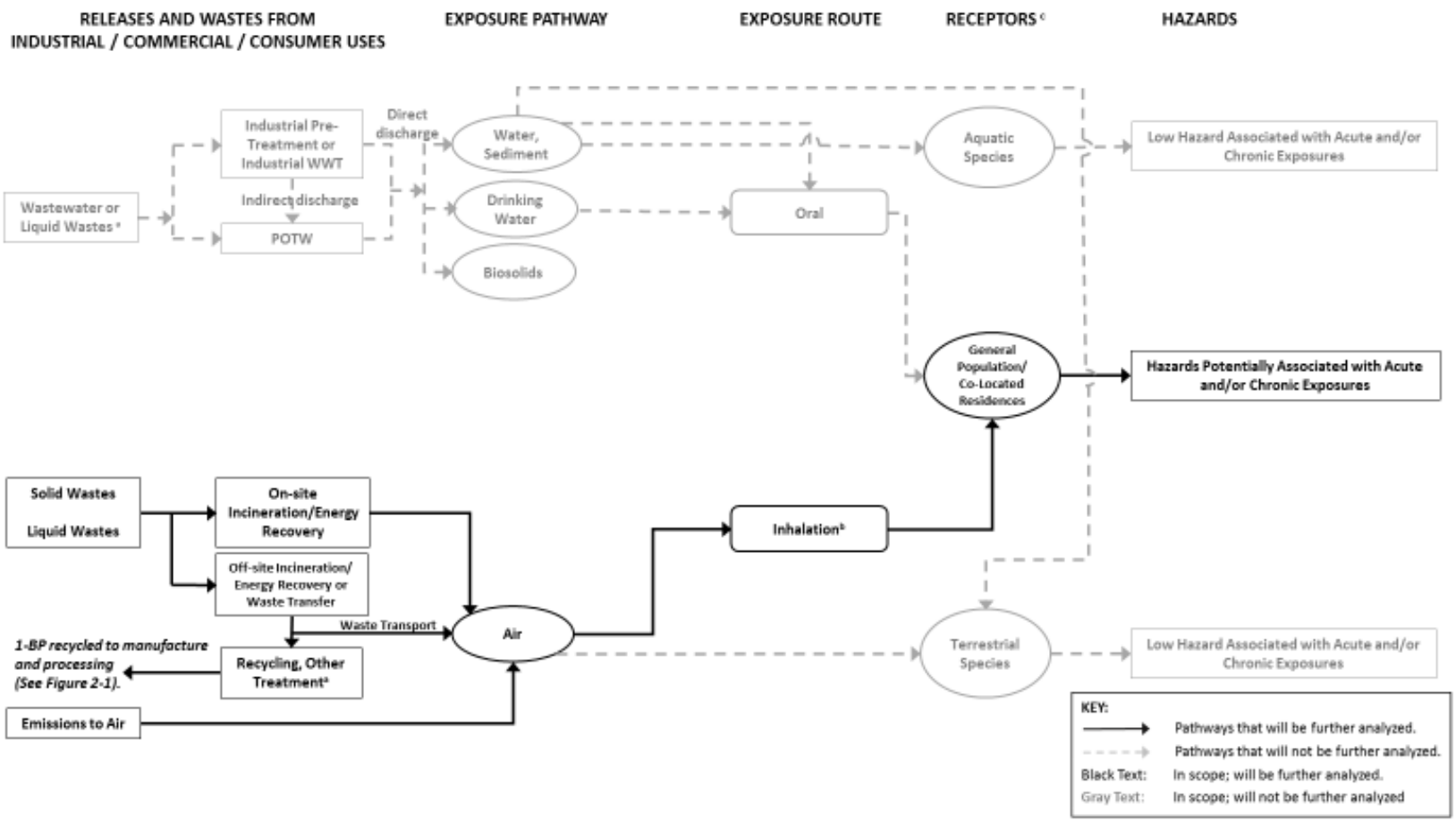


**Figure 2-4. 1-BP Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards**

The conceptual model presents the exposure pathways, exposure routes and hazards to environmental receptors from environmental releases and wastes of 1-BP.

[a]Industrial wastewater may be treated on-site and then released to surface water (direct discharge), or pre-treated and released to POTW (indirect discharge).

[b]Presence of mist is not expected. Dermal and oral exposures are expected to be low.

[c]Receptors include potentially exposed or susceptible subpopulations.

## 2.6 Analysis Plan

The analysis plan presented in the Problem Formulation elaborates on the initial analysis plan that was published in the Scope of the Risk Evaluation for 1-BP (Scope Document, EPA-HQ-OPPT-2016-0741-0049).

The analysis plan is based on the conditions of use of 1-BP, as described in Section 2.2 of this Problem Formulation. EPA is implementing systematic review approaches and/or methods to identify, select, assess, integrate and summarize the findings of studies supporting the TSCA risk evaluation. The analytical approaches and considerations in the analysis plan are used to frame the scope of the systematic review activities for this assessment. The supplemental document, *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018), provides additional information about criteria and methods that have been and will be applied to the first 10 chemical risk evaluations.

While EPA has conducted a comprehensive search for reasonably available data as described in the Scope of the Risk Evaluation for 1-BP (Scope Document, EPA-HQ-OPPT-2016-0741-0049), EPA encourages submission of additional existing data, such as full study reports or workplace monitoring from industry sources, that may be relevant for refining conditions of use, exposures, hazards and potentially exposed or susceptible subpopulations during the risk evaluation. EPA will continue to consider new information submitted by the public.

During the risk evaluation, EPA will rely on the search results [*1-Bromopropane (CASRN 106-94-5) Bibliography: Supplemental File for the TSCA Scope Document* EPA-HQ-OPPT-2016-0741-0047)], or perform supplemental searches to address specific questions. Further, EPA may consider any relevant confidential business information (CBI) in the risk evaluation in a manner that protects the confidentiality of the information from public disclosure. The analysis plan is based on EPA's knowledge of 1-BP to date, which includes partial, but not complete review of identified literature. If additional data or approaches become available, EPA may refine its analysis plan based on this information.

### 2.6.1 Exposure

Based on their physical-chemical properties, expected sources, and transport and transformation within the outdoor and indoor environment chemical substances are more likely to be present in some media and less likely to be present in others. Media-specific levels will vary based on the chemical substance of interest. For most high-priority chemical substances level(s) can be characterized through a combination of available monitoring data and modeling approaches.

#### 2.6.1.1 Environmental Releases

EPA expects to analyze releases to environmental media as follows:

1) **Review reasonably available published literature or information on processes and activities associated with the conditions of use to evaluate the types of releases and wastes generated.**

   EPA has reviewed some key data sources containing information on processes and activities resulting in releases, and the information found is shown in Appendix B.1. EPA will continue to

review potentially relevant data sources identified in Table_Apx B-3 in Appendix B during risk evaluation.

EPA plans to review the following key data sources in Table 2-8 for information on processes and activities resulting in environmental releases. The evaluation strategy for engineering and occupational data sources discussed in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018) describes how studies will be reviewed. EPA has also previously compiled process information for several conditions of use in the 2016 Draft Risk Assessment (U.S. EPA, 2016b).

**Table 2-8. Potential Sources of Environmental Release Data**

| |
|---|
| 2017 ATSDR Toxicological Profile for 1-BP: Toxicological Profile for 1-Bromopropane (2017) |
| U.S. EPA TRI Data (Reporting Year 2016 only) |
| EPA AP-42 Air Emission Factors |
| CARB ISOR for Proposed ATCM |

**2) Review reasonably available chemical-specific release data, including measured or estimated release data (e.g., data collected under the TRI and National Emissions Inventory [NEI] programs).**

EPA plans to review release data to inform releases associated with the applicable conditions of use for 1-BP. For example, EPA's Toxics Release Inventory (TRI) data will be used to inform the various subcategories, such as air releases, associated with the disposal life cycle stage. According to TRI data for Reporting Year 2016, the majority of on-site releases of 1-BP were to air (fugitive and stack), followed by land disposal. Only five pounds of 1-BP were discharged to water. Of the off-site transfers, the majority went to incineration and land disposal. No off-site transfer to wastewater treatment were reported.

Additionally, for conditions of use where no measured data on releases are available, EPA may use a variety of methods including the application of default assumptions such as standard loss fractions associated with drum cleaning (3%) or single process vessel cleanout (1%), or the use of EPA Generic Scenarios and/or OECD Emission Scenario Documents to predict releases and their corresponding media.

EPA Generic Scenarios are available at the following: https://www.epa.gov/tsca-screening-tools/using-predictive-methods-assess-exposure-and-fate-under-tsca#fate.

OECD Emission Scenario Documents are available at the following: http://www.oecd.org/chemicalsafety/risk-assessment/emissionscenariodocuments.htm

EPA will also review data sources containing estimated data and identify data gaps. The 2016 Draft Risk Assessment (U.S. EPA, 2016b) contains estimates of 1-BP emission rates for several conditions of use, including dry cleaning, spot cleaning, vapor degreasing, cold cleaning, and aerosol degreasing. EPA will use existing emission factors and emission rate data to estimate environmental releases of 1-BP to air from these uses.

**3) Understand and consider regulatory limits that may inform estimation of environmental releases.**

Information from various EPA statutes (including, for example, regulatory limits, reporting thresholds, or disposal requirements) may be used to assess releases. EPA may determine that a condition of use is unlikely to result in release to a particular media based on existing chemical-specific regulations even though an Emission Scenario or EPA Generic Scenario document indicates a likely release to that same media.

While 1-BP is not a hazardous air pollutant (HAP) regulated under the Clean Air Act, some related rules may provide relevant information on sectors using 1-BP. For example, the NESHAP for Halogenated Solvent Cleaning (40 CFR Part 63, Subpart T) may provide useful information on industry sectors that use solvents (including 1-BP) for degreasing applications.

EPA will further consider the applicability of EPA regulations to 1-BP during the development of the risk evaluation.

**4) Review and determine applicability of Organization for Economic Co-operation and Development (OECD) Emission Scenario Documents (ESDs) and EPA Generic Scenarios (GSs) to estimation of environmental releases.**

EPA will analyze the conditions of use to determine which ESDs and GSs can be applied. For example, EPA may use the ESD on Industrial Use of Industrial Cleaners, the ESD on Industrial Use of Adhesives for Substrate Bonding, and the GS on Application of Agricultural Pesticides to assess potential releases to all relevant media for some conditions of use, such as the uses of 1-BP in cleaning and degreasing, adhesive, and agricultural products.

For other conditions of use, such as manufacture and import of 1-BP, use of 1-BP in insulation material, use of cutting oils, and use of 1-BP in asphalt extraction, EPA may not be able to apply generic release scenarios. In those cases, EPA may conduct industry outreach efforts, consult process technology literature sources such as the Kirk-Othmer Encyclopedia of Chemical Technology, or perform supplemental literature searches to better understand the process steps involved in that condition of use before a release assessment can be made.

**5) Map or group each condition(s) of use to a release assessment scenario.**

EPA has identified release/occupational exposure scenarios and mapped them to relevant conditions of use in Appendix D. As presented in the fourth column of the table in this appendix, EPA has grouped the uses into 16 representative release/exposure scenarios that will be further evaluated. EPA may further refine the mapping/grouping of these scenarios based on factors (e.g., process equipment and handling, magnitude of production volume used, and exposure/release sources) corresponding to conditions of use as additional information is identified during risk evaluation.

**6) Evaluate the weight of the evidence of environmental release data.**

EPA will rely on the weight of the scientific evidence when evaluating and integrating environmental release data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data

for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

#### 2.6.1.2 Environmental Fate

EPA expects to analyze fate and transport in environmental media as follows:

1) **Review reasonably available measured or estimated environmental fate endpoint data collected through the literature search.**

   A general overview of persistence and bioaccumulation was presented in the 2016 Draft Risk Assessment (U.S. EPA, 2016b). Key environmental fate characteristics were included in the Scope Document (EPA-HQ-OPPT-2016-0741-0049) and in previous assessments of 1-BP, including that conducted by the US Agency for Toxic Substances and Disease Registry (ATSDR, 2017). These information sources will be used as a starting point for the environmental fate assessment. Other sources that will be consulted include those that are identified through the systematic review process. Studies will be evaluated using the evaluation strategies laid out in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018) document.

   If measured values resulting from sufficiently high-quality studies are not available (to be determined through the systematic review process), chemical properties will be estimated using EPI Suite, SPARC, and other chemical parameter estimation models. Estimated fate properties will be reviewed for applicability and quality.

2) **Using measured environmental fate data and/or environmental fate modeling, determine the influence of environmental fate endpoints (e.g., persistence, bioaccumulation, partitioning, transport) on exposure pathways and routes of exposure to human receptors.**

   Measured fate data including volatility and atmospheric photolysis rates along with physical-chemical properties and models, such as the EPI Suite™ Atmospheric Oxidation Program (which estimates rates of atmospheric oxidation), will be used to characterize the persistence of 1-BP in air and its impact on exposure.

3) **Evaluate the weight of the evidence of environmental fate data.**

   EPA will rely on the weight of the scientific evidence when evaluating and integrating environmental fate data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

#### 2.6.1.3 Environmental Exposures

EPA does not plan to further analyze environmental exposures to 1-BP, based on the rationale described in Section 2.3.4.

#### 2.6.1.4 General Population

EPA expects to analyze general population exposures as follows:

1) **Review reasonably available environmental and biological monitoring data for media to which general population exposures are expected. For exposure pathways where data are not available, review existing exposure models that may be applicable in estimating exposure levels.**

For 1-BP, the media of interest are expected to be ambient air and indoor air. EPA will review existing exposure models for applicability in estimating general population exposure levels associated with ongoing industrial and/or commercial releases. EPA will review reasonably available data that may be used in developing, adapting or applying exposure models. These data may include data on 1-BP or analogous chemical substances. Exposure pathways which may be modeled include air releases from point sources using air dispersion models.

Available exposure models will be evaluated and considered alongside available monitoring data to characterize environmental exposures for ambient air. Modeling approaches to estimate ambient air will generally consider the following inputs: release into air, fate and transport (partitioning within media) and characteristics of the environment (e.g., meteorological information). Some preliminary analysis may be performed to understand the impact of known releases to the overall characterization of concentrations in the environment.

Available release data (e.g. TRI data) will be used in informing releases to the environment. As data are available, EPA will estimate the air concentrations near point sources using release estimates or reported data using air dispersion models (e.g., AERMOD, AERSCREEN) incorporating what is known of incineration efficiencies (where applicable), fate and transport properties, and physical chemical properties.

2) **Consider and incorporate applicable media-specific regulations into exposure scenarios or modeling.**

1-BP is not listed on the TNSSS (Targeted National Sewage Sludge Survey), DMR (Discharge Monitoring Report), or as one of the 189 Hazardous Air Pollutants (HAPs) under Section 112(b) of the Clean Air Act. There are no specific EPA regulations regarding drinking water health advisories, ambient water quality criteria, or effluent level guidelines.

1-BP is a listed substance subject to reporting requirements under the Emergency Planning and Community Right-To-Know Act (EPCRA) – Section 313, and the TRI reporting information will be utilized for analyzing exposures to the general population via releases from manufacturing, processing and use of 1-BP. EPA may model air concentrations near facilities using air dispersion modeling applications (e.g., AERMOD or AERSCREEN).

3) **Review reasonably available data that may be used in developing, adapting or applying exposure models to the particular risk evaluation. For example, existing models developed for a chemical assessment may be applicable to another chemical assessment if model parameter data are available.**

EPA will review reasonably available data that may be used in developing, adapting or applying exposure models. These data may include modeled exposure estimates conducted by other organizations for 1-BP or analogous chemical substances. Fate and transport information will be used to inform calculations of human exposures via air. The concentrations in air will be used as inputs into exposure models to estimate general population exposures. Sources of data may

include TRI reporting for 1-BP. TRI data show air as a primary medium of environmental release. These releases include both fugitive air emissions and point source air emissions.

4) **Review reasonably available information on releases to determine how modeled estimates of concentrations near industrial point sources compare with available monitoring data.**

   General population exposure pathways expected to be relatively higher include inhalation of ambient air or inhalation in co-located buildings. EPA will review results of use specific and background exposure scenarios and select output metric relevant for exposure assessment. The metrics most likely to be relevant for 1-BP are Lifetime Average Daily Concentration ($mg/m^3$) and Average Daily Concentration ($mg/m^3$) for inhalation routes of exposure, and Lifetime Average Daily Dose (mg/kg/day) and Average Daily Dose (mg/kg/day) for dermal routes of exposure. Results within and across scenarios will be compared. For example, modeled estimates near industrial point sources can be compared with those based on available monitoring data.

5) **Review reasonably available population- or subpopulation-specific exposure factors and activity patterns to determine if potentially exposed or susceptible subpopulations need be further defined.**

   Considerations will include:

   - Age-specific differences (exposure factors and activity patterns) for populations defined in the exposure scenario table in Appendix E;
   - Exposure factors and activities patterns will be sourced from EPA's 2011 Exposure Factors Handbook (U.S. EPA, 2011);
   - Subpopulations who may have greater exposure due to magnitude, frequency or duration of exposure as they apply a person's activity patterns or exposure factors;
   - Subpopulations who may have greater exposure or susceptibility due to spatial characteristics (e.g., those who live near point sources, those who are co-located with emission sources).

6) **Analyze the weight of the evidence of general population exposure data.**

   EPA will rely on the weight of the scientific evidence when analyzing and integrating data related to general population exposures. The weight of the evidence may include qualitative and quantitative sources of information. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, analyze the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

7) **Map or group each condition of use to general population exposure assessment scenarios.**

   EPA has identified general population exposure scenarios that include sources of exposure (i.e., releases to the environment), exposure pathways, exposure routes, and populations exposed and mapped them to relevant releases and waste streams, as shown in Appendix E. EPA may refine the mapping/grouping of general population exposures scenarios as the relationship between sources of exposure and conditions of use are further characterized.

EPA will further refine and finalize exposure scenarios for the general population with the following considerations:

- Temporal trends in uses and resulting sources/releases of 1-BP to the environment over time;
- Characterization of background levels in the environment that may or may not be generally attributable to any one use or source but from a combination of uses or sources which present exposure pathways for the general population;
- Further mapping of releases to lifecycle stages and uses/sources to environmental media;
- Consideration of spatial differences between populations located near industrial point sources and those exposed at lower background levels;
- Refined definitions of potentially exposed or susceptible subpopulations.

EPA plans to analyze a variety of data types to determine which types are most appropriate when quantifying exposure scenarios. Environmental monitoring data, biomonitoring data, modeled estimates, experimental data, epidemiological data, and survey-based data can all be used to quantify exposure scenarios. In an effort to associate exposure estimates with sources of exposure and/or conditions of use, EPA will consider source apportionment across exposure scenarios during risk evaluation. EPA anticipates that there will be a wide range in the relative exposure potential of the exposure scenarios identified in Appendix E. Source apportionment characterizes the relative contribution of any of the following: a use/source toward a total media concentration, a media concentration toward a total exposure route, or an exposure route toward a total external or internal dose. This consideration may be qualitative, semi-quantitative, or quantitative, and is dependent upon available data and approaches. For example, EPA may consider the co-location of TSCA industrial facilities with available monitoring data or modeled estimates. EPA may compare modeled estimates for discrete outdoor and indoor sources/uses that apply to unique receptor groups. If available, EPA will compare multiple scenario-specific and background exposure doses estimated from media-specific concentrations and exposure factors with available biomonitoring data. The forward-calculated and back-calculated exposures could be compared to characterize the relative contribution from defined exposure scenarios.

After refining and finalizing exposure scenarios, EPA will quantify concentrations and/or doses for these scenarios. The number of scenarios will depend on how unique combinations of uses, exposure pathways, and receptors are characterized. The number of scenarios is also dependent upon the available data and approaches to quantify scenarios. When quantifying exposure scenarios, EPA plans to use a tiered approach. First-tier analysis is based on data that is readily available without a significant number of additional inputs or assumptions, and may be qualitative, semi-quantitative, or quantitative. First-tier analyses were conducted during problem formulation and are expected to continue during risk evaluation. The results of first tier analyses inform whether scenarios require more refined analysis. Refined analyses will be iterative, and require careful consideration of variability and uncertainty. Should data become available that summarily alters the overall conclusion of a scenario through iterative tiering, EPA can refine its analysis during risk evaluation.

### 2.6.1.5 Occupational Exposures

EPA expects to consider and analyze both worker and occupational non-user exposures as follows:

**1) Review reasonably available exposure monitoring data for specific condition(s) of use.**

Exposure data to be reviewed may include workplace monitoring data collected by government agencies such as OSHA and NIOSH, and monitoring data found in published literature (e.g., personal exposure monitoring data (direct measurements) and area monitoring data (indirect measurements)). Data, information, and studies will be evaluated using the evaluation strategies laid out in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018). For some OSHA data, NAICS codes included with the data will be matched with potentially applicable conditions of use, and data gaps will be identified where no data are found for particular conditions of use. EPA will attempt to address data gaps identified as described in steps 2 and 3 below. Where possible, job descriptions may be useful in distinguishing exposures to different subpopulations within a particular condition of use. EPA has also identified additional data sources that may contain relevant monitoring data for the various conditions of use. EPA will review these sources, identified in Table 2-9 and in Table_Apx B-3 in Appendix B, and will extract relevant data for consideration and analysis during risk evaluation.

EPA will evaluate and consider applicable regulatory and non-regulatory exposure limits. Available data sources that may contain relevant monitoring data for the various conditions of use are listed in Table 2-9.

OSHA has not established any occupational exposure limits for 1-BP. However, the American Conference of Governmental Industrial Hygienists (ACGIH) has adopted a recommended Threshold Limit Value (TLV) of 0.1 ppm based on a time-weighted average (TWA) over an 8-hour workday. EPA will consider the influence of the recommended exposure limits on occupational exposures in the occupational exposure assessment.

**Table 2-9. Potential Sources of Occupational Exposure Data**

| |
|---|
| 2017 ATSDR Toxicological Profile for 1-BP: Toxicological Profile for 1-Bromopropane (2017) |
| U.S. OSHA Chemical Exposure Health Data (CEHD) program data |
| U.S. NIOSH Health Hazard Evaluation (HHE) Program reports |
| 2016 Draft Risk Assessment (U.S. EPA, 2016b) |
| CARB ISOR for Proposed ATCM |
| Draft NIOSH Criteria Document for a Recommended Standard for Occupational Exposure to 1-Bromopropane |

**2) Review reasonably available exposure data for surrogate chemicals that have uses and chemical and physical properties similar to 1-BP.**

If surrogate data are identified, these data will be matched with applicable conditions of use for potentially filling data gaps. For several uses including use of adhesives, and cleaning products,

EPA believes that trichloroethylene and other similar solvents may share the same or similar conditions of use and may be considered as surrogates for 1-BP.

**3) For conditions of use where data are limited or not available, review existing exposure models that may be applicable in estimating exposure levels.**

EPA has identified potentially relevant OECD emissions scenario documents (ESDs) and EPA generic scenarios (GSs) corresponding to some conditions of use. For example, the ESD on Industrial Use of Adhesives for Substrate Bonding, the ESD on Metalworking Fluids, and the GS on Use of Vapor Degreasers are some of the ESDs and GSs that EPA may use to estimate occupational exposures. EPA will need to critically review these generic scenarios and ESDs to determine their applicability to the conditions of use assessed. EPA was not able to identify ESDs or GSs corresponding to several conditions of use, including recycling of 1-BP and solvent mixtures containing 1-BP, processing and formulation of 1-BP into industrial, commercial and consumer products, use of 1-BP in insulation materials, and use of 1-BP in asphalt extraction. EPA will perform additional targeted research, such as consulting Kirk-Othmer, in order to better understand those conditions of use, which may inform identification of exposure scenarios. EPA may also need to perform targeted research to identify applicable models that EPA may use to estimate exposures for certain conditions of use.

Furthermore, a mass-balance based model that has been used in addressing data gaps in some conditions of use is the Near-Field/Far-Field (NF/FF) model. This or other models, may be explored where models specific to conditions of use are not found. If any models are identified as applicable, EPA will search for appropriate model parameter data. If parameter data can be located or assumed, exposure estimates generated from these models may be used for potentially filling data gaps. EPA may perform additional targeted research to better understand conditions of use, which may inform identification of exposure scenarios. EPA may also need to perform targeted research to identify applicable models that EPA may use to estimate exposures for certain conditions of use.

**4) Review reasonably available data that may be used in developing, adapting or applying exposure models to the particular risk evaluation.**

If necessary, EPA will analyze relevant data to determine whether the data can be used to develop, adapt, or apply models for specific conditions of use and corresponding exposure scenarios.

In the 2016 Draft Risk Assessment (U.S. EPA, 2016b), EPA previously developed models to assess inhalation exposures to workers and occupational non-users during the use of 1-BP in dry cleaning, spot cleaning, open-top batch vapor degreasing, cold cleaning, and aerosol degreasing. The peer reviewers provided comments on EPA's modeling approach, including recommendations on specific model input parameters. During risk evaluation, EPA will further refine the exposure models for these uses based on peer reviewer feedback.

5) **Consider and incorporate applicable engineering controls and/or personal protective equipment into exposure scenarios.**

EPA will review potential data sources on engineering controls and personal protective equipment as identified in Table_Apx B-6 in Appendix B and determine their applicability and incorporation into exposure scenarios during risk evaluation.

6) **Map or group each condition of use to occupational exposure assessment scenario(s).**

EPA has identified release/occupational exposure scenarios and mapped them to relevant conditions of use in Appendix D. As presented in the fourth column of the table in this appendix, EPA has grouped the uses into 16 representative release/exposure scenarios each with 5-6 unique combinations of exposure pathway, route, and receptor that will be further analyzed. EPA may further refine the mapping/grouping of occupational exposure scenarios based on factors (e.g., process equipment and handling, magnitude of production volume used, and exposure/release sources) corresponding to conditions of use as additional information is identified during risk evaluation.

7) **Analyze the weight of evidence of occupational exposure data.**

EPA will rely on the weight of the scientific evidence when evaluating and integrating occupational exposure data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, analyze the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

#### 2.6.1.6 Consumer Exposures

EPA expects to analyze both consumers using a consumer product and bystanders associated with the consumer using the product as follows:

1) **Refine and finalize exposure scenarios for consumers by considering sources of exposure (consumer products), exposure pathways, exposure settings, exposure routes, and populations exposed.**

Considerations for constructing exposure scenarios for consumers:

- Reasonably available data on consumer products or products available for consumer use including the content of 1-BP in products;
- Information characterizing the use patterns of consumer products containing 1-BP including how the product is used, the amount of product used, frequency and duration of use, and room of use;
- The associated exposure setting and route of exposure for consumers;
- Populations who may be exposed to products, including potentially exposed and susceptible subpopulations such as children or women of child bearing age;
- Subsets of consumers who may use commercially available products which have different concentrations of 1-BP or subsets of consumers who may use products more frequently.

**2) Analyze the relative potential of exposure routes based on available data.**

Indoor exposure routes expected to be relatively higher and include inhalation of vapor. The data sources associated with these respective pathways have not been comprehensively analyzed, therefore quantitative comparisons across exposure pathways or in relation to toxicity thresholds are not yet available.

**3) Review existing consumer exposure models that may be applicable in estimating indoor air concentrations (near field and far field) for the user and bystander; and in estimating dermal exposure to the consumer in transient exposures and in longer term (e.g., occluded) exposure scenarios. Determine the applicability of the identified models for use in a quantitative exposure assessment.**

Consumer exposure based indoor exposure models that estimate emission from spray products or liquid products into the indoor environment are available. These models generally consider overall mass transfer informed by the vapor pressure of the chemical, content of the chemical in the product and use patterns and practices. OPPT's CEM or E-FAST model and other similar models can be used to estimate indoor air concentration from use of consumer products containing 1-BP.

**4) Review reasonably available empirical data that may be used in developing, adapting or applying exposure models to the exposure assessment of 1-BP. For example, existing models developed for a chemical assessment may be applicable to another chemical assessment if model parameter data are available.**

To the extent other organizations have already modeled a 1-BP consumer exposure scenario that is relevant to OPPT's assessment, EPA will analyze those modeled estimates. In addition, if modeled estimates for other chemicals with similar physical chemical properties and similar uses area available, those modeled estimates will also be evaluated. The underlying parameters and assumptions of the models will also be analyzed.

**5) Review reasonably available consumer product-specific sources to determine how those exposure estimates compare with each other and with any relevant existing monitoring data.**

The availability of 1-BP concentrations in products will be analyzed. This data provides the source term for any subsequent consumer modeling. Source attribution and comparison of indoor air monitoring will be analyzed.

**6) Review reasonably available population- or subpopulation-specific exposure factors and activity patterns to determine if potentially exposed or susceptible subpopulations need to be further refined.**

Considerations will include:

- Age-specific differences (exposure factors and activity patterns) for populations defined in the exposure scenario table in Appendix E;

- Exposure factors and activities patterns will be sourced from EPA's 2011 Exposure Factors Handbook (U.S. EPA, 2011)
- The characteristics of the user of the consumer product and the bystander in the room, including for example, women of child bearing age and children;
- Subpopulations who may have greater exposure due to magnitude, frequency or duration of exposure as they apply to specific consumer products.

**7) Analyze the weight of the evidence of consumer exposure estimates based on different approaches.**

EPA will rely on the weight of the scientific evidence when evaluating and integrating data related to consumer exposure. The weight of the evidence may include qualitative and quantitative sources of information. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, analyze the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

### 2.6.2 Hazards (Effects)

#### 2.6.2.1 Environmental Hazards

Environmental hazards will not be further analyzed because exposure analysis conducted using physical and chemical properties, fate information and TRI environmental releases for 1-BP show that ecological receptors are not significantly exposed to TSCA-related environmental releases of this chemical.

#### 2.6.2.2 Human Health Hazards

EPA expects to analyze human health hazards as follows:

**1) Review reasonably available human health hazard data, including data from alternative test methods (e.g., computational toxicology and bioinformatics; high-throughput screening methods; data on categories and read-across; *in vitro* studies; systems biology).**

Human health studies will be evaluated using the evaluation strategies laid out in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018) document. Human and animal data will be identified and included as described in the inclusions and exclusion criteria in Appendix F. EPA plans to prioritize the evaluation of mechanistic evidence. Specifically, EPA does not plan to evaluate mechanistic studies unless needed to clarify questions about associations between 1-BP and health effects and its relevance to humans. The *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018), document describes the process of how studies will be evaluated using specific data evaluation criteria and a predetermined approach. Study results will be extracted and presented in evidence tables by hazard endpoint. EPA plans to evaluate relevant studies identified in the 2016 Draft Risk Assessment (U.S. EPA, 2016b) of 1-BP as well as those that were captured in the comprehensive literature search conducted by the Agency for *1-Bromopropane (CASRN 106-94-5) Bibliography: Supplemental File for the TSCA Scope Document;* [EPA-HQ-OPPT-2016-0741-0047; (U.S. EPA, 2017a)]. EPA intends to review studies published after the 2016 Draft Risk Assessment (U.S. EPA,

2016b) to ensure that EPA is considering information that has been made available since that assessment was conducted.

2) **In analyzing reasonably available data, determine whether particular human receptor groups may have greater susceptibility to the chemical's hazard(s) than the general population.**

Reasonably available human health hazard data will be analyzed to ascertain whether some human receptor groups may have greater susceptibility than the general population to 1-BP hazard(s). Susceptibility of particular human receptor groups to 1-BP will be determined by evaluating information on factors that influence susceptibility.

3) **Conduct hazard identification (the qualitative process of identifying non-cancer and cancer endpoints) and dose-response assessment (the quantitative relationship between hazard and exposure) for all identified human health hazard endpoints.**

Human health hazards from acute and chronic exposures will be identified by analyzing the human and animal data that meet the systematic review data quality criteria described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018) document. Data quality evaluation will be performed on key studies identified from the 2016 Draft Risk Assessment (U.S. EPA, 2016b) of 1-BP, and studies published after 2016 that were identified in the comprehensive literature search (see *1-Bromopropane (CASRN 106-94-5) Bibliography: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0741-0047)). Hazards identified by studies meeting data quality criteria will be grouped by routes of exposure relevant to humans (oral, dermal, inhalation) and by cancer and noncancer endpoints.

Dose-response assessment will be performed in accordance with EPA guidance (U.S. EPA, 2012a, 2011, 1994). Dose-response analyses performed for the 2016 Draft Risk Assessment (U.S. EPA, 2016b) of 1-BP may be used if the data meet data quality criteria and if additional information on the identified hazard endpoints or additional hazard endpoints would not alter the analysis.

4) **Derive points of departure (PODs) where appropriate; conduct benchmark dose modeling (BMD) depending on the available data. Adjust the PODs as appropriate to conform (e.g., adjust for duration of exposure) to the specific exposure scenarios evaluated.**

Hazard data will be evaluated to determine the type of dose-response modeling that is applicable. Where modeling is feasible, a set of dose-response models that are consistent with a variety of potentially underlying biological processes will be applied to empirically model the dose-response relationships in the range of the observed data consistent with the EPA *Benchmark Dose Technical Guidance Document* (U.S. EPA, 2012a). Where dose-response modeling is not feasible, NOAELs or LOAELs will be identified.

EPA will evaluate whether the available PBPK and empirical kinetic models are adequate for route-to-route and interspecies extrapolation of the POD, or for extrapolation of the POD to appropriate exposure durations for the risk evaluation.

5) **Consider the route(s) of exposure (oral, inhalation, dermal), available route-to-route extrapolation approaches, available biomonitoring data and available approaches to correlate internal and external exposures to integrate exposure and hazard assessment.**

EPA believes there are sufficient health effects data to conduct dose-response analysis and/or benchmark dose modeling or NOAELs or LOAELs for inhalation route of exposure.

If sufficient dermal toxicity studies are not identified in the literature search to assess risks from dermal exposures, then a route-to-route extrapolation from the inhalation and oral toxicity studies would be needed to assess systemic risks from dermal exposures. Without an adequate PBPK model, the approaches described in the EPA guidance document *Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part E, Supplemental Guidance for Dermal Risk Assessment)* (U.S. EPA, 2004b) could be applied. These approaches may be able to further inform the relative importance of dermal exposures compared with other routes of exposure.

6) **Evaluate the weight of the evidence of human health hazard data.**

EPA will rely on the weight of the scientific evidence when analyzing and integrating human health hazard data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

### 2.6.3 Risk Characterization

Risk characterization is an integral component of the risk assessment process for both ecological and human health risks. EPA will derive the risk characterization in accordance with EPA's *Risk Characterization Handbook* (U.S. EPA, 2000). As defined in EPA's Risk Characterization Policy, "the risk characterization integrates information from the preceding components of the risk evaluation and synthesizes an overall conclusion about risk that is complete, informative and useful for decision makers." Risk characterization is considered to be a conscious and deliberate process to bring all important considerations about risk, not only the likelihood of the risk but also the strengths and limitations of the assessment, and a description of how others have assessed the risk into an integrated picture.

Risk characterization at EPA assumes different levels of complexity depending on the nature of the risk assessment being characterized. The level of information contained in each risk characterization varies according to the type of assessment for which the characterization is written. Regardless of the level of complexity or information, the risk characterization for TSCA risk evaluations will be prepared in a manner that is transparent, clear, consistent, and reasonable (TCCR) (U.S. EPA, 2000). EPA will also present information in this section consistent with approaches described in the *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act* (82 FR 33726). For instance, in the risk characterization summary, EPA will further carry out the obligations under TSCA section 26; for example, by identifying and assessing uncertainty and variability in each step of the risk evaluation, discussing considerations of data quality such as the reliability, relevance and whether the methods utilized were reasonable and consistent, explaining any assumptions used, and discussing information generated from independent peer review. EPA will also be guided by EPA's Information Quality Guidelines (U.S. EPA, 2002) as it provides guidance for presenting risk information. Consistent with those guidelines, in the risk characterization, EPA will also identify: (1) Each population addressed by

an estimate of applicable risk effects; (2) the expected risk or central estimate of risk for the potentially exposed or susceptible subpopulations affected; (3) each appropriate upper-bound or lower bound estimate of risk; (4) each significant uncertainty identified in the process of the assessment of risk effects and the studies that would assist in resolving the uncertainty; and (5) peer reviewed studies known to the Agency that support, are directly relevant to, or fail to support any estimate of risk effects and the methodology used to reconcile inconsistencies in the scientific information.

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# APPENDICES

# APPENDIX A REGULATORY HISTORY

## A.1 Federal Laws and Regulations

**Table_Apx A-1. Federal Laws and Regulations**

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| **US EPA Regulations** | | |
| Toxic Substances Control Act (TSCA) – Section 6(b) | EPA is directed to identify and begin risk evaluations on 10 chemical substances drawn from the 2014 update of the TSCA Work Plan for Chemical Assessments. | 1-BP is on the initial list of chemicals to be evaluated for unreasonable risk under TSCA (81 FR 91927, December 19, 2016) |
| Toxic Substances Control Act (TSCA) – Section 8(a) | The TSCA section 8(a) Chemical Data Reporting (CDR) Rule requires manufacturers (including importers) to give EPA basic exposure-related information on the types, quantities and uses of chemical substances produced domestically and imported into the US. | 1-BP manufacturing, importing, processing, and use information is reported under the Chemical Data Reporting (CDR) rule (76 FR 50816, August 16, 2011). |
| Toxic Substances Control Act (TSCA) – Section 8(b) | EPA must compile, keep current, and publish a list (the TSCA Inventory) of each chemical substance manufactured, processed, or imported in the United States. | 1-BP was on the initial TSCA Inventory and therefore was not subject to EPA's new chemicals review process (60 FR 16309, March 29, 1995). |
| Toxic Substances Control Act (TSCA) – Section 8(e) | Manufacturers (including importers), processors, and distributors must immediately notify EPA if they obtain information that supports the conclusion that a chemical substance or mixture presents a substantial risk of injury to health or the environment. | Eleven notifications of substantial risk (Section 8(e)) received before 2001 (US EPA, ChemView. Accessed April 13, 2017). |
| Toxic Substances Control Act (TSCA) – Section 4 | Provides EPA with authority to issue rules and orders requiring manufacturers (including importers) and processors to test chemical substances and mixtures. | One submission from a test rule (Section 4) received in 1981 (US EPA, ChemView. Accessed April 13, 2017). |
| Emergency Planning and Community Right-To-Know Act (EPCRA) – Section 313 | Requires annual reporting from facilities in specific industry sectors that employ 10 or more full time equivalent employees and that manufacture, process, or otherwise use a Toxics Release Inventory (TRI)-listed chemical in quantities above threshold levels. | 1-BP is a listed substance subject to reporting requirements under 40 CFR 372.65 effective as of January 1, 2016, with reporting due July 1, 2017 (80 FR 72906, November 23, 2015). |

**Table_Apx A-1. Federal Laws and Regulations**

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| Clean Air Act (CAA) – Section 112(b) | This section lists 189 Hazardous Air Pollutants (HAPs) that must be addressed by EPA and includes authority for EPA to add or delete pollutants. EPA may, by rule, add pollutants that present, or may present, a threat of adverse human health effects or adverse environmental effects. | EPA received petitions from the Halogenated Solvent Industry Alliance and the New York State Department of Environmental Conservation to list 1-BP as a *hazardous air pollutant* (HAP) under section 112(b)(1) of the Clean Air Act (80 FR 6676, February 6, 2015). On January 9, 2017, EPA published a draft notice on the rational for granting the petitions to add 1-BP to the list of hazardous air pollutants. Comments are due June 8, 2017 (82 FR 2354, January 9, 2017). Since 1-BP is not a HAP, currently, there are no National Emissions Standards for Hazardous Air Pollutants (NESHAPs) that apply to the life cycle. |
| Clean Air Act (CAA) – Section 183(e) | Section 183(e) requires EPA to list the categories of consumer and commercial products that account for at least 80 percent of all VOC emissions in areas that violate the National Ambient Air Quality Standards (NAAQS) for ozone and to issue standards for these categories that require "best available controls." In lieu of regulations, EPA may issue control techniques guidelines if the guidelines are determined to be substantially as effective as regulations. | 1-BP is listed under the National Volatile Organic Compound Emission Standards for Aerosol Coatings (40 CFR part 59, subpart E). 1-BP has a reactivity factor of 0.35 g O3/g VOC. |
| Clean Air Act (CAA) – Section 612 | Under Section 612 of the Clean Air Act (CAA), EPA's Significant New Alternatives Policy (SNAP) program reviews substitutes for ozone depleting substances within a comparative risk framework. EPA publishes lists of acceptable and unacceptable alternatives. A determination that an alternative is unacceptable, or acceptable only with conditions, is made through rulemaking. | Under EPA's SNAP program, EPA evaluated 1-BP as an acceptable substitute for ozone-depleting substances. In 2007, EPA listed 1-BP as an acceptable substitute for chlorofluorocarbon (CFC)-113 and methyl chloroform in the solvent and cleaning sector for metals cleaning, electronics cleaning, and precision cleaning. EPA recommended the use of personal protective equipment, including chemical goggles, flexible laminate protective gloves and chemical-resistant clothing (72 FR 30142, May 30, 2007). In 2007, the Agency also proposed to list 1-BP as an unacceptable substitute for CFC-113, hydrochlorofluorocarbon (HCFC)- 114b and methyl chloroform when used in adhesives or in aerosol solvents; and in |

**Table_Apx A-1. Federal Laws and Regulations**

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | | the coatings end use (subject to use conditions) (72 FR 30168, May 30, 2007). The proposed rule has not been finalized by the Agency. The rule identifies 1-BP as acceptable and unacceptable substitute for ozone-depleting substances in several sectors. |
| **Other Federal Regulations** | | |
| Occupational Safety and Health Act (OSHA) | Requires employers to provide their workers with a place of employment free from recognized hazards to safety and health, such as exposure to toxic chemicals, excessive noise levels, mechanical dangers, heat or cold stress, or unsanitary conditions.<br>Under the Act, OSHA can issue occupational safety and health standards including such provisions as Permissible Exposure Limits (PELs), exposure monitoring, engineering and administrative control measures, and respiratory protection. | OSHA has not issued a PEL for 1-BP.<br>OSHA and the National Institute for Occupational Safety and Health (NIOSH) issued a Hazard Alert regarding 1-BP (OSHA-NIOSH, 2013) providing information regarding health effects, how workers are exposed, how to control the exposures and how OSHA and NIOSH can help. |
| Department of Energy (DOE) | The Atomic Energy Act authorizes DOE to regulate the health and safety of its contractor employees. | 10 CFR 851.23, Worker Safety and Health Program, requires the use of the 2005 ACGIH TLVs if they are more protective than the OSHA PEL. The 2005 TLV for 1-BP is 10 ppm (8hr Time Weighted Average). |

## A.2 State Laws and Regulations

**Table_Apx A-2. State Laws and Regulations**

| State Actions | Description of Action |
|---|---|
| State Air Regulations | Allowable Ambient Levels<br>Rhode Island (Air Pollution Regulation No. 22)<br>New Hampshire (Env-A 1400: Regulated Toxic Air Pollutants) |
| Chemicals of High Concern | Massachusetts designated 1-BP as a higher hazard substance requiring reporting starting in 2016 (301 CMR 41.00).<br>Minnesota listed 1-BP as chemical of high concern to children (Minnesota Statutes 116.9401 to 116.9407). |
| State Permissible Exposure Limits | California PEL: 5 ppm as an 8-hr-time-weighted average (TWA) (California Code of Regulations, title 8, section 5155). |
| State Right-to-Know Acts | New Jersey (42 N.J.R. 1709(a)), Pennsylvania (Chapter 323. Hazardous Substance List). |
| Other | In California, 1-BP was added to proposition 65 list in December 2004 due to developmental, female and male, toxicity; and in 2016 due to cancer. (Cal. Code Regs. title 27, section 27001).<br>1-BP is listed as a Candidate Chemical under California's Safer Consumer Products Program (Health and Safety Code sections 25252 and 25253).<br>California also selected 1-BP as the first chemical for early warning and prevention activities under SB 193 Early Warning Authority and issued a Health Hazard Alert for 1-BP (Hazard Evaluation System and Information Service, 2016). |

## A.3 International Laws and Regulations

**Table_Apx A-3. Regulatory Actions by other Governments and Tribes**

| Country /Organization | Requirements and Restrictions |
|---|---|
| European Union | In 2012, 1-BP was listed on the Candidate list as a Substance of Very High Concern (SVHC) under regulation (EC) No 1907/2006 - REACH (Registration, Evaluation, Authorization and Restriction of Chemicals due to its reproductive toxicity (category 1B).<br><br>In June 2017, 1-BP was added to Annex XIV of REACH (Authorisation List) with a sunset date of July 4, 2020 (European Chemicals Agency (ECHA) database. Accessed December 6, 2017). |
| Australia | 1-BP was assessed under Environment Tier II of the Inventory Multi-tiered Assessment and Prioritisation (IMAP) (National Industrial Chemicals Notification and Assessment Scheme (NICNAS), 2017, *Human Health Tier II Assessment for Propane, 1-bromo-*. Accessed April, 18 2017). |
| Japan | 1-BP is regulated in Japan under the following legislation:<br><br>Act on the Evaluation of Chemical Substances and Regulation of Their Manufacture, etc. (Chemical Substances Control Law; CSCL)<br><br>Act on Confirmation, etc. of Release Amounts of Specific Chemical Substances in the Environment and Promotion of Improvements to the Management Thereof<br><br>Industrial Safety and Health Act (ISHA)<br><br>Air Pollution Control Law<br><br>(National Institute of Technology and Evaluation (NITE) Chemical Risk Information Platform (CHIRP). Accessed April 13, 2017). |
| Belgium, Canada, Finland, Japan, Poland, South Korea and Spain | Occupational exposure limits for 1-BP. (GESTIS International limit values for chemical agents (Occupational exposure limits, OELs) database. Accessed April 18, 2017). |
| Basel Convention | Halogenated organic solvents (Y41) are listed as a category of waste under the Basel Convention – Annex I. Although the United States is not currently a party to the Basel Convention, this treaty still affects U.S. importers and exporters. |
| OECD Control of Transboundary Movements of Wastes Destined for Recovery Operations | Halogenated organic solvents (A3150) are listed as a category of waste subject to The Amber Control Procedure under Council Decision C (2001) 107/Final. |

# APPENDIX B PROCESS, RELEASE AND OCCUPATIONAL EXPOSURE INFORMATION

This appendix provides information and data found in preliminary data gathering for 1-BP.

## B.1 Process Information

Process-related information for the risk evaluation may include process diagrams, descriptions and equipment. Such information may inform potential release sources and worker exposure activities. EPA will consider this information in combination with available monitoring data and estimation methods and models, as appropriate, to quantity occupational exposure and releases for the various conditions of use in the risk evaluation. Most of the process-related information provided below, especially descriptions pertaining to 1-BP use in degreasing (vapor, cold and aerosol), spray adhesive, dry cleaning and spot cleaning, has been previously compiled, described and peer reviewed in EPA's 2016 Draft Risk Assessment (U.S. EPA, 2016b).

### B.1.1 Manufacture (Including Import)

#### B.1.1.1 Domestic Manufacture

1-BP is produced by reacting n-propyl alcohol with hydrogen bromide and then removing the excess water that forms in the process (NTP, 2013). The reaction product may then be distilled, neutralized with sodium hydrogen carbonate, packaged and stored (Ichihara et al., 2004).

#### B.1.1.2 Import

EPA expects that imported chemicals are often stored in warehouses prior to distribution for further processing and use. In some cases, the chemicals may be repackaged into differently sized containers, depending on customer demand, and QC samples may be taken for analyses.

#### B.1.1.3 Processing and Distribution

Based on the reported industrial processing operations in the 2016 CDR, 1-BP may be incorporated into a variety of formulations, products and articles, or used industrially as a chemical intermediate (U.S. EPA, 2016a). Some industrial or commercial products may also be repackaged into appropriately-sized containers to meet specific customer demands (U.S. EPA, 2016a).

#### B.1.1.4 Processing as a Reactant

Processing as a reactant or intermediate is the use of 1-BP as a feedstock in the production of another chemical via a chemical reaction in which 1-BP is consumed to form the product. EPA has not identified specific information for the processing of 1-BP as a reactant.

#### B.1.1.5 Incorporated into Formulation, Mixture or Reaction Product

Incorporation into a formulation, mixture or reaction product refers to the process of mixing or blending of several raw materials to obtain a product or mixture (e.g., adhesives and sealants). EPA has not identified 1-BP specific formulation processes.

### B.1.1.6 Incorporated into Article

Incorporation into an article typically refers to a process in which a chemical becomes an integral component of an article that is distributed for industrial, trade, or consumer use. Exact process operations involved in the incorporation of 1-BP are dependent on the article. EPA will further investigate the potential use of 1-BP in this type of process during the risk evaluation.

### B.1.1.7 Repackaging

Typically, repackaging sites receive the chemical in bulk containers and transfer the chemical from the bulk container into another smaller container in preparation for distribution in commerce. Based on EPA's knowledge of the chemical industry, worker activities at repackaging sites may involve manually unloading 1-BP from bulk containers into the smaller containers for distribution or connecting/disconnecting transfer lines used to transfer 1-BP product between containers and analyzing QC samples. EPA will further investigate the potential use of 1-BP in this type of process during the risk evaluation.

### B.1.1.8 Recycling

A general description of waste solvent recovery processes was identified. Waste solvents are generated when it becomes contaminated with suspended and dissolved solids, organics, water, or other substance (U.S. EPA, 1980). Waste solvents can be restored to a condition that permits reuse via solvent reclamation/recycling (U.S. EPA, 1980). The recovery process involves an initial vapor recovery (e.g., condensation, adsorption and absorption) or mechanical separation (e.g., decanting, filtering, draining, setline and centrifuging) step followed by distillation, purification and final packaging (U.S. EPA, 1980).

## B.1.2 Uses

In the Scope Document (EPA-HQ-OPPT-2016-0741-0049), EPA has grouped uses based on CDR categories and identified examples within these categories as subcategories of use. Note that some subcategories of use may be grouped under multiple CDR categories. The differences between these uses will be further investigated during risk evaluation.

### B.1.2.1 Solvents for Cleaning and Degreasing

Solvents for Cleaning and Degreasing category encompasses chemical substances used to dissolve oils, greases and similar materials from a variety of substrates including metal surfaces, glassware and textiles. This category includes the use of 1-BP in vapor degreasing, cold cleaning and in industrial and commercial aerosol degreasing products.

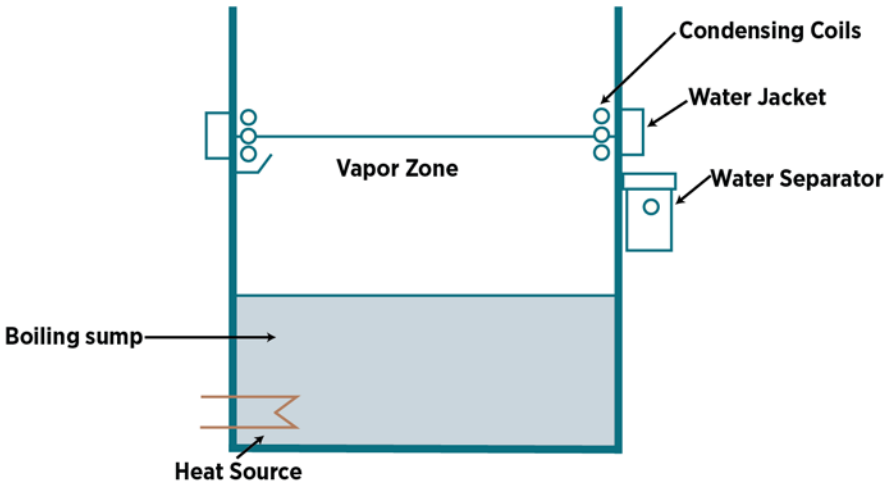
***Vapor Degreasing***

Vapor degreasing is a process used to remove dirt, grease and surface contaminants in a variety of metal cleaning industries. 1-BP is often used to replace chlorinated solvents in vapor degreasing applications. Vapor degreasing may take place in batches or as part of an in-line (i.e., continuous) system. In batch machines, each load (parts or baskets of parts) is loaded into the machine after the previous load is completed. With in-line systems, parts are continuously loaded into and through the vapor degreasing equipment as well as the subsequent drying steps. Vapor degreasing equipment can generally be categorized into one of the three categories: (1) batch vapor degreasers, (2) conveyorized vapor degreasers and (3) web vapor degreasers.

Each category of vapor degreaser is described below.

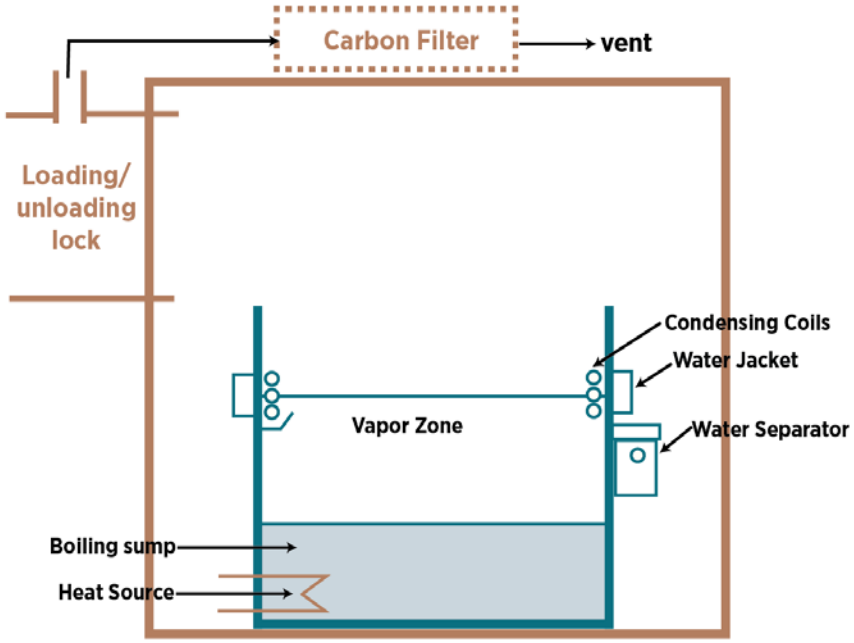
**Batch Vapor Degreasers**

- *Open top vapor degreasers (OTVD)*: In OTVDs, a vapor cleaning zone is created by heating the liquid solvent in the OTVD causing it to volatilize. Workers manually load or unload fabricated parts directly into or out of the vapor cleaning zone. The tank usually has chillers along the side of the tank to prevent losses of the solvent to the air. However, these chillers are not able to eliminate emissions, and throughout the degreasing process, significant air emissions of the solvent can occur. These air emissions can cause issues with both worker health and safety as well as environmental issues. Additionally, the cost of replacing solvent lost to emissions can be expensive (NEWMOA, 2001). Figure_Apx B-1 illustrates a standard OTVD. The use of 1-BP in OTVD has been previously described in EPA's 2016 Draft Risk Assessment (U.S. EPA, 2016b).



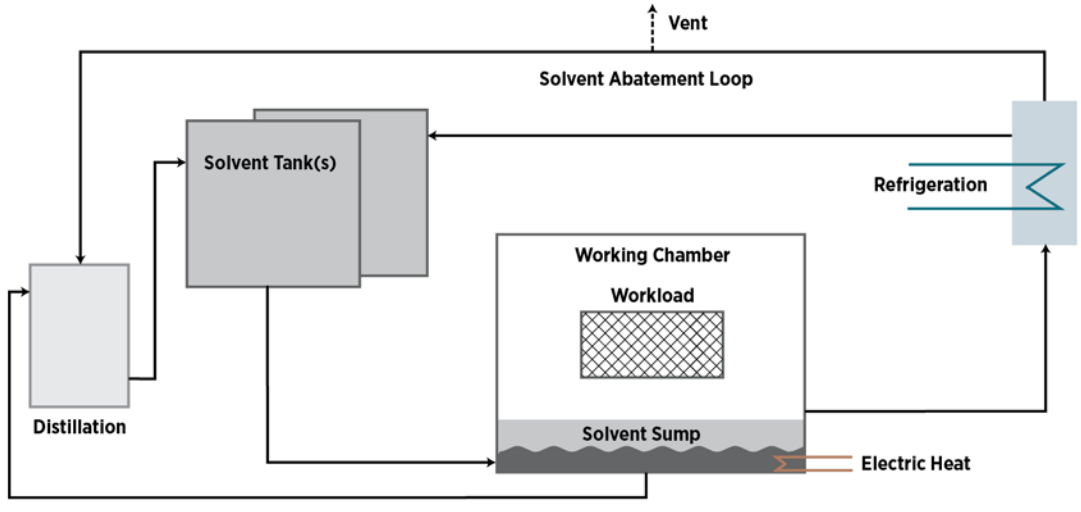

**Figure_Apx B-1. Open Top Vapor Degreaser**

- *OTVD with enclosure:* OTVDs with enclosures operate the same as standard OTVDs except that the OTVD is enclosed on all sides during degreasing. The enclosure is opened and closed to add or remove parts to/from the machine, and solvent is exposed to the air when the cover is open. Enclosed OTVDs may be vented directly to the atmosphere or first vented to an external carbon filter and then to the atmosphere (U.S. EPA, 2004a). Figure_Apx B-2 illustrates an OTVD with an enclosure. The dotted lines in Figure_Apx B-2 represent the optional carbon filter that may or may not be used with an enclosed OTVD.




**Figure_Apx B-2. Open Top Vapor Degreaser with Enclosure**

- *Closed-loop degreasing system (airtight):* In closed-loop degreasers, parts are placed into a basket, which is then placed into an airtight work chamber. The door is closed and solvent vapors are sprayed onto the parts. Solvent can also be introduced to the parts as a liquid spray or liquid immersion. When cleaning is complete, vapors are exhausted from the chamber and circulated over a cooling coil where the vapors are condensed and recovered. The parts are dried by forced hot air. Air is circulated through the chamber and residual solvent vapors are captured by carbon adsorption. The door is opened when the residual solvent vapor concentration has reached a specified level (Kanegsberg and Kanegsberg, 2011). Figure_Apx B-3 illustrates a standard closed-loop vapor degreasing system.




**Figure_Apx B-3. Closed-Loop/Vacuum Vapor Degreaser**

- *Airless degreasing system (vacuum drying):* Airless degreasing systems are also sealed, closed-loop systems, but remove air at some point of the degreasing process. Removing air typically takes the form of drawing vacuum, but could also include purging air with nitrogen at some point of the process (in contrast to drawing vacuum, a nitrogen purge operates at a slightly positive pressure). In airless degreasing systems with vacuum drying only, the cleaning stage works similarly as with the airtight closed-loop degreaser. However, a vacuum is generated during the drying stage, typically below 5 torr (5 mmHg). The vacuum dries the parts and a vapor recovery system captures the vapors (Kanegsberg and Kanegsberg, 2011; NEWMOA, 2001; U.S. EPA, 2001).
- *Airless vacuum-to-vacuum degreasing system:* Airless vacuum-to-vacuum degreasers are true "airless" systems because the entire cycle is operated under vacuum. Typically, parts are placed into the chamber, the chamber sealed, and then vacuum drawn within the chamber. The typical solvent cleaning process is a hot solvent vapor spray. The introduction of vapors in the vacuum chamber raises the pressure in the chamber. The parts are dried by again drawing vacuum in the chamber. Solvent vapors are recovered through compression and cooling. An air purge then purges residual vapors over an optional carbon adsorber and through a vent. Air is then introduced in the chamber to return the chamber to atmospheric pressure before the chamber is opened (Durkee, 2014; NEWMOA, 2001).

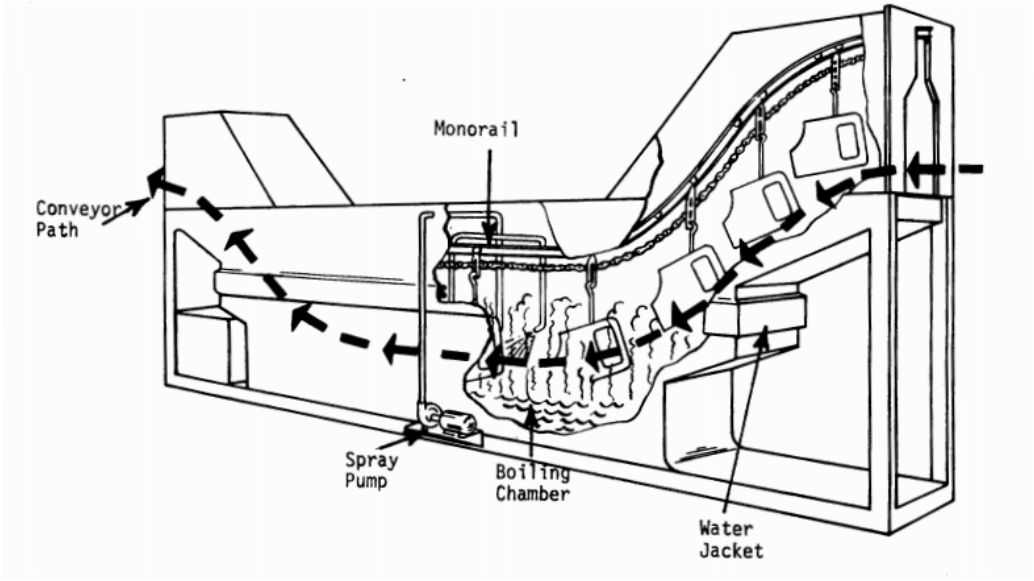
The general design of vacuum vapor degreasers and airless vacuum degreasers is similar as illustrated in Figure_Apx B-3 for closed-loop systems except that the work chamber is under vacuum during various stages of the cleaning process.

**Conveyorized Vapor Degreasers**

Conveyorized vapor degreasing systems are solvent cleaning machines that use an automated parts handling system, typically a conveyor, to automatically provide a continuous supply of parts to be cleaned. Conveyorized degreasing systems are usually fully enclosed except for the conveyor inlet and outlet portals. Conveyorized degreasers are likely used in similar shop types as batch vapor degreasers except for repair shops, where the number of parts being cleaned is likely not large enough to warrant the use of a conveyorized system.

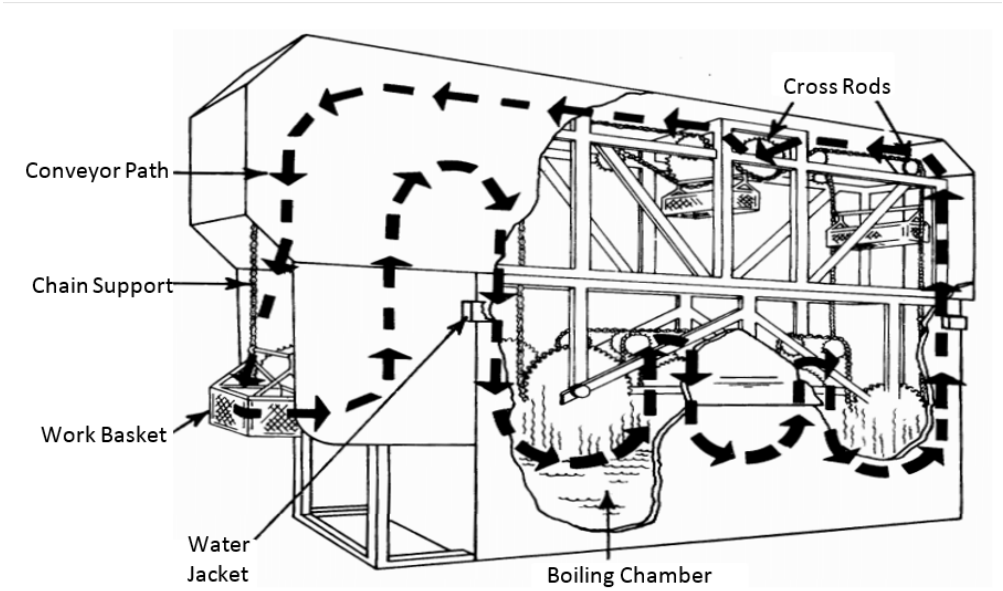
There are seven major types of conveyorized degreasers (U.S. EPA, 1977):

- *Monorail degreasers*: Monorail degreasing systems are typically used when parts are already being transported throughout the manufacturing areas by a conveyor (U.S. EPA, 1977). They use a straight-line conveyor to transport parts into and out of the cleaning zone. The parts may enter one side and exit and the other or may make a 180° turn and exit through a tunnel parallel to the entrance (U.S. EPA, 1977). Figure_Apx B-4 illustrates a typical monorail degreaser (U.S. EPA, 1977).



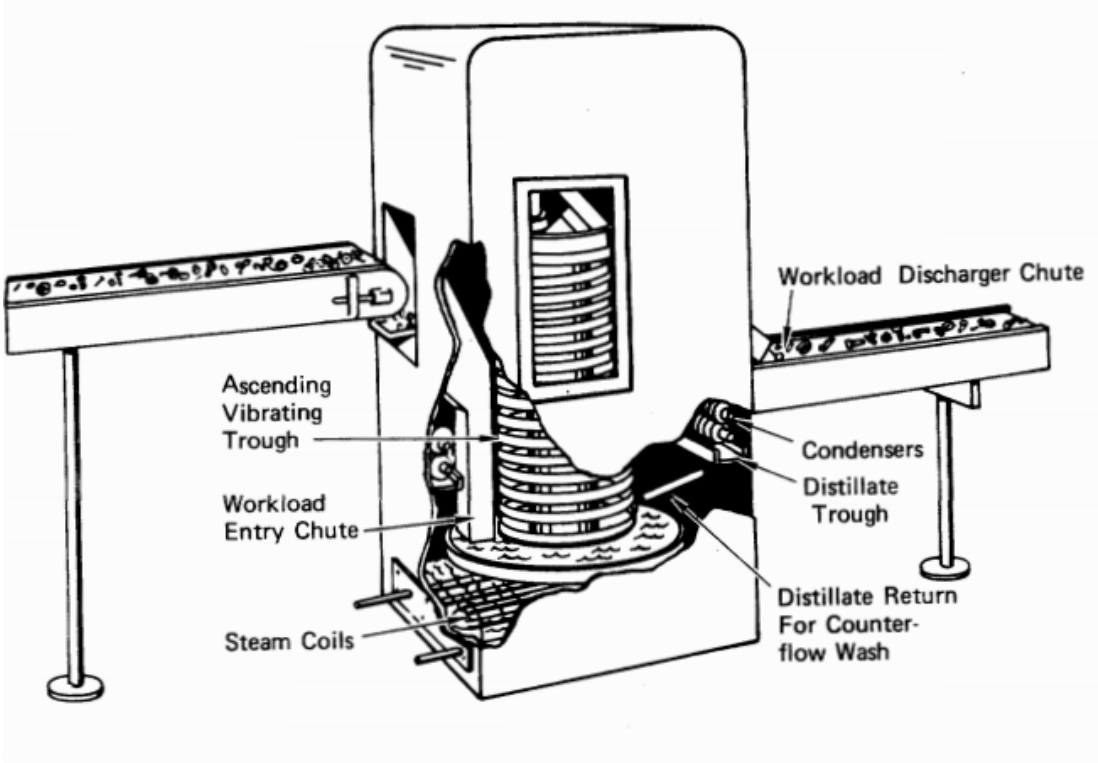

**Figure_Apx B-4. Monorail Degreaser**

- *Cross-rod degreasers:* Cross-rod degreasing systems utilize two parallel chains connected by a rod that support the parts throughout the cleaning process. The parts are usually loaded into perforated baskets or cylinders and then transported through the machine by the chain support system. The baskets and cylinders are typically manually loaded and unloaded (U.S. EPA, 1977). Cylinders are used for small parts or parts that need enhanced solvent drainage because of crevices and cavities. The cylinders allow the parts to be tumbled during cleaning and drying and thus increase cleaning and drying efficiency. Figure_Apx B-5 illustrates a typical cross-rod degreaser (U.S. EPA, 1977).



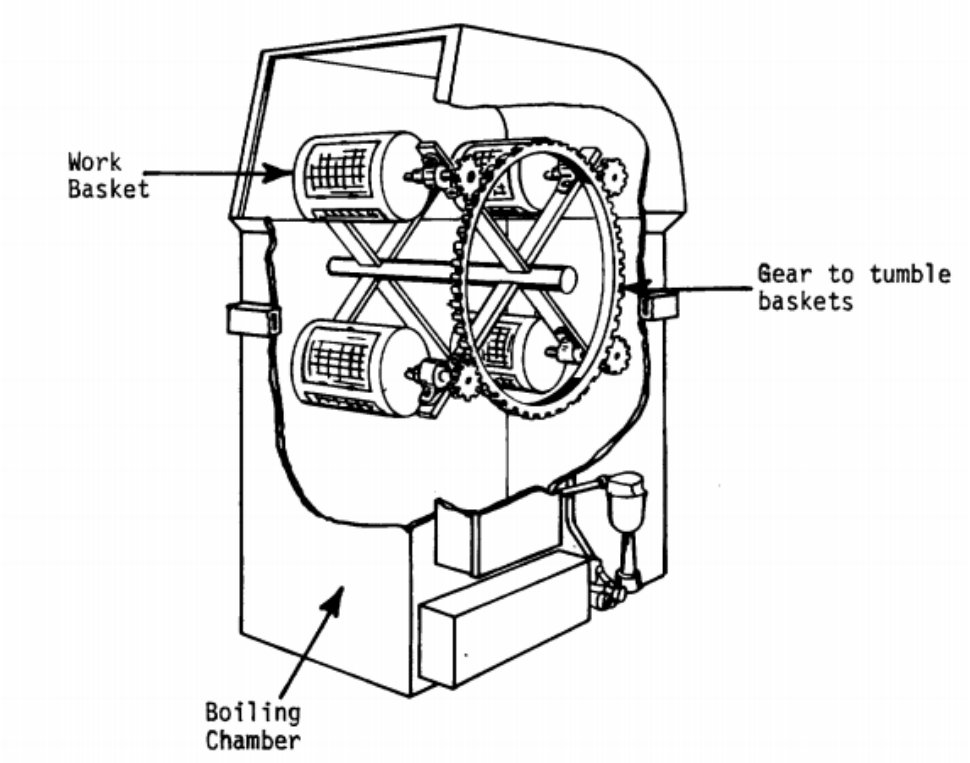

**Figure_Apx B-5. Cross-Rod Degreaser**

- *Vibra degreasers:* In vibra degreasing systems, parts are fed by conveyor through a chute that leads to a pan flooded with solvent in the cleaning zone. The pan and the connected spiral elevator are continuously vibrated throughout the process, causing the parts to move from the pan and up a spiral elevator to the exit chute. As the parts travel up the elevator, the solvent condenses and the parts are dried before exiting the machine (U.S. EPA, 1977).



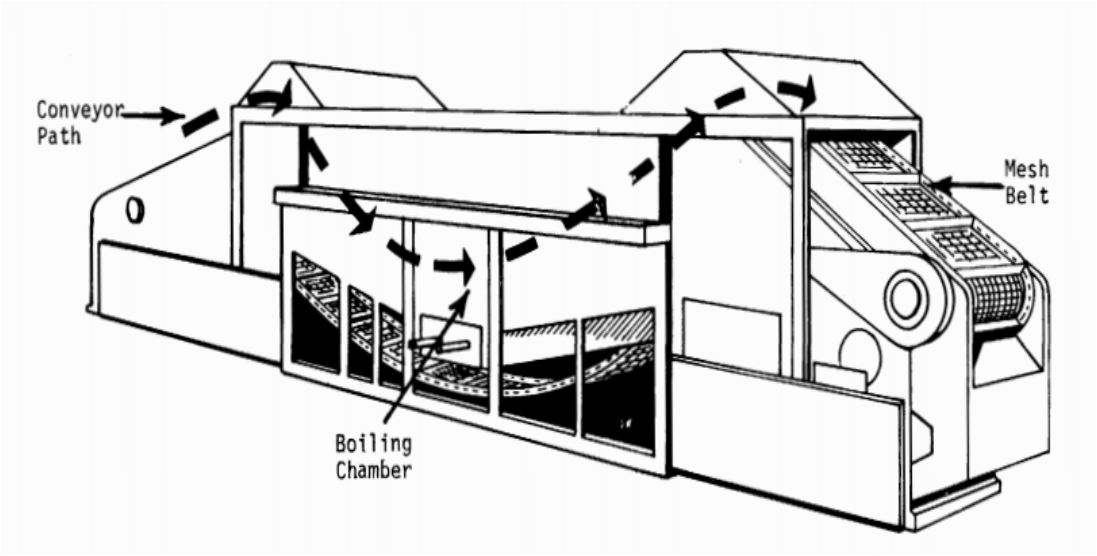

**Figure_Apx B-6. Vibra Degreaser**

- *Ferris wheel degreasers:* Ferris wheel degreasing systems are generally the smallest of all the conveyorized degreasers (U.S. EPA, 1977). In these systems, parts are manually loaded into perforated baskets or cylinders and then rotated vertically through the cleaning zone and back out. Figure_Apx B-7 illustrates a typical ferris wheel degreaser (U.S. EPA, 1977).




**Figure_Apx B-7. Ferris Wheel Conveyorized Vapor Degreasing System**

- *Belt degreasers:* Belt degreasing systems (similar to strip degreasers; see next bullet) are used when simple and rapid loading and unloading of parts is desired (U.S. EPA, 1977). Parts are loaded onto a mesh conveyor belt that transports them through the cleaning zone and out the other side. Figure_Apx B-8 illustrates a typical belt or strip degreaser (U.S. EPA, 1977).

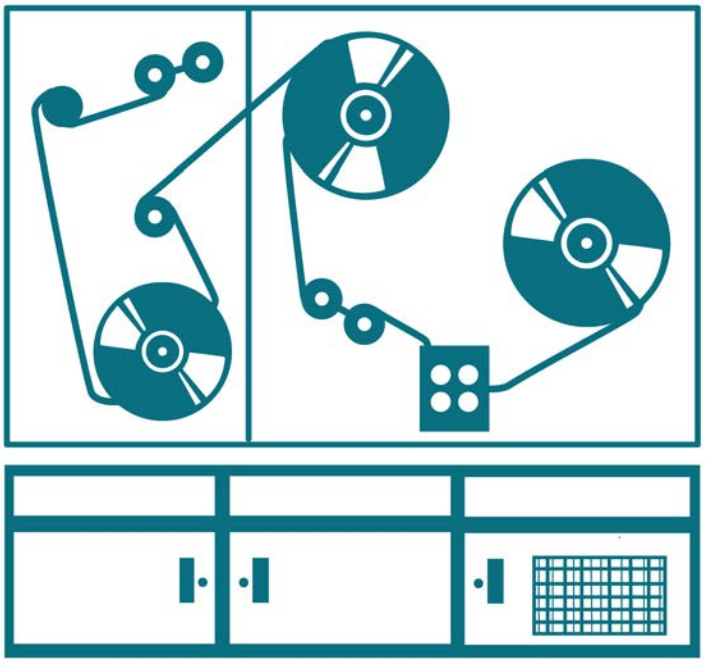



**Figure_Apx B-8. Belt/Strip Conveyorized Vapor Degreasing System**

- *Strip degreasers*: Strip degreasing systems operate similar to belt degreasers except that the belt itself is being cleaned rather than parts being loaded onto the belt for cleaning.
- *Circuit board cleaners:* Circuit board degreasers use any of the conveyorized designs. However, in circuit board degreasing, parts are cleaned in three different steps due to the manufacturing processes involved in circuit board production (U.S. EPA, 1977).

**Continuous Web Vapor Degreasers**

Continuous web cleaning machines differ from typical conveyorized degreasers in that they are specifically designed for cleaning parts that are coiled or on spools such as films, wires and metal strips (Kanegsberg and Kanegsberg, 2011; U.S. EPA, 2006b). In continuous web degreasers, parts are uncoiled and loaded onto rollers that transport the parts through the cleaning and drying zones at speeds >11 feet/minute (U.S. EPA, 2006b). The parts are then recoiled or cut after exiting the cleaning machine (Kanegsberg and Kanegsberg, 2011; U.S. EPA, 2006b). Figure_Apx B-9 illustrates a typical continuous web cleaning machine.



**Figure_Apx B-9. Continuous Web Vapor Degreasing System**

***Cold Cleaning***

1-BP can also be used as a solvent in cold cleaners, which are non-boiling solvent degreasing units. Cold cleaning operations include spraying, brushing, flushing and immersion. In a typical batch-loaded, maintenance cold cleaner, dirty parts are cleaned manually by spraying and then soaking in the tank. After cleaning, the parts are either suspended over the tank to drain or are placed on an external rack that routes the drained solvent back into the cleaner. Batch manufacturing cold cleaners could vary widely, but have two basic equipment designs: the simple spray sink and the dip tank. The dip tank design typically provides better cleaning through immersion, and often involves an immersion tank equipped with agitation (U.S. EPA, 1981). Emissions from batch cold cleaning machines typically result from (1) evaporation of the solvent from the solvent-to-air interface, (2) “carry out” of excess solvent on cleaned

parts and (3) evaporative losses of the solvent during filling and draining of the machine (U.S. EPA, 2006b).

***Aerosol Degreasing***

Aerosol degreasing is a process that uses an aerosolized solvent spray, typically applied from a pressurized can, to remove residual contaminants from fabricated parts. The aerosol droplets bead up on the fabricated part and then drip off, carrying away any contaminants and leaving behind a clean surface. One example of commercial setting that uses aerosol degreasing operation is repair shops, where service items are cleaned to remove any contaminants that would otherwise compromise the service item's operation. Internal components may be cleaned in place or removed from the service item, cleaned, and then re-installed once dry (U.S. EPA, 2014a). Aerosol degreasing may occur at either industrial facilities or at commercial repair shops to remove contaminants on items being serviced.

### B.1.2.2 Adhesives and Sealants

1-BP is a component of spray adhesive. In foam cushion manufacturing, workers use a spray gun to spray-apply adhesive containing 1-BP onto flexible foam surfaces. Adhesive spraying typically occurs either on an open top workbench with side panels that may have some local ventilation, or in an open workspace with general room ventilation. After the adhesive is applied, workers hand-press the flexible foam pieces together to assemble the cushions.

### B.1.2.3 Cleaning and Furniture Care Products

1-BP can be used as a solvent in dry cleaning machines and 1-BP formulations such as DrySolv® are often marketed as "drop-in" replacements for PERC, which indicates that they can be used in third-generation or higher PERC equipment (TURI, 2012). Dry cleaners who opt to use 1-BP can either convert existing PERC machines or purchase a new dry cleaning machine specifically designed for 1-BP. To convert existing PERC machines to use 1-BP, machine settings and components must be changed to prevent machine overheating and solvent leaks (Blando et al., 2010). 1-BP is known to damage rubber gaskets and seals. It can also degrade cast aluminum, which is sometimes used on equipment doors and other dry cleaning machine components. In addition, 1-BP is not compatible with polyurethane and silicone (TURI, 2012). Worker who handle 1-BP at dry cleaning facilities may be exposed when 1) adding makeup solvent, typically by manually dumping it through the front hatch, 2) opening the machine door during the wash cycle, and 3) removing loads from the machines (Blando et al., 2010).

In addition, 1-BP is found in products used to spot clean garments. Spot cleaning products can be applied to the garment either before or after the garment is dry cleaned. Spot cleaning occurs on a spotting board and spotting agent can be applied from squeeze bottles, hand-held spray bottles or even from spray guns connected to pressurized tanks. Once applied, the dry cleaner may come into further contact with the 1-BP if using a brush, spatula, pressurized air or steam or their fingers to scrape or flush away the stain (Young, 2012; NIOSH, 1997).

### B.1.2.4 Other Uses

Based on products identified in EPA's preliminary data gathering and information received in public comments, a variety of other uses may exist for 1-BP including in lubricants, insulation, mold release products, refrigerants, adhesive accelerants, asphalt extraction, and temperature indicators for laboratory applications [see *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: 1-Bromopropane,* EPA-HQ-OPPT-2016-0741-0003 (U.S. EPA, 1977)]. EPA has not

identified any process-specific information to further refine the use of 1-BP in these applications at this time and more information on these uses will be gathered through expanded literature searches during risk evaluation.

### B.1.3 Disposal

Disposal of a chemical should take into consideration the chemical's potential impact on air quality, migration to groundwater, effect on biological species, and disposal regulations (if any) (ATSDR, 2017). Due to the high volatility of 1-BP, releases to the atmosphere are expected to be the primary release route of 1-BP (ATSDR, 2017). Currently, 1-BP is not regulated under federal regulations as a hazardous waste (U.S. EPA, 1977). However, 1-BP may be disposed of as a hazardous waste if it is present in or co-mingled with solvent mixtures that are RCRA regulated substances. EPA has not identified further process information specific to disposal of 1-BP at this time, but will review TRI data submitted for 1-BP, as it becomes available, for information on how wastes containing 1-BP are disposed.

## B.2 Occupational Exposure Data

EPA presents below examples of occupational exposure-related information from the preliminary data gathering. EPA will consider this information and data in combination with other data and methods for use in the risk evaluation.

Table_Apx B-1 summarizes the release/exposure scenarios and industry sectors with available 1-BP personal monitoring data from OSHA inspections conducted between 2013 and 2016 (OSHA, 2017).

**Table_Apx B-1. Summary of Release/Exposure Scenarios and Industry Sectors with 1-BP Personal Monitoring Air Samples Obtained from OSHA Inspections Conducted Between 2013 and 2016**

| Release/ Exposure Scenario | NAICS | NAICS Description |
|---|---|---|
| Solvents (for cleaning or degreasing) | 336412 | Aircraft Engine and Engine Parts Manufacturing |
| Commercial spot cleaning | 448190 | Other Clothing Stores |
| Solvents (for cleaning or degreasing) | 333517 | Machine Tool Manufacturing |
| Solvents (for cleaning or degreasing) | 334418 | Printed Circuit Assembly |
| Solvents (for cleaning or degreasing) | 331210 | Iron and Steel Pipe and Tube Manufacturing from Purchased Steel |
| Solvents (for cleaning or degreasing) | 336413 | Other Aircraft Parts and Auxiliary Equipment Manufacturing |
| Solvents (for cleaning or degreasing) | 332813 | Electroplating, Plating, Polishing, Anodizing, and Coloring |
| Other | 926150 | Regulation, Licensing, and Inspection of Miscellaneous Commercial Sectors |
| Unknown, likely commercial spot cleaning | 323113 | Commercial Screen Printing |

**Table_Apx B-1. Summary of Release/Exposure Scenarios and Industry Sectors with 1-BP Personal Monitoring Air Samples Obtained from OSHA Inspections Conducted Between 2013 and 2016**

| Release/ Exposure Scenario | NAICS | NAICS Description |
|---|---|---|
| Solvents (for cleaning or degreasing) | 332913 | Plumbing Fixture Fitting and Trim Manufacturing |
| Solvents (for cleaning or degreasing) | 332721 | Precision Turned Product Manufacturing |
| Solvents (for cleaning or degreasing) | 333911 | Pump and Pumping Equipment Manufacturing |

Table_Apx B-2 summarizes the release/exposure scenarios and industry sectors with available area monitoring data.

**Table_Apx B-2. Summary of Release/Exposure Scenarios and Industry Sectors with 1-BP Area Monitoring Air Samples Obtained from OSHA Inspections Conducted Between 2013 and 2016**

| Release/ Exposure Scenario | NAICS | NAICS Description |
|---|---|---|
| Solvents (for cleaning or degreasing) | 332721 | Precision Turned Product Manufacturing |
| Solvents (for cleaning or degreasing) | 333911 | Pump and Pumping Equipment Manufacturing |

## B.3 References related to Risk Evaluation – Environmental Release and Occupational Exposure

As part of the Systematic Review process, EPA has conducted a full-text screening of literature sources and identified sources that may be relevant for risk evaluation. This section presents a list of data sources that may contain process description, environmental release estimate, occupational exposure data, engineering control and personal protective equipment information for 1-BP. EPA will further review these data sources and determine their utility for risk evaluation.

**Table_Apx B-3. Potentially Relevant Data Sources for Process Description Related Information for 1-BP [a]**

| Bibliography | url |
|---|---|
| NIOSH (1997). Control of health and safety hazards in commercial drycleaners: chemical exposures, fire hazards, and ergonomic risk factors. Education and Information Division. Atlanta, GA. | NIOSH (1997) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3044963 |
| U.S. EPA (2016). TSCA work plan chemical risk assessment: Peer review draft 1-bromopropane: (n-Propyl bromide) spray adhesives, dry cleaning, and degreasing uses CASRN: 106-94-5. Washington, DC. | U.S. EPA (2016b) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3355305 |

## Table_Apx B-3. Potentially Relevant Data Sources for Process Description Related Information for 1-BP [a]

| Bibliography | url |
|---|---|
| NIOSH (2007). Workers' exposures to n-propyl bromide at a printed electronics circuit assembly manufacturer. Cincinnati, OH, NIOSH Division of Surveillance, Hazard Evaluation and Field Studies. | NIOSH (2007b) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3355604 |
| NIOSH (2007). Workers' exposures to n-propyl bromide at a hydraulic power control component manufacturer. Cincinnati, OH, NIOSH Division of Surveillance, Hazard Evaluation and Field Studies. | NIOSH (2007a) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3355621 |
| U.S. EPA (1995). Guidance document for the halogenated solvent cleaner NESHAP. Research Triangle Park, NC, Office of Air Quality Planning and Standards, Information Transfer and Program Integration Division, Control Technology Center, Federal Small Business Assistance Program. | U.S. EPA (1995) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3827323 |
| NIOSH (2003). NIOSH Health Hazard Evaluation Report: HETA No. 99-0260-2906, Marx Industries, Inc., Sawmills, North Carolina. Hazard Evaluation and Technical Assistance Branch. Cincinnati, OH, National Institute for Occupational Health and Safety. | Harney et al. (2003) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3970467 |
| U.S. EPA; ICF Consulting (2004). The U.S. solvent cleaning industry and the transition to non ozone depleting substances. | U.S. EPA; ICF Consulting (2004) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3982140 |
| HSIA (2008). Chlorinated solvents - The key to surface cleaning performance. | HSIA (2008) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3982144 |

[a] The data sources identified are based on preliminary results to date of the full-text screening step of the Systematic Review process. Further screening and quality control are on-going.

## Table_Apx B-4. Potentially Relevant Data Sources for Estimated or Measured Release Data for 1-BP [a]

| Bibliography | url |
|---|---|
| Japanese Ministry of Environment (2017). 1-Bromopropane. Tokyo, Japan. | Japanese Ministry of Environment (2017) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3980936 |
| CAMP, Inc., (2000). Final report: Beyond pollution prevention: Removal of organochlorines from industrial feedstocks and processes in the Great Lakes Basin, The Great Lakes Protection Fund, The Joyce Foundation. | CAMP (2000) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3981054 |
| HSIA (2008). Chlorinated solvents - The key to surface cleaning performance. | (HSIA, 2008) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3982144 |

[a] The data sources identified are based on preliminary results to date of the full-text screening step of the Systematic Review process. Further screening and quality control are on-going.

## Table_Apx B-5. Potentially Relevant Data Sources for Personal Exposure Monitoring and Area Monitoring Data for 1-BP [a]

| Bibliography | url |
|---|---|
| Hanley, K. W., et al. (2006). "Urinary bromide and breathing zone concentrations of 1-bromopropane from workers exposed to flexible foam spray adhesives." Annals of Occupational Hygiene **50**(6): 599-607. | Hanley et al. (2006a) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/607476 |
| NIOSH (2003). NIOSH Health Hazard Evaluation Report: HETA No. 99-0260-2906, Marx Industries, Inc., Sawmills, North Carolina. Hazard Evaluation and Technical Assistance Branch. Cincinnati, OH, National Institute for Occupational Health and Safety. | Harney et al. (2003) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/1379492 |

## Table_Apx B-5. Potentially Relevant Data Sources for Personal Exposure Monitoring and Area Monitoring Data for 1-BP [a]

| Bibliography | url |
|---|---|
| Toraason, M., et al. (2003). "Assessment of DNA strand breaks in leukocytes of workers occupationally exposed to 1-bromopropane." Toxicological Sciences **72**(S-1): 250. | Toraason et al. (2003) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/1733747 |
| OSHA (2013). OSHA/NIOSH hazard alert: 1-bromopropane. Washington, DC, U.S. Department of Labor. | OSHA (2013) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/2347177 |
| NIOSH (1997). Control of health and safety hazards in commercial drycleaners: chemical exposures, fire hazards, and ergonomic risk factors. Education and Information Division. Atlanta, GA. | NIOSH (1997) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3044963 |
| NIOSH (2007). Workers' exposures to n-propyl bromide at a printed electronics circuit assembly manufacturer. Cincinnati, OH, NIOSH Division of Surveillance, Hazard Evaluation and Field Studies. | NIOSH (2007b) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3355604 |
| NIOSH (2007). Workers' exposures to n-propyl bromide at a hydraulic power control component manufacturer. Cincinnati, OH, NIOSH Division of Surveillance, Hazard Evaluation and Field Studies. | NIOSH (2007a) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3355621 |
| CDC (2016). Criteria for a recommended standard: Occupational exposure to 1-bromopropane. Cincinnati, OH, National Institute for Occupational Safety and Health. | CDC (2016) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3827326 |
| NIOSH (2003). NIOSH Health Hazard Evaluation Report: HETA No. 99-0260-2906, Marx Industries, Inc., Sawmills, North Carolina. Hazard Evaluation and Technical Assistance Branch. Cincinnati, OH, National Institute for Occupational Health and Safety. | Harney et al. (2003) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3970467 |
| Hanley, K. W., et al. (2006). "Urinary bromide and breathing zone concentrations of 1-bromopropane from workers exposed to flexible foam spray adhesives, Part3." Annals of Occupational Hygiene **6**: 599-607. | Hanley et al. (2006b) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3974876 |
| OSHA (2010). Input received through web forum for identifying hazardous chemicals for which OSHA should develop exposure reduction strategies. Washington, DC, U.S. Department of Labor, Occupational Safety and Health Administration. | OSHA (2010) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3978176 |
| ATSDR (2017). Toxicological profile for1-bromopropane. Atlanta, GA, Division of Toxicology and Human Health Sciences, Environmental Toxicology Branch. | ATSDR (2017) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3982334 |
| OSHA; NIOSH (2013). Hazard alert: 1-Bromopropane. Washington, DC, Occupational Safety and Health Administration & National Institute for Occupational Safety and Health. | OSHA; NIOSH (2013) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3994171 |

[a] The data sources identified are based on preliminary results to date of the full-text screening step of the Systematic Review process. Further screening and quality control are on-going.

## Table_Apx B-6. Potentially Relevant Data Sources for Engineering Controls and Personal Protective Equipment Information for 1-BP [a]

| Bibliography | url |
|---|---|
| Raymond, L. W. and M. D. Ford (2007). "Severe illness in furniture makers using a new glue: 1-bromopropane toxicity confounded by arsenic." Journal of Occupational and Environmental Medicine **49**(9): 1009-1019. | Raymond and Ford (2007) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/1025819 |
| NIOSH (2003). NIOSH Health Hazard Evaluation Report: HETA No. 99-0260-2906, Marx Industries, Inc., Sawmills, North Carolina. Hazard Evaluation and Technical Assisstance Branch. Cincinnati, OH, National Institute for Occupational Health and Safety. | Harney et al. (2003) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/1379492 |

## Table_Apx B-6. Potentially Relevant Data Sources for Engineering Controls and Personal Protective Equipment Information for 1-BP [a]

| Bibliography | url |
|---|---|
| Hanley, K. W., et al. (2009). "N-acetyl-S-(n-propyl)-l-cysteine in urine from workers exposed to 1-bromopropane in foam cushion spray adhesives." Annals of Occupational Hygiene **53**(7): 759-769. | Hanley et al. (2009) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/1689272 |
| Kawai, T., et al. (2001). "Biological monitoring of occupational exposure to 1-bromopropane by means of urinalysis for 1-bromopropane and bromide ion." Biomarkers **6**(5): 303-312. | Kawai et al. (2001) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/1733873 |
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| NIOSH (1997). Control of health and safety hazards in commercial drycleaners: chemical exposures, fire hazards, and ergonomic risk factors. Education and Information Division. Atlanta, GA. | NIOSH (1997) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3044963 |
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| NIOSH (2007). Workers' exposures to n-propyl bromide at a hydraulic power control component manufacturer. Cincinnati, OH, NIOSH Division of Surveillance, Hazard Evaluation and Field Studies. | NIOSH (2007a) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3355621 |
| U.S. EPA (1995). Guidance document for the halogenated solvent cleaner NESHAP. Research Triangle Park, NC, Office of Air Quality Planning and Standards, Information Transfer and Program Integration Division, Control Technology Center, Federal Small Business Assistance Program. | U.S. EPA (1995) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3827323 |
| CDC (2016). Criteria for a recommended standard: Occupational exposure to 1-bromopropane. Cincinnati, OH, National Institute for Occupational Safety and Health. | CDC (2016) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3827326 |
| CDPH (2017). 1-Bromopropane. Richmond, CA, California Department of Public Health, California Department of Industrial Relations**:** 6. | CDPH (2017) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3969295 |
| NIOSH (2003). NIOSH Health Hazard Evaluation Report: HETA No. 99-0260-2906, Marx Industries, Inc., Sawmills, North Carolina. Hazard Evaluation and Technical Assisstance Branch. Cincinnati, OH, National Institute for Occupational Health and Safety. | Harney et al. (2003) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3970467 |
| NIOSH (2014). International chemical safety cards (ICDC): 1-bromopropane. Atlanta, GA. | NIOSH (2014) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3978148 |
| HSIA (2008). Chlorinated solvents - The key to surface cleaning performance. | HSIA (2008) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3982144 |
| OSHA; NIOSH (2013). Hazard alert: 1-Bromopropane. Washington, DC, Occupational Safety and Health Administration & National Institute for Occupational Safety and Health. | OSHA; NIOSH (2013) https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3994171 |

[a] The data sources identified are based on preliminary results to date of the full-text screening step of the Systematic Review process. Further screening and quality control are on-going.

# APPENDIX C ESTIMATES OF SURFACE WATER CONCENTRATION

## SCENARIO 1. REPORTED RELEASES TO TRI

For 1-BP, there is one facility reporting water releases from the 2016 TRI reporting period, the Flint Hills Resources facility. This facility, located in Corpus Christi, TX, has reported 1 lb of 1-BP released to the Nueces River with 100% from stormwater on an annual basis. They also reported 4 lbs of 1-BP released to an unnamed water body with 83% from stormwater on an annual basis. These are direct releases to water and thus are presumed to be untreated at a POTW. A quick calculation of site specific surface water concentration was performed using E-FAST assuming that the total release occurs over 1 day, 20 days or 100 days. Two receiving waters were used:

a. Nueces River – the NPDES permit for Corpus Christ City POTW TX0047082 was used as a surrogate for this direct release. 0% removal was assumed since this is listed as a direct release.

b. Unnamed Waterbody – the NPDES permit for the reporting facility was available in EFAST with the receiving water body listed as the Corpus Christi Bay. Acute dilution factors were used to estimate the surface water concentration, again with 0% removal.

The resulting estimated surface water concentrations, based on the reported releases and locations, are well below the acute and chronic concentrations of concern even if the annual release amount occurs over 1 day. The maximum estimated surface water concentration is 78 µg/L for this scenario. The acute concentration of concern is 4860 ppb and the chronic concentration of concern is 243 ppb.

**Table_Apx C-1. Estimated Surface Concentrations from Water Releases Reported to TRI**

**SCENARIO 1: REPORTED RELEASES TO TRI**

Acute COC = 4860 ppb

Chronic COC = 2430 ppb

From TRI reporting: 1 reporting facility: Flint Hills Resources Corpus Christi LLC – West Plant
1 lb to Nueces River (100% from stormwater);
4 lbs to 'unnamed water body' (83% from stormwater)

Wastewater Treatment Removal= 0%; direct release
(Note: NPDES for Corpus Christi City POTW used as surrogate for Nueces River. Flint Hills Resources facility modeled directly)

| | **Nueces River (Corpus Christi City - TX0047082)** | | | | **Flint Hills Resources - Corpus Christi Bay, (TX0006289)** | | |
|---|---|---|---|---|---|---|---|
| | **7Q10 SWC µg/L** | | | | **SWC* µg/L** | | |
| **Annual Release Amount lb (kg)** | 1 day/yr | 20 days/yr | 100 days/yr | | 1 day/yr | 20 days/yr | 100 days/yr |
| **1 (0.45)** | 7.86 | 0.39 | 0.08 | | 19.4 | 0.97 | 0.19 |
| **4 (1.81)** | 31.60 | 1.58 | 0.31 | | 77.90 | 3.90 | 0.77 |
| | | | | | *Acute dilution factor for bay | | |

# APPENDIX D SUPPORTING TABLE FOR INDUSTRIAL AND COMMERCIAL ACTIVITIES AND USES CONCEPTUAL MODEL

(Note that rows shaded in gray are not proposed for further analysis)

**Table_Apx D-1. Industrial and Commercial Activities and Uses Conceptual Model Supporting Table**

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| Manufacture | Domestic Manufacture | Domestic Manufacture | Manufacture of 1-BP via reaction of n-propyl alcohol and hydrogen bromide | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization and the fraction absorbed was measured to be low (0.16%) by NIOSH. The number of sites mfg 1-BP is limited per CDR (3 sites). |
| | | | | Vapor | Inhalation | Workers | Yes | Due to high volatility (VP = 146 torr at 20°C), inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | Due to high volatility (VP = 146 torr at 20°C), inhalation pathway will be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation is not expected during mfg and will not be further analyzed. |
| Manufacture | Import | Import | Repackaging of import containers | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization and the fraction absorbed was measured to be low (0.16%) by NIOSH. The number of import sites is limited (<9 sites) per CDR. Exposure will only occur in the event the imported material is repackaged. |
| | | | | Vapor | Inhalation | Workers | Yes | Exposure expected only in the event the imported material is repackaged into different sized containers. Exposure frequency may be low. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Exposure expected only in the event the imported material is repackaged into different sized containers. Exposure frequency may be low. |

## Table_Apx D-1. Industrial and Commercial Activities and Uses Conceptual Model Supporting Table

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation is not expected during import and will not be further analyzed. |
| Processing | Processing as a reactant | Intermediate in all other basic inorganic chemical manufacturing, all other basic organic chemical manufacturing, and pesticide, fertilizer and other agricultural chemical manufacturing | Chemical manufacture / Pesticide, fertilizer, and other agricultural chemical manufacture | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization and the fraction absorbed was measured to be low (0.16%) by NIOSH. The number of workers is expected to be low per CDR (2 submissions in CDR, 10-25 workers per submission). |
| | | | | Vapor | Inhalation | Workers | Yes | Due to high volatility (VP = 146 torr at 20°C), inhalation pathway should be further analyzed. However, potential for exposure may be low in scenarios where 1-BP is consumed as a chemical intermediate. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | | Due to high volatility (VP = 146 torr at 20°C), inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation is not expected during processing as an intermediate and will not be further analyzed. |
| Processing | Incorporated into formulation, mixture or reaction product | Solvent for cleaning or degreasing in manufacturing of:<br>- all other chemical product and preparation<br>- computer and electronic product<br>- electrical equipment, appliance and component<br>- soap, cleaning compound and toilet preparation<br>- services | Formulation of cleaning fluids | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization and the fraction absorbed was measured to be low (0.16%) by NIOSH. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected at processing sites that formulate products containing 1-BP. Due to high volatility (VP = 146 torr at 20°C), inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected at processing sites that formulate products containing 1-BP. Due to high volatility (VP = 146 torr at 20°C), inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation is not expected during processing/formulation operations and will not be further analyzed. |

## Table_Apx D-1. Industrial and Commercial Activities and Uses Conceptual Model Supporting Table

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| Processing | Incorporated into articles | Solvents (which become part of product formulation or mixture) in construction | Production of insulation material | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization and the fraction absorbed was measured to be low (0.16%) by NIOSH. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected at processing sites. Due to high volatility (VP = 146 torr at 20°C), inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected at processing sites. Due to high volatility (VP = 146 torr at 20°C), inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation is not expected during processing operations and will not be further analyzed. |
| Processing | Repackaging | Solvent for cleaning or degreasing in all other basic organic chemical manufacturing | Repackaging into large and small containers | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization and the fraction absorbed was measured to be low (0.16%) by NIOSH. |
| | | | | Vapor | Inhalation | Workers | Yes | Exposure frequency may be low. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Exposure frequency may be low. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation is not expected during repackaging and will not be further analyzed. |
| Processing | Recycling | Recycling | Recycling of process solvents containing 1-BP | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization and the fraction absorbed was measured to be low (0.16%) by NIOSH. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected at recycling sites. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected at recycling sites. |

## Table_Apx D-1. Industrial and Commercial Activities and Uses Conceptual Model Supporting Table

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation is not expected during recycling and will not be further analyzed. |
| Distribution in commerce | Distribution | Distribution | Distribution of bulk shipment of 1-BP | Liquid Contact, Vapor | Dermal/ Inhalation | Workers, ONU | Yes | EPA will further analyze activities resulting in exposures associated with distribution in commerce (e.g. loading, unloading) throughout the various lifecycle stages and conditions of use (e.g. manufacturing, processing, industrial use, consumer use, disposal) rather than as a single distribution scenario. |
| | Distribution | Distribution | Distribution of formulated products | | | | | |
| Industrial / commercial / consumer use | Solvents (for cleaning or degreasing) | Batch vapor degreaser (e.g., open-top, closed-loop)<br><br>In-line vapor degreaser (e.g., conveyorized, web cleaner) | Open top vapor degreasing (OTVD)<br>OTVD with enclosures<br>Conveyorized vapor degreasing<br>Cross-rod and ferris wheel vapor degreasing<br>Web vapor degreasing<br>Airtight closed-loop degreasing system<br>Airless vacuum-to-vacuum degreasing system<br>Airless vacuum drying degreasing system | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization and the fraction absorbed was measured to be low (0.16%) by NIOSH. However, repeat contact or dermal immersion may occur, especially while cleaning and maintaining degreasing equipment. |
| | | | | Vapor | Inhalation | Workers | Yes | EPA has previously assessed OTVD in the 2016 RA. EPA will further refine and expand its assessment for all degreasing systems by addressing comments received from peer review, or by incorporating additional data identified through systematic review, if found.<br>For closed-systems, EPA expects inhalation exposure to be lower than exposure associated with open systems such as OTVD. |
| | | | | Vapor | Inhalation | ONU | Yes | |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation is not expected during this use and will not be further analyzed. |
| Industrial / commercial / consumer use | Solvents (for cleaning or degreasing) | Cold cleaner | | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization and the fraction absorbed was measured to be low (0.16%) by NIOSH. However, repeat contact or dermal immersion may occur. |

## Table_Apx D-1. Industrial and Commercial Activities and Uses Conceptual Model Supporting Table

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | Spray use in cold cleaning - maintenance (manual spray; spray sink; dip tank) | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | Workers | Yes | EPA has previously assessed this use in the 2016 RA. EPA will further refine its assessment by addressing comments received from peer review, or by incorporating additional data identified through systematic review, if found. |
| | | | | Vapor | Inhalation | ONU | Yes | |
| | | | | Mist | Dermal/ Inhalation | Workers | Yes | EPA will further analyze the potential for mist generation. |
| | | | | Mist | Dermal | ONU | No | Exposure to mist is generally not expected as occupational non-users do not directly handle 1-BP. This pathway will not be further analyzed. |
| | | | | Mist | Inhalation | ONU | Yes | EPA will further analyze the potential for mist generation. |
| Industrial / commercial / consumer use | Solvents (for cleaning or degreasing) | Aerosol spray degreaser/ cleaner | Aerosol use in degreasing/ cleaning | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization and the fraction absorbed was measured to be low (0.16%) by NIOSH. However, repeat contact may occur. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | Workers | Yes | EPA has previously assessed this use in the 2016 RA. EPA will further refine its assessment by addressing comments received from peer review, or by incorporating additional data identified through systematic review, if found. |
| | | | | Vapor | Inhalation | ONU | Yes | |
| | | | | Mist | Dermal/ Inhalation | Workers | Yes | EPA will further analyze the potential for mist generation. |
| | | | | Mist | Dermal | ONU | No | Exposure to mist is generally not expected as occupational non-users do not directly handle 1-BP. This pathway will not be further analyzed. |
| | | | | Mist | Inhalation | ONU | Yes | EPA will further analyze the potential for mist generation. |
| Industrial / commercial / consumer use | Adhesives and sealants | Adhesive chemicals - spray adhesive for foam cushion | Industrial spray adhesive application | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization and the fraction absorbed was measured to be low (0.16%) by NIOSH. However, repeat contact may occur. |

## Table_Apx D-1. Industrial and Commercial Activities and Uses Conceptual Model Supporting Table

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | manufacturing and other uses | Other adhesive, sealant, or coating applications (e.g. roll) | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | Workers | Yes | EPA has previously assessed the use of spray adhesive in the 2016 RA. EPA will further refine its assessment by addressing comments received from peer review, or by incorporating additional data identified through systematic review, if found.<br>For other adhesives, inhalation pathway should be analyzed due to high volatility (VP = 146 torr at 20°C). |
| | | | | Vapor | Inhalation | ONU | Yes | |
| | | | | Mist | Dermal/ Inhalation | Workers | Yes | Mist generation is expected for spray adhesives. EPA will further analyze to determine if mist generation is applicable for each adhesive/sealant product. |
| | | | | Mist | Dermal | ONU | No | Exposure to mist is generally not expected as occupational non-users do not directly handle 1-BP. This pathway will not be further analyzed. |
| | | | | Mist | Inhalation | ONU | Yes | EPA will further analyze the potential for mist generation. |
| Industrial / commercial / consumer use | Cleaning and furniture care products | Dry cleaning solvent<br>Spot cleaner, stain remover | Commercial dry cleaning and spot cleaning | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization and the fraction absorbed was measured to be low (0.16%) by NIOSH. However, repeat contact may occur. Peer reviewers also indicated the potential for occluded exposure. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | Workers | Yes | EPA has previously assessed this use in the 2016 RA. EPA will further refine its assessment by addressing comments received from peer review, or by incorporating additional data identified through systematic review, if found. |
| | | | | Vapor | Inhalation | ONU | Yes | |
| | | | | Mist | Dermal/ Inhalation | Workers | Yes | EPA will further analyze the potential for mist generation. |
| | | | | Mist | Dermal | ONU | No | Exposure to mist is generally not expected as occupational non-users do not directly handle 1-BP. This pathway will not be further analyzed. |
| | | | | Mist | Inhalation | ONU | Yes | EPA will further analyze the potential for mist generation. |
| | | | | Indoor vapor | Dermal | Co-located population | No | Exposure via dermal and oral routes may be unlikely. |

## Table_Apx D-1. Industrial and Commercial Activities and Uses Conceptual Model Supporting Table

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | Indoor vapor | Oral | Co-located population | No | Exposure via dermal and oral routes may be unlikely. |
| | | | | Indoor vapor | Inhalation | Co-located population | Yes | EPA expects persons living in residences co-located with dry cleaners to be exposed to vapor. EPA will further analyze exposure via the inhalation route. |
| Industrial / commercial / consumer use | Cleaning and furniture care products | Liquid spray / aerosol cleaner | Commercial use of aerosol cleaner | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization and the fraction absorbed was measured to be low (0.16%) by NIOSH. However, repeat contact may occur. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers | Yes | Due to high volatility (VP = 146 torr at 20°C), inhalation pathway should be further analyzed. |
| | | | | Vapor | Inhalation | ONU | Yes | Due to high volatility (VP = 146 torr at 20°C), inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers | Yes | Mist generation expected for aerosol applications. |
| | | | | Mist | Dermal | ONU | No | Exposure to mist is generally not expected as occupational non-users do not directly handle 1-BP. This pathway will not be further analyzed. |
| | | | | Mist | Inhalation | ONU | Yes | EPA will further analyze the potential for mist generation. |
| Industrial / commercial / consumer use | Other uses | Other aerosol uses, e.g. automotive degreasing/brake cleaning, cutting oils | See Table 2-3 for specific scenario corresponding to the condition of use. | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization and the fraction absorbed was measured to be low (0.16%) by NIOSH. However, repeat contact may occur. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | Workers | Yes | Due to high volatility (VP = 146 torr at 20°C), inhalation pathway should be further analyzed. |
| | | | | Vapor | Inhalation | ONU | Yes | Due to high volatility (VP = 146 torr at 20°C), inhalation pathway should be further analyzed. |

## Table_Apx D-1. Industrial and Commercial Activities and Uses Conceptual Model Supporting Table

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | Mist | Dermal/ Inhalation | Workers | Yes | Mist generation expected for aerosol applications. |
| | | | | Mist | Dermal | ONU | No | Exposure to mist is generally not expected as occupational non-users do not directly handle 1-BP. This pathway will not be further analyzed. |
| | | | | Mist | Inhalation | ONU | Yes | EPA will further analyze the potential for mist generation. |
| Industrial / commercial / consumer use | Other uses | Other non-aerosol uses, e.g. insulation materials, asphalt extraction, temperature indicator | See Table 2-3 for specific scenario corresponding to the condition of use. | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization and the fraction absorbed was measured to be low (0.16%) by NIOSH. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | Workers | Yes | Due to high volatility (VP = 146 torr at 20°C), inhalation pathway should be further analyzed. However, the potential for exposure is unknown where 1-BP is incorporated into articles. |
| | | | | Vapor | Inhalation | ONU | Yes | |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation is not expected for non-aerosol applications and will not be further analyzed. |
| Disposal | Waste Handling, Treatment and Disposal | Disposal of 1-BP wastes | Worker handling of wastes | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization and the fraction absorbed was measured to be low (0.16%) by NIOSH. However, EPA will further analyze exposure where occluded exposure, repeated contact, and dermal immersion may occur. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | Workers | Yes | Due to high volatility (VP = 146 torr at 20°C), inhalation pathway should be further analyzed. |
| | | | | Vapor | Inhalation | ONU | Yes | |

# APPENDIX E SUPPORTING TABLE FOR CONSUMER ACTIVITIES AND USES, GENERAL POPULATIONS, ECOLOGICAL RECEPTORS, AND ENVIRONMENTAL RELEASES AND WASTES CONCEPTUAL MODEL

(Note that rows shaded in gray are not proposed for further analysis)

**Table_Apx E-1. Consumer Scenario Table**

| Life Cycle Stage | Category | Subcategory | Release from source | Exposure Pathway | Route | Receptor | Further Analysis | Rationale for Further Analysis / No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| Co-Location with dry cleaners | Cleaning and Furniture Care Products | | Vapor | Vapor | Inhalation | Co-located populations | Yes | Based on the VP (146 mm Hg) of 1-BP and the conditions of use, inhalation exposures to 1-BP in the vapor phase is expected. |
| | | | Vapor | Vapor | Oral Dermal | Co-located populations | No | Ingestion of 1-BP is anticipated to be low since 1-BP is expected to be absorbed in the lung quickly and not have appreciable ability to travel up the mucosal elevator and be swallowed. |
| Consumer Use | Solvent (for cleaning or degreasing) | Aerosol spray degreaser/cleaner | Spray | Vapor/Mist | Inhalation | Consumers Bystanders | Yes | Based on the VP (146 mm Hg) of 1-BP and the conditions of use, inhalation exposures to 1-BP in the vapor phase from use of consumer products is expected. |
| | | | Spray | Direct dermal contact; incl occluded dermal contact | Dermal | Consumers | Yes | Based on conditions of use, consumers may have direct dermal contact to 1-BP. Occluded exposures may be higher. |
| | | | Spray | Direct dermal contact; incl occluded dermal contact | Dermal | Bystanders | No | Bystanders are not expected to have direct dermal contact to 1-BP |
| | | | Spray | Vapor/Mist | Oral | Consumers Bystanders | No | Ingestion of 1-BP is anticipated to be low since 1-BP is expected to be absorbed in the lung quickly and not have appreciable ability |

**Table_Apx E-1. Consumer Scenario Table**

| Life Cycle Stage | Category | Subcategory | Release from source | Exposure Pathway | Route | Receptor | Further Analysis | Rationale for Further Analysis / No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | | to travel up the mucosal elevator and be swallowed. |
| Consumer Use | Cleaning and Furniture Care Products | Spot Cleaner, Stain Remover | Spray | Vapor/Mist | Inhalation | Consumers Bystanders | Yes | Based on the VP (146 mm Hg) of 1-BP and the conditions of use, inhalation exposures to 1-BP in the vapor phase from use of consumer products is expected. |
| | | | Spray | Direct dermal contact; incl occluded dermal contact | Dermal | Consumers | Yes | Based on conditions of use, consumers may have direct dermal contact to 1-BP. Occluded exposures may be higher. |
| | | | Spray | Direct dermal contact; incl occluded dermal contact | Dermal | Bystanders | No | Bystanders are not expected to have direct dermal contact to 1-BP |
| | | | Spray | Vapor/Mist | Oral | Consumers Bystanders | No | Ingestion of 1-BP is anticipated to be low since 1-BP is expected to be absorbed in the lung quickly and not have appreciable ability to travel up the mucosal elevator and be swallowed. |
| Consumer Use | Cleaning and Furniture Care Products | Liquid Cleaner (e.g. coin and scissor cleaner) | Volatilization | vapor | Inhalation | Consumers Bystanders | Yes | Based on the VP (146 mm Hg) of 1-BP and the conditions of use, inhalation exposures to 1-BP in the vapor phase from use of consumer products is expected. |
| | | | Liquid | Direct dermal contact; incl occluded dermal contact | Dermal | Consumers | Yes | Based on conditions of use, consumers may have direct dermal contact to 1-BP. Occluded exposures may be higher. |
| | | | Liquid | Direct dermal contact | Dermal | Bystanders | No | Bystanders are not expected to have direct dermal contact to 1-BP |
| | | | Liquid or vapor/mist | Ingestion | Oral | Consumers Bystanders | No | Ingestion of 1-BP is anticipated to be low since 1-BP is expected to be absorbed in the lung quickly and not have appreciable ability |

**Table_Apx E-1. Consumer Scenario Table**

| Life Cycle Stage | Category | Subcategory | Release from source | Exposure Pathway | Route | Receptor | Further Analysis | Rationale for Further Analysis / No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | | to travel up the mucosal elevator and be swallowed. |
| Consumer Use | Cleaning and Furniture Care Products | Liquid Spray/aerosol Cleaner | Spray | Vapor/mist | Inhalation | Consumers Bystanders | Yes | Based on the VP (146 mm Hg) of 1-BP and the conditions of use, inhalation exposures to 1-BP in the vapor phase is expected. |
| | | | Spray | Dermal contact; incl occluded dermal contact | Dermal | Consumers | Yes | Based on conditions of use, consumers may have direct dermal contact to 1-BP. Occluded exposures may be higher. |
| | | | Spray | Direct Dermal Contact; | Dermal | Bystanders | No | Bystanders are not expected to have direct dermal contact to 1-BP |
| | | | Spray | Vapor/mist | Oral | Consumers Bystanders | No | Ingestion of 1-BP is anticipated to be low since 1-BP is expected to be absorbed in the lung quickly and not have appreciable ability to travel up the mucosal elevator and be swallowed. |
| Consumer Use | Other Uses | Arts, crafts and hobby materials – adhesive accelerant | Spray | Vapor/mist | Inhalation | Consumers Bystanders | Yes | Based on the VP (146 mm Hg) of 1-BP and the conditions of use, inhalation exposures to 1-BP in the vapor phase is expected. |
| | | | Spray | Dermal contact; incl occluded dermal contact | Dermal | Consumers | Yes | Based on conditions of use, consumers may have direct dermal contact to 1-BP. Occluded exposures may be higher. |
| | | | Spray | Direct Dermal Contact | Dermal | Bystanders | No | Bystanders are not expected to have direct dermal contact to 1-BP |
| | | | Spray | Vapor/mist | Oral | Consumers Bystanders | No | Ingestion of 1-BP is anticipated to be low since 1-BP is expected to be absorbed in the lung quickly and not have appreciable ability to travel up the mucosal elevator and be swallowed. |

**Table_Apx E-1. Consumer Scenario Table**

| Life Cycle Stage | Category | Subcategory | Release from source | Exposure Pathway | Route | Receptor | Further Analysis | Rationale for Further Analysis / No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| Consumer Use | Other Uses | Anti-adhesive agents – mold cleaning and release product | Spray | Vapor/mist | Inhalation | Consumers Bystanders | Yes | Based on the VP (146 mm Hg) of 1-BP and the conditions of use, inhalation exposures to 1-BP in the vapor phase is expected. |
| | | | Spray | Dermal contact; incl occluded dermal contact | Dermal | Consumers | Yes | Based on conditions of use, consumers may have direct dermal contact to 1-BP. Occluded exposures may be higher. |
| | | | Spray | Direct Dermal Contact | Dermal | Bystanders | No | Bystanders are not expected to have direct dermal contact to 1-BP |
| | | | Spray | Vapor/mist | Oral | Consumers Bystanders | No | Ingestion of 1-BP is anticipated to be low since 1-BP is expected to be absorbed in the lung quickly and not have appreciable ability to travel up the mucosal elevator and be swallowed. |
| Consumer Use | Other Uses | Automotive Care Products, refrigerant flush | Spray | Vapor/mist | Inhalation | Consumers Bystanders | Yes | Emissions to air from spray applied consumer uses is expected. |
| | | | Spray | Dermal contact; incl occluded dermal contact | Dermal | Consumers | Yes | Dermal contact from emissions to air from spray applied consumer uses is expected. |
| | | | Spray | Direct Dermal Contact | Dermal | Bystanders | No | Direct dermal contact by bystanders from is not expected. |
| | | | Spray | Vapor/mist | Oral | Consumers Bystanders | No | Ingestion of 1-BP is anticipated to be low since 1-BP is expected to be absorbed in the lung quickly and not have appreciable ability to travel up the mucosal elevator and be swallowed. |
| Consumer Use | Other Uses | Building/Construction materials not covered elsewhere - insulation | Offgassing | Vapor | Inhalation | Consumers Bystanders | Yes | Based on the VP (146 mm Hg) of 1-BP and the conditions of use, inhalation exposures to 1-BP in the vapor phase is expected. |

**Table_Apx E-1. Consumer Scenario Table**

| Life Cycle Stage | Category | Subcategory | Release from source | Exposure Pathway | Route | Receptor | Further Analysis | Rationale for Further Analysis / No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | Offgassing | Vapor | Dermal<br>Oral | Consumers<br>Bystanders | No | Bystanders are not expected to have direct dermal contact to 1-BP. Ingestion of 1-BP is anticipated to be low. |
| All | All | All | n/a | Solid/Liquid Contact from Handling and Disposal of Waste | Inhalation, Dermal, Ingestion | Consumers | No | 1-BP is expected to be disposed of in closed containers. |

**Table_Apx E-2. General Population, Ecological Receptors, and Environmental Releases and Wastes Scenario Table**

| Life Cycle Stage | Release | Exposure Pathway / Media | Exposure Routes | Receptor / Population | Further Analysis | Rationale for Further Analysis / No Further Analysis |
|---|---|---|---|---|---|---|
| All | Stack Emissions to Air | Near Facility Ambient Air Concentrations | Inhalation | General Population: Adults and Children living near facilities | Yes | Releases of 1-BP to air are expected based on TRI data. Based on the relatively long hydroxy radical oxidation half-life ($t_{½}$ = 14 days) emissions to ambient air could travel far enough from the release point to reach both near facility human receptors and the general population. |
| All | Fugitive Emissions to Air | Near Facility Ambient Air Concentrations | Inhalation | General Population: Adults and Children living near facilities | Yes | |
| All | Stack Emissions to Air | Indirect deposition to nearby bodies of water and soil catchments | Surface water and sediment (lakes)-Ingestion<br>Soil (catchments)-Ingestion | General Population: Adults and Children living near facilities | No | Based on the Koc of 40, 1-BP is not expected to adsorb strongly to sediment or soil. 1-BP is volatile and has a relatively high Henry's law constant. It is somewhat biodegradable and is not expected to sorb to solids in water. |
| All | Stack Emissions to Air | Indirect deposition to nearby bodies of water and soil catchments | Surface water and sediment (lakes)<br>Soil (catchments) | Aquatic and Terrestrial Receptors | No | |

**Table_Apx E-2. General Population, Ecological Receptors, and Environmental Releases and Wastes Scenario Table**

| Life Cycle Stage | Release | Exposure Pathway / Media | Exposure Routes | Receptor / Population | Further Analysis | Rationale for Further Analysis / No Further Analysis |
|---|---|---|---|---|---|---|
| All | Fugitive Emissions to Air | Indirect deposition to nearby bodies of water and soil catchments | Surface water and sediment (lakes)- Ingestion Soil (catchments)- Ingestion Uptake from environment into food sources- Ingestion | General Population: Adults and Children living near facilities | No | |
| All | Fugitive Emissions to Air | Indirect deposition to nearby bodies of water and soil catchments | Surface water and sediment (lakes) Soil (catchments) | Aquatic and Terrestrial Receptors | No | |
| All | Industrial pre-treatment and wastewater treatment- | Direct release into surface water and partitioning to sediment | Surface water and Sediment (rivers) | Aquatic and Terrestrial Receptors | No | Recent TRI reporting indicated 0 pounds released to POTWs and 5 pounds released directly to water in 2016. Based on 1-BP surface water concentrations estimated using TRI 2016 releases to water, EFAST modeling and the acute fish toxicity $EC_{50}$ value 24.3 mg/L, the concentration of concern is not expected to be exceeded. Based on the Koc of 40, 1-BP is not expected to adsorb strongly to sediment. Ingestion of surface water is not expected to be a significant route of exposure. |
| All | Industrial pre-treatment and wastewater treatment- | Direct release into surface water and partitioning to sediment | Surface water and Sediment (rivers)- Ingestion | General Population: Adults and Children living near facilities | No | |
| All | Industrial pre-treatment and wastewater treatment- | Biosolids application to soil | Soil ingestion | General Population: Adults and Children living near facilities | No | Based on the Koc of 40, 1-BP is not expected to adsorb strongly to sediment or soil. If present in biosolids, 1-BP would be expected to associate with the aqueous component and volatilize to air as the biosolids are applied to soil and allowed to dry. |
| All | Industrial pre-treatment and | Biosolids application to soil | Soil | Terrestrial receptors | No | Based on the Koc of 40, 1-BP is not expected to adsorb strongly to sediment or soil. |

**Table_Apx E-2. General Population, Ecological Receptors, and Environmental Releases and Wastes Scenario Table**

| Life Cycle Stage | Release | Exposure Pathway / Media | Exposure Routes | Receptor / Population | Further Analysis | Rationale for Further Analysis / No Further Analysis |
|---|---|---|---|---|---|---|
| | wastewater treatment- | | | | | |
| All | Wastewater injected underground | Any | Any | Any | No | TRI reporting only indicated 10 pounds released to underground injection to a Class I well in 2016. The underground injection of certain classes of chemicals/wastes (i.e., hazardous) may be limited to practices that mitigate groundwater impacts. |
| All | Industrial pre-treatment and wastewater treatment- | Direct release into surface water and indirect partitioning to sediment | Surface water and Sediment (rivers) | Aquatic and Terrestrial Receptors | No | Recent TRI reporting indicated 0 pounds released to POTWs and 5 pounds released directly to water in 2016. Based on 1-BP surface water concentrations estimated using TRI 2016 releases to water, EFAST modeling and the acute fish toxicity $EC_{50}$ value 24.3 mg/L, the concentration of concern is not expected to be exceeded. Based on the Koc of 40, 1-BP is not expected to adsorb strongly to sediment.<br>Ingestion of surface water is not expected to be a significant route of exposure. |
| All | Industrial pre-treatment and wastewater treatment- | Direct release into surface water and partitioning to sediment | Surface water and Sediment (rivers)- Ingestion | General Population: Adults and Children living near facilities | No | |
| All | Industrial pre-treatment and wastewater treatment- | Biosolids application to soil | Soil | Terrestrial receptors | No | Based on the Koc of 40, 1-BP is not expected to adsorb strongly to sediment or soil. HBCD has not been detected in soil samples. |
| Disposal | Hazardous Waste Landfill | All | All | All | No | Due to design and operating practices for Subtitle C landfills, general population exposure to 1-BP in groundwater from Subtitle C hazardous waste landfill leachate is not expected to be a significant pathway and will not be further analyzed. |
| Disposal | Solid and Liquid Wastes sent to On or Off-site Incineration/ Energy Recovery | Near Facility Ambient Air Concentrations | Inhalation | General Population: Adults and Children living near facilities | Yes | Air emissions resulting from these operations are included in the TRI reports. Municipal incinerators may release 1-BP due to incomplete removal during burning. |

**Table_Apx E-2. General Population, Ecological Receptors, and Environmental Releases and Wastes Scenario Table**

| Life Cycle Stage | Release | Exposure Pathway / Media | Exposure Routes | Receptor / Population | Further Analysis | Rationale for Further Analysis / No Further Analysis |
|---|---|---|---|---|---|---|
| Disposal | Solid and Liquid Wastes sent to On-Site or Off-site Incineration/ Energy Recovery | Near Facility Ambient Air Concentrations | Inhalation | Terrestrial Receptors | No | Low Hazard: No available sediment, soil, nor avian toxicity studies found in the scientific literature for 1-BP. The toxicity of 1-BP is expected to be low based on the lack of on-topic environmental hazard data for 1-BP to sediment and terrestrial organisms in the published literature and the physical/chemical/fate properties (relatively high volatility (Henry's Law constant of $7.3X10^{-3}$ atm-$m^3$/mole), high water solubility (2.4 g/L), and low log $K_{oc}$ (1.6) suggesting that 1-BP will only be present at low concentrations in these environmental compartments. |
| Disposal | Municipal landfill and other land disposal | Soil | Soil | Terrestrial Receptors | No | Low Hazard: No available sediment, soil, nor avian toxicity studies found in the scientific literature for 1-BP. The toxicity of 1-BP is expected to be low based on the lack of on-topic environmental hazard data for 1-BP to sediment and terrestrial organisms in the published literature and the physical/chemical/fate properties (relatively high volatility (Henry's Law constant of $7.3X10^{-3}$ atm-$m^3$/mole), high water solubility (2.4 g/L), and low log $K_{oc}$ (1.6) suggesting that 1-BP will only be present at low concentrations in these environmental compartments. |
| Disposal | Municipal landfill and other land disposal | Soil to air | Inhalation | General Population: Adults and Children living near facilities | No | Releases from municipal landfill to soil are not expected. States ensure the federal criteria for operating RCRA Subtitle D municipal solid waste and industrial waste landfills regulations are met. |
| Recycling | Recycling of 1-BP | All | All | All | No | Recycling of 1-BP is not expected. |

**Table_Apx E-2. General Population, Ecological Receptors, and Environmental Releases and Wastes Scenario Table**

| Life Cycle Stage | Release | Exposure Pathway / Media | Exposure Routes | Receptor / Population | Further Analysis | Rationale for Further Analysis / No Further Analysis |
|---|---|---|---|---|---|---|
| All | Background | Surface water | Ingestion | General Population: Adults and Children Aquatic and Terrestrial Receptors | No | TRI reporting indicates little to no releases to water. |
| All | Background | Sediment | Ingestion | Aquatic Receptors | No | TRI reporting indicates little to no releases to water. Based on the Koc of 40, 1-BP is not expected to adsorb strongly to sediment. |
| All | Background | Soil | Ingestion | General Population: Adults and Children Terrestrial Receptors | No | Based on the Koc of 40, 1-BP is not expected to adsorb strongly to sediment or soil. HBCD has not been detected in soil samples. |
| All | Background | Aquatic Biota | n/a | Aquatic Receptors | No | |
| All | Background | Terrestrial Biota | n/a | Terrestrial receptors | No | |
| All | Background | Ambient Air | Inhalation | General Population | Yes | Based on the VP (146 mm Hg) of 1-BP and the conditions of use, inhalation exposures to 1-BP in the vapor phase is expected. |
| All | Background | Indoor Air | Inhalation | General Population | Yes | Based on the VP (146 mm Hg) of 1-BP and the conditions of use, inhalation exposures to 1-BP in the vapor phase is expected. |
| All | Background | Indoor Dust | Ingestion, Dermal | General Population | No | There are no data indicating 1-BP is present in dust. |
| All | Background | Dietary Food Sources | Ingestion | General Population | No | There are no data indicating 1-BP is present in food. |
| All | Background | Human Biomonitoring - breast milk | n/a | General Population | No | |

# APPENDIX F INCLUSION AND EXCLUSION CRITERIA FOR FULL TEXT SCREENING

Appendix F contains the eligibility criteria for various data streams informing the TSCA risk evaluation: environmental fate; engineering and occupational exposure; exposure to consumers; and human health hazard. The criteria are applied to the *on-topic* references that were identified following title and abstract screening of the comprehensive search results published on June 22, 2017.

Systematic reviews typically describe the study eligibility criteria in the form of PECO statements or a modified framework. PECO stands for Population, Exposure, Comparator and Outcome and the approach is used to formulate explicit and detailed criteria about those characteristics in the publication that should be present in order to be eligible for inclusion in the review. EPA/OPPT adopted the PECO approach to guide the inclusion/exclusion decisions during full text screening.

Inclusion and exclusion criteria were also used during the title and abstract screening, and documentation about the criteria can be found in the *Strategy for Conducting Literature Searches* document published in June 2017 along with each of the TSCA Scope documents. The list of *on-topic* references resulting from the title and abstract screening is undergoing full text screening using the criteria in the PECO statements. The overall objective of the screening process is to select the most relevant evidence for the TSCA risk evaluation. As a general rule, EPA is excluding non-English data/information sources and will translate on a case by case basis.

The inclusion and exclusion criteria for ecotoxicological data have been documented in the ECOTOX SOPs. The criteria can be found at https://cfpub.epa.gov/ecotox/help.cfm?helptabs=tab4) and in the *Strategy for Conducting Literature Searches* document published along with each of the TSCA Scope documents.

## F.1 Inclusion Criteria for Data Sources Reporting Environmental Fate Data

EPA/OPPT developed a generic PESO statement to guide the full text screening of environmental fate data sources. PESO stands for Pathways and Processes, Exposure, Setting or Scenario, and Outcomes. Subsequent versions of the PESO statement may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the inclusion criteria in the PESO statement are eligible for inclusion, considered for evaluation, and possibly included in the environmental fate assessment. On the other hand, data sources are excluded if they do not meet the criteria in the PESO statement.

Assessors seek information on various chemical-specific fate endpoints and associated fate processes, environmental media and exposure pathways as part of the process of developing the environmental fate assessment (Table_Apx F-2). The PESO statement and information in Table_Apx F-1 will be used when screening the fate data sources to ensure complete coverage of the processes, pathways and data relevant to the fate of the chemical substance of interest.

| Table_Apx F-1. Inclusion Criteria for Data Sources Reporting Environmental Fate Data | |
|---|---|
| **PESO Element** | **Evidence** |
| **P**athways and **P**rocesses | • Environmental fate, transport, partitioning and degradation behavior across environmental media to inform exposure pathways of the chemical substance of interest<br>• Media of interest may include:<br>– Air<br>Please refer to the conceptual models for more information about the exposure pathways included in the TSCA risk evaluation. |
| **E**xposure | • Environmental exposure of ecological receptors (i.e., aquatic and terrestrial organisms) to the chemical substance of interest and/or its degradation products and metabolites<br>• Environmental exposure of human receptors, including any potentially exposed or susceptible subpopulations, to the substance of interest and/or its degradation products and metabolites<br><br>Please refer to the conceptual models for more information about the ecological and human receptors included in the TSCA risk evaluation. |
| **S**etting or **S**cenario | Any setting or scenario resulting in releases of the chemical substance of interest into the natural or built environment (e.g., buildings including homes or workplaces, or wastewater treatment facilities) that would expose ecological (i.e., aquatic and terrestrial organisms) or human receptors (i.e., general population, and potentially exposed or susceptible subpopulation) |
| **O**utcomes | • Fate properties which allow assessments of exposure pathways:<br>o Abiotic and biotic degradation rates, mechanisms, pathways, and products<br>o Bioaccumulation magnitude and metabolism rates<br>o Partitioning within and between environmental media (see Pathways and Processes) |

**Table_Apx F-2. Fate Endpoints and Associated Processes, Media and Exposure Pathways Considered in the Development of the Environmental Fate Assessment**

| Fate Data Endpoint | Associated Process(es) | Associated Media/Exposure Pathways | | | | |
|---|---|---|---|---|---|---|
| | | Surface water, Sediment | Soil, Biosolids | Ground-water | Air | [Indoor environment, anthropogenic materials, other media] |
| **Required Environmental Fate Data** | | | | | | |
| Abiotic reduction rates or half-lives | Abiotic reduction, Abiotic dehalogenation | X | | | | |
| Aerobic biodegradation rates or half-lives | Aerobic biodegradation | X | X | | | |
| Anaerobic biodegradation rates or half-lives | Anaerobic biodegradation | X | X | X | | |
| Aqueous photolysis (direct and indirect) rates or half-lives | Aqueous photolysis (direct and indirect) | X | | | | |
| Atmospheric photolysis (direct and indirect) rates or half-lives | Atmospheric photolysis (direct and indirect) | | | | X | |
| Bioconcentration factor (BCF), Bioaccumulation factor (BAF) | Bioconcentration, Bioaccumulation | X | | | | |
| Hydrolysis rates or half-lives | Hydrolysis | X | | | | |
| $K_{AW}$, Henry's Law constant, and other volatilization information | Volatilization | X | X | | X | |
| $K_{OC}$ and other sorption information | Sorption, Mobility | X | X | X | | |
| [Other required data) | | | | | | |
| **Optional Environmental Fate Data** | | | | | | |
| Abiotic transformation products | Hydrolysis, Photolysis | X | | | X | |
| Aerobic biotransformation products | Aerobic biodegradation | X | X | | | |

| Table_Apx F-2. Fate Endpoints and Associated Processes, Media and Exposure Pathways Considered in the Development of the Environmental Fate Assessment | | | | | | |
|---|---|---|---|---|---|---|
| Anaerobic biotransformation products | Anaerobic biodegradation | X | X | X | | |
| Atmospheric deposition information | Atmospheric deposition | | | | X | |
| Biomagnification and related information | Trophic magnification | X | | | | |
| Coagulation information | Coagulation, Mobility | X | | | | |
| Desorption information | Sorption, Mobility | X | X | X | | |
| Incineration removal information | Incineration | | | | X | |
| Suspension/resuspension information | Suspension/resuspension, Mobility | X | | | | |
| Wastewater treatment removal information | Wastewater treatment | X | | | | |
| [Other optional data] | | | | | | |

## F.2 Inclusion Criteria for Data Sources Reporting Exposure Data on Consumers, General Population, and Ecological Receptors

EPA/OPPT developed PECO statements to guide the full text screening of exposure data/information for human (i.e., consumers, potentially exposed or susceptible subpopulations). Subsequent versions of the PECO statements may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the inclusion criteria in the PECO statement are eligible for inclusion, considered for evaluation, and possibly included in the exposure assessment. On the other hand, data sources are excluded if they do not meet the criteria in the PECO statement. The 1-BP-specific PECO is provided in **Table_Apx F-3**.

| Table_Apx F-3. Inclusion Criteria for the Data Sources Reporting 1-BP Exposure Data on Consumers and General Population | |
|---|---|
| **PECO Element** | **Evidence** |
| **P**opulation | **Human:** General population, consumers (i.e., receptors who use a product directly) and bystanders (i.e., receptors who are non-product users that are incidentally exposed to the product or article) in residential settings, near-facility populations (includes industrial and commercial facilities manufacturing, processing or using 1-BP); populations in co-located residences or businesses; including potentially exposed or susceptible subpopulations such as infants, children, pregnant women, lactating women, women of child bearing age, and high-end consumers. |
| | **Ecological:** None. |
| **E**xposure | **Expected Primary Exposure Sources, Pathways, Routes:** *See Figure 2-3 and Figure 2-4* |

| Table_Apx F-3. Inclusion Criteria for the Data Sources Reporting 1-BP Exposure Data on Consumers and General Population | |
|---|---|
| **PECO Element** | **Evidence** |
| | Source: Manufacturing, processing, commercial and consumer use of products containing 1-BP as an ingredient, and associated emissions to air or dermal contact.<br>Pathway: indoor air (including transfer from outdoor air), outdoor air, dermal contact with 1-BP in consumer products<br>Routes of Exposure: Inhalation of outdoor air or indoor air (consumer and bystander populations) and dermal exposure via contact with consumer products containing 1-BP. |
| **C**omparator (Scenario) | **Human:** Consider media-specific background exposure scenarios and use/source specific exposure scenarios as well as which receptors are and are not reasonably exposed across the projected exposure scenarios. |
| | **Ecological:** None. |
| **O**utcomes for Exposure Concentration or Dose | **Human:** Acute, subchronic, and/or chronic external dose estimates (mg/kg/day); acute, subchronic, and/or chronic air concentration estimates (µg/m$^3$, mg/m$^3$). Both external potential dose and internal dose based on biomonitoring and reverse dosimetry mg/kg/day will be considered. |
| | **Ecological:** None. |

## F.3 Inclusion Criteria for Data Sources Reporting Engineering and Occupational Exposure Data

EPA/OPPT developed a generic RESO statement to guide the full text screening of engineering and occupational exposure literature (Table_Apx F-4). RESO stands for Receptors, Exposure, Setting or Scenario, and Outcomes. Subsequent versions of the RESO statement may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the inclusion criteria specified in the RESO statement will be eligible for inclusion, considered for evaluation, and possibly included in the environmental release and occupational exposure assessments, while those that do not meet these criteria will be excluded.

The RESO statement should be used along with the engineering and occupational exposure data needs table (Table_Apx F-5) when screening the literature.

| Table_Apx F-4. Inclusion Criteria for Data Sources Reporting Engineering and Occupational Exposure Data | |
|---|---|
| **RESO Element** | **Evidence** |
| **R**eceptors | • **Humans:**<br>Workers, including occupational non-users<br><br>Please refer to the conceptual models for more information about the human receptors included in the TSCA risk evaluation. |

| Table_Apx F-4. Inclusion Criteria for Data Sources Reporting Engineering and Occupational Exposure Data | |
|---|---|
| **E**xposure | • Worker exposure to and relevant environmental releases of the chemical substance of interest<br>o Any exposure route (list included: dermal, inhalation, oral) as indicated in the conceptual model<br>o Any relevant media/pathway [list included: water, land, air, incineration, and other(s)] as indicated in the conceptual model<br>Please refer to the conceptual models for more information about the routes and media/pathways included in the TSCA risk evaluation. |
| **S**etting or **S**cenario | • Any occupational setting or scenario resulting in worker exposure and relevant environmental releases (includes all manufacturing, processing, use, disposal indicated in Table_Apx F-5 below except (state none excluded or list excluded uses) |
| **O**utcomes | • Quantitative estimates* of worker exposures and of relevant environmental releases from occupational settings<br>• General information and data related and relevant to the occupational estimates* |

* Metrics (e.g., mg/kg/day or mg/m$^3$ for worker exposures, kg/site/day for releases) are determined by toxicologists for worker exposures and by exposure assessors for releases; also, the Engineering Data Needs (Table_Apx F-5) provides a list of related and relevant general information.

| Table_Apx F-5. Engineering, Environmental Release and Occupational Data Necessary to Develop the Environmental Release and Occupational Exposure Assessments | |
|---|---|
| **Objective Determined during Scoping** | **Type of Data** |
| General Engineering Assessment (may apply for either or both Occupational Exposures and / or Environmental Releases) | 1. Description of the life cycle of the chemical(s) of interest, from manufacture to end-of-life (e.g., each manufacturing, processing, or use step), and material flow between the industrial and commercial life cycle stages. {Tags: Life cycle description, Life cycle diagram}[a]<br>2. The total annual U.S. volume (lb/yr or kg/yr) of the chemical(s) of interest manufactured, imported, processed, and used; and the share of total annual manufacturing and import volume that is processed or used in each life cycle step. {Tags: Production volume, Import volume, Use volume, Percent PV} [a]<br>3. Description of processes, equipment, unit operations, and material flows and frequencies (lb/site-day or kg/site-day and days/yr; lb/site-batch and batches/yr) of the chemical(s) of interest during each industrial/ commercial life cycle step. Note: if available, include weight fractions of the chemicals (s) of interest and material flows of all associated primary chemicals (especially water). {Tags: Process description, Process material flow rate, Annual operating days, Annual batches, Weight fractions (for each of above, manufacture, import, processing, use)} [a]<br>4. Basic chemical properties relevant for assessing exposures and releases, e.g., molecular weight, normal boiling point, melting point, physical forms, and room temperature vapor pressure. {Tags: Molecular weight, Boiling point, Melting point, Physical form, Vapor pressure, Water solubility} [a]<br>5. Number of sites that manufacture, process, or use the chemical(s) of interest for each industrial/ commercial life cycle step and site locations. {Tags: Numbers of sites (manufacture, import, processing, use), Site locations} [a] |
| Occupational Exposures | 6. Description of worker activities with exposure potential during the manufacture, processing, or use of the chemical(s) of interest in each industrial/commercial life cycle stage. {Tags: Worker activities (manufacture, import, processing, use)} [a] |

**Table_Apx F-5. Engineering, Environmental Release and Occupational Data Necessary to Develop the Environmental Release and Occupational Exposure Assessments**

| Objective Determined during Scoping | Type of Data |
|---|---|
| | 7. Potential routes of exposure (e.g., inhalation, dermal). {Tags: Routes of exposure (manufacture, import, processing, use)} [a]<br>8. Physical form of the chemical(s) of interest for each exposure route (e.g., liquid, vapor, mist) and activity. {Tags: Physical form during worker activities (manufacture, import, processing, use)} [a]<br>9. Breathing zone (personal sample) measurements of occupational exposures to the chemical(s) of interest, measured as time-weighted averages (TWAs), short-term exposures, or peak exposures in each occupational life cycle stage (or in a workplace scenario similar to an occupational life cycle stage). {Tags: PBZ measurements (manufacture, import, processing, use)} [a]<br>10. Area or stationary measurements of airborne concentrations of the chemical(s) of interest in each occupational setting and life cycle stage (or in a workplace scenario similar to the life cycle stage of interest). {Tags: Area measurements (manufacture, import, processing, use)} [a]<br>11. For solids, bulk and dust particle size characterization data. {Tags: PSD measurements (manufacture, import, processing, use)} [a]<br>12. Dermal exposure data. {Tags: Dermal measurements (manufacture, import, processing, use)}<br>13. Data needs associated with mathematical modeling (will be determined on a case-by-case basis). {Tags: Worker exposure modeling data needs (manufacture, import, processing, use)} [a]<br>14. Exposure duration (hr/day). {Tags: Worker exposure durations (manufacture, import, processing, use)} [a]<br>15. Exposure frequency (days/yr). {Tags: Worker exposure frequencies (manufacture, import, processing, use)} [a]<br>16. Number of workers who potentially handle or have exposure to the chemical(s) of interest in each occupational life cycle stage. {Tags: Numbers of workers exposed (manufacture, import, processing, use)} [a]<br>17. Personal protective equipment (PPE) types employed by the industries within scope. {Tags: Worker PPE (manufacture, import, processing, use)} [a]<br>18. Engineering controls employed to reduce occupational exposures in each occupational life cycle stage (or in a workplace scenario similar to the life cycle stage of interest), and associated data or estimates of exposure reductions. {Tags: Engineering controls (manufacture, import, processing, use), Engineering control effectiveness data} [a] |
| Environmental Releases (to relevant environmental media) | 19. Description of relevant sources of potential environmental releases, including cleaning of residues from process equipment and transport containers, involved during the manufacture, processing, or use of the chemical(s) of interest in each life cycle stage. {Tags: Release sources (manufacture, import, processing, use)} [a]<br>20. Estimated mass (lb or kg) of the chemical(s) of interest released from industrial and commercial sites to each environmental medium (water) and treatment and disposal methods (POTW), including releases per site and aggregated over all sites (annual release rates, daily release rates) {Tags: Release rates (manufacture, import, processing, use)} [a]<br>21. Release or emission factors. {Tags: Emission factors (manufacture, import, processing, use)} [a]<br>22. Number of release days per year. {Tags: Release frequencies (manufacture, import, processing, use)} [a]<br>23. Data needs associated with mathematical modeling (will be determined on a case-by-case basis). {Tags: Release modeling data needs (manufacture, import, processing, use)} [a]<br>24. Waste treatment methods and pollution control devices employed by the industries within scope and associated data on release/emission reductions. {Tags: Treatment/ emission controls (manufacture, import, processing, use), Treatment/ emission controls removal/ effectiveness data} [a] |

**Notes:**

[a]These are the tags included in the full text screening form. The screener makes a selection from these specific tags, which describe more specific types of data or information.

## F.4 Inclusion Criteria for Data Sources Reporting Human Health Hazards

EPA/OPPT developed a 1-BP-specific PECO statement (Table_Apx F-6) to guide the full text screening of the human health hazard literature. Subsequent versions of the PECOs may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the criteria specified in the PECO statement will be eligible for inclusion, considered for evaluation, and possibly included in the human health hazard assessment, while those that do not meet these criteria will be excluded according to the exclusion criteria.

In general, the PECO statements were based on (1) information accompanying the TSCA Scope document, and (2) preliminary review of the health effects literature from sources cited in the TSCA Scope documents. When applicable, these sources (e.g., IRIS assessments, EPA/OPPT's Work Plan Problem Formulations or risk assessments) will serve as starting points to identify PECO-relevant studies.

**Table_Apx F-6. Inclusion and Exclusion Criteria for the Data Sources Reporting Human Health Hazards Related to 1-BP Exposure[a]**

| PECO Element | Evidence Stream | Papers/Features Included | Papers/Features Excluded |
|---|---|---|---|
| **Population [b]** | *Human* | • Any population<br>• All lifestages<br>• Study designs:<br>o Controlled exposure, cohort, case-control, cross-sectional, case-crossover<br>o Case studies and case series that are related to deaths from acute exposure | • Case studies and case series for all endpoints ***other than*** death from acute exposure |
| | *Animal* | • All non-human whole-organism mammalian species<br>• All lifestages | • Non-mammalian species |
| **Exposure** | *Human* | • Exposure based on administered dose or concentration of 1-BP, biomonitoring data (e.g., urine, blood or other specimens), environmental or occupational-setting monitoring data (e.g., air, water levels), job title or residence<br>• Primary metabolites of interest as identified in biomonitoring studies<br>• Exposure identified as ***or presumed to be*** from oral, dermal, inhalation routes<br>• Any number of exposure groups<br>• Quantitative, semi-quantitative or qualitative estimates of exposure<br>• Exposures to multiple chemicals/mixtures only if 1-BP or related metabolites were independently measured and analyzed | • Route of exposure ***not*** by inhalation, oral or dermal type (e.g., intraperitoneal, injection)<br>• Multiple chemical/mixture exposures with no independent measurement of or exposure to 1-BP (or related metabolite) |
| | *Animal* | • A minimum of 2 quantitative dose or concentration levels of 1-BP plus a negative control group[a]<br>• Acute, subchronic, chronic exposure from oral, dermal, inhalation routes<br>• Exposure to 1-BP only (no chemical mixtures)<br>• Quantitative and/or qualitative relative/rank-order estimates of exposure | • Only 1 quantitative dose or concentration level in addition to the control<br>• Route of exposure ***not*** by inhalation, oral or dermal type (e.g., intraperitoneal, injection)<br>• No duration of exposure stated<br>• Exposure to 1-BP in a chemical mixture |
| **Comparator** | *Human* | • A comparison population [not exposed, exposed to lower levels, exposed below detection] for endpoints ***other than*** | • No comparison population for endpoints other than death from acute |

| Table_Apx F-6. Inclusion and Exclusion Criteria for the Data Sources Reporting Human Health Hazards Related to 1-BP Exposure[a] | | | |
|---|---|---|---|
| | | death from acute exposure | exposure |
| | *Animal* | • Negative controls that are vehicle-only treatment and/or no treatment | • Negative controls ***other than*** vehicle-only treatment or no treatment |
| **Outcome** | *Human* | • Endpoints described in the 1-BP scope document [c]:<br>o Kidney toxicity<br>o Liver toxicity<br>o Neurotoxicity<br>o Reproductive toxicity<br>o Developmental toxicity<br>o Cancer<br>• Other endpoints [d] | |
| | *Animal* | | |
| **General Considerations** | | **Papers/Features Included** | **Papers/Features Excluded** |
| | | • Written in English [e]<br>• Reports primary source or meta-analysis. [a]<br>• Full-text available<br>• Reports both 1-BP exposure ***and*** a health outcome | • Not written in English<br>• Reports a secondary source (e.g., review papers) [a]<br>• No full-text available (e.g., only a study description/abstract, out-of-print text)<br>• Reports a 1-BP-related exposure ***or*** a health outcome, but not both (e.g. incidence, prevalence report) |

[a]Some of the studies that are excluded based on the PECO statement may be considered later during the systematic review process. For 1-BP, EPA will evaluate studies related to susceptibility and may evaluate, toxicokinetics and physiologically based pharmacokinetic models after other data (e.g., human and animal data identifying adverse health outcomes) are reviewed. EPA may need to evaluate mechanistic data depending on the review of health effects data. Finally, EPA may also review other data as needed (e.g., animal studies using one concentration, review papers).

[b] Mechanistic data are excluded during the full text screening phase of the systematic review process but may be considered later (see footnote *a*).

[c] EPA will review key and supporting studies that were considered in the 2016 Draft Risk Assessment (U.S. EPA, 2016b) for 1-BP for non-cancer and cancer endpoints as well as studies published after the draft. assessment.

[d] EPA may screen for hazards other than those listed in the scope document if they were identified in the updated literature search that accompanied the scope document.

[e] EPA may translate studies as needed.

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Office of Chemical Safety and
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United States
Environmental Protection Agency

# Problem Formulation of the Risk Evaluation for Asbestos

*May 2018*

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## ACKNOWLEDGEMENTS

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**Docket**

Supporting information can be found in public docket: EPA-HQ-OPPT-2016-0736.

**Disclaimer**

Reference herein to any specific commercial products, process or service by trade name, trademark, manufacturer or otherwise does not constitute or imply its endorsement, recommendation or favoring by the United States Government.

## ABBREVIATIONS

| | |
|---|---|
| ABPO | 1989 Asbestos Ban and Phase Out Rule |
| ACC | American Chemistry Council |
| ACGIH TLV | American Conference of Governmental Industrial Hygienists Threshold Limit Value |
| AHERA | Asbestos Hazard Emergency Response Act |
| ASHAA | Asbestos School Hazard Abatement Act |
| ASHARA | Asbestos School Hazard Abatement Reauthorization Act |
| ATSDR | Agency for Toxic Substances and Disease Registries |
| CAA | Clean Air Act |
| CASRN | Chemical Abstract Service Registry Number |
| CBI | Confidential Business Information |
| CDR | Chemical Data Reporting |
| CEPA | Canadian Environmental Protection Act |
| CERCLA | Comprehensive Environmental Response, Compensation and Liability Act |
| ChV | Chronic Value |
| COC | Concentration of Concern |
| CPCat | Chemical and Product Categories |
| CPID | Consumer Product Information Database |
| CPSC | Consumer Product Safety Commission |
| CWA | Clean Water Act |
| DHHS | Department of Health and Human Services |
| EG | Effluent Guideline |
| EMP | Elongated Mineral Particle |
| EPA | Environmental Protection Agency |
| EPCRA | Emergency Planning and Community Right-to-Know Act |
| EU | European Union |
| FDA | Food and Drug Administration |
| f/cc | Fibers per cubic centimeter |
| FHSA | Federal Hazardous Substance Act |
| g | Gram(s) |
| HEPA | High-Efficiency Particulate Air |
| HTS | Harmonized Tariff Schedule |
| IARC | International Agency for Research on Cancer |
| IgA | Immunoglobulin A |
| IgG | Immunoglobulin G |
| IRIS | Integrated Risk Information System |
| lb | Pound |
| LOEC | Lowest Observable Effect Concentration |
| MAP | Model Accreditation Plan |
| MCLG | Maximum Contaminant Level Goal |
| µm | Micrometers |
| MFL | Million Fibers per Liter |
| mg | Milligram(s) |
| MPa | Megapascal |
| MSDS | Material Safety Data Sheet |
| MSHA | Mine Safety and Health Administration |
| mV | Millivolt |
| NAICS | North American Industrial Classification System |
| ND | Non-detects (value is < analytical detection limit) |

| | |
|---|---|
| NEI | National Emissions Inventory |
| NESHAP | National Emission Standard for Hazardous Air Pollutants |
| NIH | National Institutes of Health |
| NIOSH | National Institute for Occupational Safety and Health |
| NOEC | No Observable Effect Concentration |
| NOI | Notice of Intent |
| NPL | National Priorities List |
| NTP | National Toxicology Program |
| OCSPP | Office of Chemical Safety and Pollution Prevention |
| OECD | Organisation for Economic Co-operation and Development |
| ONU | Occupational Non-User |
| OPPT | Office of Pollution Prevention and Toxics |
| OSHA | Occupational Safety and Health Administration |
| PBPK | Physiologically Based Pharmacokinetic |
| PECO | Population, Exposure, Comparator and Outcome |
| PEL | Permissible Exposure Level |
| PESO | Pathways/Processes, Exposure, Setting and Outcomes |
| POD | Point of Departure |
| POTW | Publicly Owned Treatment Works |
| PPE | Personal Protective Equipment |
| ppm | Part(s) per Million |
| RCRA | Resource Conservation and Recovery Act |
| PV | Production Volume |
| QSAR | Quantitative Structure Activity Relationship |
| RA | Risk Assessment |
| RESO | Receptors, Exposure, Setting/Scenario and Outcomes |
| RfC | Reference Concentration |
| RIA | Regulatory Impact Analysis |
| SDS | Safety Data Sheet |
| SDWA | Safe Drinking Water Act |
| TCCR | Transparent, Clear, Consistent, and Reasonable |
| TRI | Toxics Release Inventory |
| TSCA | Toxic Substances Control Act |
| TURA | Toxics Use Reduction Act |
| TWA | Time Weighted Average |
| UCMR 3 | Unregulated Contaminant Monitoring Rule 3 |
| U.S. | United States |
| USGS | United States Geological Survey |
| WHO | World Health Organization |

# EXECUTIVE SUMMARY

TSCA § 6(b)(4) requires the U.S. Environmental Protection Agency (EPA) to establish a risk evaluation process. In performing risk evaluations for existing chemicals, EPA is directed to "determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of costs or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator under the conditions of use." In December of 2016, EPA published a list of 10 chemical substances that are the subject of the Agency's initial chemical risk evaluations (81 FR 91927), as required by TSCA § 6(b)(2)(A). Asbestos was one of these chemicals.

TSCA § 6(b)(4)(D) requires that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use and potentially exposed or susceptible subpopulations that the Administrator expects to consider and in June 2017, EPA published the Scope of the Risk Evaluation for Asbestos. As explained in the scope document, because there was insufficient time for EPA to provide an opportunity for comment on a draft of the scope, as EPA intends to do for future scope documents, EPA is publishing and taking public comment on a problem formulation document to refine the current scope, as an additional interim step prior to publication of the draft risk evaluation for asbestos. Comments received on this problem formulation document will inform development of the draft risk evaluation.

This problem formulation document refines the conditions of use, exposures and hazards presented in the scope of the risk evaluation for asbestos and presents refined conceptual models and analysis plans that describe how EPA expects to evaluate the risk for asbestos.

For the purposes of scoping, problem formulation and risk evaluation, EPA has adopted the definition of asbestos as defined by TSCA Title II (added to TSCA in 1986), Section 202 as the "asbestiform varieties of six fiber types – chrysotile (serpentine), crocidolite (riebeckite), amosite (cummingtonite-grunerite), anthophyllite, tremolite or actinolite." The latter five fiber types are amphibole varieties. The general CAS Registry Number (CASRN) of asbestos is 1332-21-4; this is the only asbestos CASRN on the TSCA Inventory. However, other CASRNs are available for specific fiber types.

Asbestos has not been mined or otherwise produced in the United States since 2002; therefore, any new asbestos entering this country is imported. In 2017, the United States imported approximately 300 metric tons of raw asbestos, all of it comprised of chrysotile asbestos.

EPA has identified the ongoing use of chrysotile asbestos in: industrial processes in the chlor-alkali industry, asbestos sheet gaskets for use in equipment used in the manufacture of titanium dioxide and asbestos brake blocks in oilfield equipment and aftermarket asbestos brake linings. In addition, certain asbestos containing products can be imported into the U.S., but the amounts are not known. These products are mostly used in industrial processes (e.g. cement products) but could also be used by consumers, and include woven products and automotive brakes and linings.

In the case of asbestos, legacy uses, associated disposals, and legacy disposals will be excluded from the problem formulation and risk evaluation, as they were in the Scope document. These include asbestos-containing materials that remain in older buildings or are part of older products but for which manufacture, processing and distribution in commerce are not currently intended, known or reasonably foreseen. EPA is excluding these activities because EPA generally interprets the mandates under section TSCA § 6(a)-(b) to conduct risk evaluations and any corresponding risk management to focus on uses for which manufacture, processing or distribution is intended, known to be occurring, or reasonably

foreseen, rather than reaching back to evaluate the risks associated with legacy uses, associated disposal, and legacy disposal, and interprets the definition of conditions of use in that context.

During scoping and problem formulation EPA reviewed the existing EPA IRIS health assessments to ascertain the established health hazards and any known toxicity values. EPA had previously, in the IRIS assessments, identified asbestos as a carcinogen causing both lung cancer and mesothelioma from inhalation exposures and derived a unit risk to address both cancers. No toxicity values or unit risks have yet been estimated for other cancers that have been identified by the International Agency for Research on Cancer (IARC) and others. Given the well-established carcinogenicity of asbestos for lung cancer and mesothelioma, EPA has decided to limit the scope of its systematic review to these two specific cancers with the goal of updating, or reaffirming, the existing unit risk. No clear association was found for drinking water asbestos exposure and cancer. Dermal exposures may cause non-cancerous skin lesions. Since neither oral nor dermal exposures are expected to contribute to the risks of lung cancer and mesothelioma, which are the basis of the 1988 cancer unit risk, exposures from the oral and dermal routes will not be assessed. These inhalation hazards will be evaluated based on the specific exposure scenarios identified for workers, consumers and the general population where applicable.

Most of the ongoing uses of asbestos pertain to industrial and commercial uses. Exposures to workers, consumers and the general population, as well as environmental receptors may occur from industrial releases and use of asbestos-containing products. Only environmental releases of friable asbestos are reported in the Toxics Release Inventory. Asbestos fibers are largely chemically inert under environmental conditions. They may undergo minor physical changes, such as changes in fiber length, but do not degrade, react, or dissolve to any appreciable extent in the environment.

The revised conceptual models presented in this problem formulation identify conditions of use; exposure pathways (e.g., media); exposure routes (inhalation); potentially exposed or susceptible subpopulations; and hazards EPA expects to consider in the risk evaluation. The initial conceptual models provided in the scope document were revised during problem formulation based on evaluation of reasonably available information for physical and chemical properties, fate, exposures, hazards, and conditions of use and based upon consideration of other statutory and regulatory authorities.

EPA's overall objectives in the risk evaluation process are to conduct timely, relevant, high-quality, and scientifically credible risk evaluations within the statutory deadlines, and to evaluate the conditions of use that raise greatest potential for risk 82 FR 33726, 33728 (July 20, 2017).

# 1 INTRODUCTION

This document presents for comment the problem formulation of the risk evaluation to be conducted for asbestos under the Frank R. Lautenberg Chemical Safety for the 21st Century Act. The Frank R. Lautenberg Chemical Safety for the 21st Century Act amended the Toxic Substances Control Act (TSCA), the Nation's primary chemicals management law, on June 22, 2016. The new law includes statutory requirements and deadlines for actions related to conducting risk evaluations of existing chemicals.

In December of 2016, EPA published a list of 10 chemical substances that are the subject of the Agency's initial chemical risk evaluations (81 FR 91927), as required by TSCA § 6(b)(2)(A). These 10 chemical substances were drawn from the 2014 update of EPA's TSCA Work Plan for Chemical Assessments, a list of chemicals that EPA identified in 2012 and updated in 2014 (currently totaling 90 chemicals) for further assessment under TSCA. EPA's designation of the first 10 chemical substances constituted the initiation of the risk evaluation process for each of these chemical substances, pursuant to the requirements of TSCA § 6(b)(4).

TSCA § 6(b)(4)(D) requires that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use and potentially exposed or susceptible subpopulations that the Administrator expects to consider, within 6 months after the initiation of a risk evaluation. The scope documents for all first 10 chemical substances were issued on June 22, 2017. The first 10 Problem Formulation documents are a refinement of what was presented in the first 10 scope documents. TSCA § 6(b)(4)(D) does not distinguish between scoping and problem formulation, and requires EPA to issue scope documents that include information about the chemical substance, including the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations that the Administrator expects to consider in the risk evaluation. In the future, EPA expects scoping and problem formulation to be completed prior to the issuance of scope documents and intends to issue scope documents that include problem formulation.

As explained in the scope document, because there was insufficient time for EPA to provide an opportunity for comment on a draft of the scope, as EPA intends to do for future scope documents, EPA is publishing and taking public comment on a problem formulation document to refine the current scope, as an additional interim step prior to publication of the draft risk evaluation for asbestos. Comments received on this problem formulation document will inform development of the draft risk evaluation.

The Agency defines problem formulation as the analytical phase of the risk assessment in which "the purpose of the assessment is articulated, the problem is defined, and a plan for analyzing and characterizing risk is determined" [see Section 2.2 of the *Framework for Human Health Risk Assessment to Inform Decision Making*, (U.S. EPA, 2014a)]. The outcome of problem formulation is a conceptual model(s) and an analysis plan. The conceptual model describes the linkages between stressors and adverse human health and environmental effects, including the stressor(s), exposure pathway(s), exposed life stage(s) and population(s), and endpoint(s) that will be addressed in the risk evaluation (U.S. EPA, 2014a). The analysis plan follows the development of the conceptual model(s) and is intended to describe the approach for conducting the risk evaluation, including its design, methods and key inputs and intended outputs as described in the EPA Human Health Risk Assessment Framework (U.S. EPA, 2014a). The problem formulation documents refine the initial conceptual models and analysis plans that were provided in the scope documents.

First, EPA has removed from the risk evaluation any activities and exposure pathways and hazards that EPA has concluded do not warrant inclusion in the risk evaluation. For example, for some activities that

were listed as "conditions of use" in the scope document, EPA has insufficient information following the further investigations during problem formulation to find they are circumstances under which the chemical is actually "intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of."

Second, EPA also identified certain exposure pathways that are under the jurisdiction of regulatory programs and associated analytical processes carried out under other EPA-administered environmental statutes – namely, the Clean Air Act (CAA), the Safe Drinking Water Act (SDWA), the Clean Water Act (CWA), and the Resource Conservation and Recovery Act (RCRA) – and which EPA does not expect to include in the risk evaluation.

As a general matter, EPA believes that certain programs under other Federal environmental laws adequately assess and effectively manage the risks for the covered exposure pathways. To use Agency resources efficiently under the TSCA program, to avoid duplicating efforts taken pursuant to other Agency programs, to maximize scientific and analytical efforts, and to meet the three-year statutory deadline, EPA is planning to exercise its discretion under TSCA 6(b)(4)(D) to focus its analytical efforts on exposures that are likely to present the greatest concern and consequently merit a risk evaluation under TSCA, by excluding, on a case-by-case basis, certain exposure pathways that fall under the jurisdiction of other EPA-administered statutes.[1] EPA does not expect to include any such excluded pathways as further explained below in the problem formulation. The provisions of various EPA-administered environmental statutes and their implementing regulations represent the judgment of Congress and the Administrator, respectively, as to the degree of health and environmental risk reduction that is sufficient under the various environmental statutes.

Third, EPA identified any conditions of use, hazards, or exposure pathways which were included in the scope document and that EPA expects to include in the risk evaluation but which EPA does not expect to further analyze in the risk evaluation. EPA expects to be able to reach conclusions about particular conditions of use, hazards or exposure pathways without further analysis and therefore plans to conduct no further analysis on those conditions of use, hazards or exposure pathways in order to focus the Agency's resources on more extensive or quantitative analyses. Each risk evaluation will be "fit-for-purpose," meaning not all conditions of use will warrant the same level of evaluation and the Agency may be able to reach some conclusions without comprehensive or quantitative risk evaluations. 82 FR 33726, 33734, 33739 (July 20, 2017).

EPA received comments on the published scope document for asbestos and has considered the comments specific to asbestos in this problem formulation document. EPA is soliciting public comment on this problem formulation document and when the draft risk evaluation is issued the Agency intends to respond to comments that are submitted. In its draft risk evaluation, EPA may revise the conclusions and approaches contained in this problem formulation, including the conditions of use and pathways covered and the conceptual models and analysis plans, based on comments received.

## 1.1 Regulatory History

EPA conducted a search of existing domestic and international laws, regulations and assessments pertaining to asbestos. EPA compiled this summary from data available from federal, state, international and other government sources, as cited in Appendix A. EPA evaluated and considered the impact of at

[1] As explained in the final rule for chemical risk evaluation procedures, "EPA may, on a case-by case basis, exclude certain activities that EPA has determined to be conditions of use in order to focus its analytical efforts on those exposures that are likely to present the greatest concern, and consequently merit an unreasonable risk determination [82FR 33726, 33729] (July 20, 2017).

least some of these existing laws and regulations in the problem formulation step to determine what, if any further analysis might be necessary as part of the risk evaluation. Consideration of the nexus between these existing regulations and TSCA conditions of use may additionally be made as detailed/specific conditions of use and exposure scenarios are developed in conducting the analysis phase of the risk evaluation.

***Federal Laws and Regulations***

Asbestos is subject to federal statutes or regulations, other than TSCA, that are implemented by other offices within EPA and/or other federal agencies/departments. A summary of federal laws, regulations and implementing authorities is provided in Appendix A-1; including adding the Department of Transportation regulations on asbestos since the scope document.

***State Laws and Regulations***

Asbestos is subject to statutes or regulations implemented by state agencies or departments. A summary of state laws, regulations and implementing authorities is provided in Appendix A-2 (updated since the scope document).

***Laws and Regulations in Other Countries and International Treaties or Agreements***

Asbestos is subject to statutes or regulations in countries other than the United States and/or international treaties and/or agreements. A summary of these laws, regulations, treaties and/or agreements is provided in Appendix A-3.

## 1.2 Assessment History

EPA has identified assessments conducted by other EPA Programs and other organizations (see Table 1-1). Depending on the source, these assessments may include information on conditions of use, hazards, exposures and potentially exposed or susceptible subpopulations—information useful to EPA in preparing the scope and problem formulation documents for the risk evaluation. Table 1-1 shows the assessments that have been conducted. Since publication of the Scope document in June 2017 EPA has added documents to Table 1-1 that supported the 1988 Asbestos Ban and Phase Out rule (54 FR 29460) which were consulted for background information on uses, exposures, and risk assessment, as well as the ecological risk assessment conducted at the Libby Asbestos Superfund Site.

In addition to using this information, EPA intends to conduct a full review of the relevant data/information collected in the initial comprehensive search (see *Asbestos (CASRN 1332-21-4) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0736) following the literature search and screening strategies documented in the *Strategy for Conducting Literature Searches for Asbestos: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0736). This will ensure that EPA considers data/information that has been made available since these assessments were conducted.

**Table 1-1. Assessment History of Asbestos**

| Authoring Organization | Assessment |
|---|---|
| **EPA assessments** | |
| EPA, Integrated Risk Information System (IRIS) | IRIS Assessment on Asbestos (1988b) |
| EPA, Integrated Risk Information System (IRIS) | IRIS Assessment on Libby Amphibole Asbestos (2014c) |

| Authoring Organization | Assessment |
|---|---|
| EPA, Region 8 | Site-Wide Baseline Ecological Risk Assessment, Libby Asbestos Superfund Site, Libby Montana (U.S. EPA, 2014b) |
| EPA, Drinking Water Criteria Document | U.S. EPA Drinking Water Criteria Document for Asbestos (1985) |
| EPA, Ambient Water Quality Criteria for Asbestos | Asbestos: Ambient Water Quality Criteria (1980a) |
| EPA, Final Rule (40 CFR Part 763) | Asbestos; Manufacture, Importation, Processing and Distribution in Commerce Prohibitions (1988) |
| EPA, Asbestos Modeling Study | Final Report; Asbestos Modeling Study (U.S. EPA, 1988a) |
| EPA, Asbestos Exposure Assessment | Revised Report to support ABPO rule (1988) |
| EPA, Nonoccupational Exposure Report | Revised Draft Report, Nonoccupational Asbestos Exposure (Versar, 1987) |
| EPA, Airborne Asbestos Health Assessment Update | Support document for NESHAP review (1986) |
| **Other U.S.-based organizations** | |
| National Institute for Occupational Safety and Health (NIOSH) | Asbestos Fibers and Other Elongate Mineral Particles: State of the Science and Roadmap for Research (2011) |
| Agency for Toxic Substances and Disease Registry (ATSDR) | Toxicological Profile for Asbestos (2001) |
| National Toxicology Program (NTP) | Report on Carcinogens, Fourteenth Edition (2016) |
| CA Office of Environmental Health Hazard Assessment (OEHHA), Pesticide and Environmental Toxicology Section | Public Health Goal for Asbestos in Drinking Water (2003) |
| **International** | |
| International Agency for Research on Cancer (IARC) | IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Arsenic, Metals, Fibres, and Dusts. Asbestos (Chrysotile, Amosite, Crocidolite, Tremolite, Actinolite, and Anthophyllite) (2012) |
| World Health Organization (WHO) | World Health Organization (WHO) Chrysotile Asbestos (2014) |

## 1.3 Data and Information Collection

EPA/OPPT generally applies a systematic process and workflow that includes: (1) data collection; (2) data evaluation; and (3) data integration of the scientific information used in risk evaluations developed under TSCA. Scientific analysis is often iterative in nature as new knowledge is obtained. Hence, EPA/OPPT expects that multiple refinements regarding data collection will occur during the process of

risk evaluation. Additional information that may be considered and was not part of the initial comprehensive bibliographies will be documented in the Draft Risk Evaluation for asbestos.

***Data Collection: Data Search***

EPA/OPPT conducted chemical-specific searches for data and information on: physical and chemical properties; environmental fate and transport; conditions of use information; environmental and human exposures, including potentially exposed or susceptible subpopulations; and, ecological and human health hazard, including potentially exposed or susceptible subpopulations.

EPA/OPPT designed its initial data search to be broad enough to capture a comprehensive set of sources containing data and/or information potentially relevant to the risk evaluation. For most disciplines, the search was not limited by date and was conducted on a wide range of data sources, including but not limited to: peer-reviewed literature and gray literature (e.g., publicly-available industry reports, trade association resources, government reports). When available, EPA/OPPT relied on the search strategies from recent assessments, such as EPA Integrated Risk Information System (IRIS) assessments and the National Toxicology Program's (NTP) *Report on Carcinogens*, to identify relevant references and supplemented these searches to identify relevant information published after the end date of the previous search to capture more recent literature. *Strategy for Conducting Literature Searches for Asbestos: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0736) provides details about the data sources and search terms that were used in the initial search.

***Data Collection: Data Screening***

Following the data search, references were screened and categorized using selection criteria outlined in *Strategy for Conducting Literature Searches for Asbestos: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0736). Titles and abstracts were screened against the criteria as a first step with the goal of identifying a smaller subset of the relevant data to move into the subsequent data extraction and data evaluation steps. Prior to full-text review, EPA/OPPT anticipates refinements to the screening strategies, as informed by an evaluation of the performance of the initial title/abstract screening and categorization process.

The categorization scheme (or tagging structure) used for data screening varies by scientific discipline (i.e., physical and chemical properties; environmental fate and transport; chemical use/conditions of use information; human and environmental exposures, including potentially exposed or susceptible subpopulations identified by virtue of greater exposure; human health hazard, including potentially exposed or susceptible subpopulations identified by virtue of greater susceptibility; and ecological hazard). However, within each data set, there are two broad categories or data tags: (1) o*n-topic* references or (2) *off-topic* references. *On-topic* references are those that may contain data and/or information relevant to the risk evaluation. O*ff-topic* references are those that do not appear to contain data or information relevant to the risk evaluation. The *Strategy for Conducting Literature Searches for Asbestos: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0736) discusses the inclusion and exclusion criteria that EPA/OPPT used to categorize references as *on-topic* or *off-topic*.

Additional data screening using sub-categories (or sub-tags) was also performed to facilitate further sorting of data/information. For example, identifying references by source type (e.g., published peer-reviewed journal article, government report); data type (e.g., primary data, review article); human health hazard (e.g., liver toxicity, cancer, reproductive toxicity); or chemical-specific and use-specific data or information. These sub-categories are described in the *Strategy for Conducting Literature Searches for Asbestos: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0736) and will be

used to organize the different streams of data during the stages of data evaluation and data integration steps of systematic review.

Results of the initial search and categorization results can be found in the *Asbestos (CASRN 1332-21-4) Bibliography: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0736). The scope document provided a comprehensive list (bibliography) of the sources of data identified by the initial search and the initial categorization for *on-topic* and *off-topic* references. Because systematic review is an iterative process, EPA/OPPT expects that some references may move from the *on-topic* to the *off-topic* categories, and vice versa. Moreover, targeted supplemental searches may also be conducted to address specific needs for the analysis phase (e.g., to locate specific data needed for modeling); hence, additional *on-topic* references not initially identified in the initial search may be identified as the systematic review process proceeds.

## 1.4 Data Screening during Problem Formulation

EPA/OPPT is in the process of completing the full text screening of the on-topic references identified in the *Asbestos (CASRN: 1332-21-4) Bibliography: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0736). The screening process at the full-text level is described in the *Application of Systematic Review in TSCA Risk Evaluations* document (U.S. EPA, 2018). Appendix D provides the inclusion and exclusion criteria applied at the full text screening. The eligibility criteria are guided by the analytical considerations in the revised conceptual models and analysis plan, as discussed in the problem formulation document. Thus, it is expected the number of data/information sources entering evaluation is reduced to those that are relevant to address the technical approach and issues described in the analysis plan of this document.

Following the screening process, the quality of the included studies will be assessed using the evaluation strategies that are described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018).

# 2 PROBLEM FORMULATION

As required by TSCA, the scope of the risk evaluation identifies the conditions of use, hazards, exposures and potentially exposed or susceptible subpopulations that the Administrator expects to consider. To communicate and visually convey the relationships between these components, EPA included in the scope document a life cycle diagram and conceptual models that describe the actual or potential relationships between asbestos and human and ecological receptors. During the problem formulation, EPA revised the conceptual models based on further data gathering and analysis, as presented in this problem formulation document. An updated analysis plan is also included which identifies, to the extent feasible, the approaches and methods that EPA may use to assess exposures, effects (hazards) and risks under the conditions of use of asbestos.

## 2.1 Definition, Structure and Physical and Chemical Properties

### 2.1.1 Definition of Asbestos

Asbestos is a "generic commercial designation for a group of naturally occurring mineral silicate fibers of the serpentine and amphibole series" (IARC, 2012). The Chemical Abstract Service (CAS) definition of asbestos is "a grayish, non-combustible fibrous material. It consists primarily of impure magnesium silicate minerals." The general CAS Registry Number (CASRN) of asbestos is 1332-21-4; this is the

only asbestos CASRN on the TSCA Inventory. However, other CASRNs are available for specific fiber types.

TSCA Title II (added to TSCA in 1986), Section 202 defines asbestos as the "*asbestiform varieties of six fiber types – chrysotile (serpentine), crocidolite (riebeckite), amosite (cummingtonite-grunerite), anthophyllite, tremolite or actinolite*." The latter five fiber types are amphibole varieties. EPA is using this definition of asbestos for the risk evaluation for asbestos. EPA received public comment on the definition and fiber types of asbestos used in the Scope document and adjusted Table 2-1 to clarify the fiber types and size included in the definition. EPA will continue to use the TSCA Title II definition of asbestos in the risk evaluation.

The most common form of asbestos used in the United States is chrysotile, which is found in serpentine rock formations (chrysotile content average 5%, with a maximum 50%) (WHO, 2014). Chrysotile was the predominant type of asbestos used in the United States and is currently the only type of raw asbestos imported. The United States Geological Survey (USGS) estimated that 300 metric tons of asbestos were imported into the U.S. in 2017, 57% less than 702 metric tons in 2016, and 22% less than 386 metric tons in 2015 (USGS, 2018). It is used wholly by the chlor-alkali industry.

The three varieties of amphibole fibers that are the most commonly found are crocidolite, amosite and tremolite. Crocidolite and amosite were the only amphiboles with significant industrial uses in recent years. Tremolite, although having essentially no industrial application, may be found as a contaminant associated with other fibers or in other industrial minerals (e.g., chrysotile and talc) (Virta, 2011).

### 2.1.2 Structure

As with all silicate minerals, the basic building blocks of asbestos fibers are silicate tetrahedra $[SiO_4]^{4-}$ where four oxygen atoms are covalently bound to the central silicon. These tetrahedrons occur as sheets $[Si_4O_{10}]$ in chrysotile (U.S. EPA, 2014a). In the case of chrysotile, an octahedral brucite layer having the formula $[Mg_6O_4(OH)_8]$ is intercalated between each silicate tetrahedral sheet.

### 2.1.3 Physical and Chemical Properties of Asbestos

Physical-chemical properties influence the environmental behavior and the toxic properties of a chemical, thereby informing the potential conditions of use, exposure pathways and routes, and hazards EPA intends to consider. For scope development, EPA considered the measured or estimated physical-chemical properties set forth in Table 2-1.

Asbestos fibers are basically chemically inert, and they do not evaporate, dissolve, burn or undergo significant reactions with most chemicals. They are insoluble in water and organic solvents. In acid and neutral aqueous media, magnesium is lost from the outer brucite layer of chrysotile. Amphibole fibers are more resistant to acid attack and all varieties of asbestos are resistant to attack by alkalis (Virta, 2011).

**Table 2-1. Physical and Chemical Properties of Asbestos Fiber Types [a]**

| | Chrysotile | Amosite | Crocidolite | Asbestiform Tremolite | Asbestiform Anthophyllite | Asbestiform Actinolite |
|---|---|---|---|---|---|---|
| Essential composition | Mg silicate with some water | Fe, Mg silicate with some water | Na, Fe silicate with some water | Ca, Mg silicate with some water | Mg silicate with some iron | Ca, Mg, Fe silicate with some water |

| | Chrysotile | Amosite | Crocidolite | Asbestiform Tremolite | Asbestiform Anthophyllite | Asbestiform Actinolite |
|---|---|---|---|---|---|---|
| Color | Usually white to grayish green; may have tan coloration | Yellowish gray to dark brown | Cobalt blue to lavender blue | Gray-white, green, yellow, blue | Grayish white, also brown-gray or green | Greenish |
| Luster | Silky | Vitreous to pearly | Silky to dull | Silky | Vitreous to pearly | Silky |
| Surface area [b, c] ($m^2/g$) | 13-18 | 2-9 | 2-9 | 2-9 | 2-9 | 2-9 |
| Hardness (Mohs) | 2.5-4.0 | 5.5-6.0 | 4.0 | 5.5 | 5.5-6.0 | 6.0 |
| Specific gravity | 2.4-2.6 | 3.1-3.25 | 3.2-3.3 | 2.9-3.2 | 2.85-3.1 | 3.0-3.2 |
| Optical properties | Biaxial positive parallel extinction | Biaxial positive parallel extinction | Biaxial oblique extinction | Biaxial negative oblique extinction | Biaxial positive extinction parallel | Biaxial negative extinction inclined |
| Refractive index | 1.53-1.56 | 1.63-1.73 | 1.65-1.72 | 1.60- 1.64 | 1.61 | 1.63 weakly pleochroic |
| Flexibility | High | Fair | Fair to good | Poor, generally brittle | Poor | Poor |
| Texture | Silky, soft to harsh | Coarse but somewhat pliable | Soft to harsh | Generally harsh | Harsh | Harsh |
| Spinnability | Very good | Fair | Fair | Poor | Poor | Poor |
| Tensile strength (MPa) | 1,100-4,400 | 1,500-2,600 | 1,400-4,600 | <500 | ≤27 | ≤7 |
| Fiber size, median true diameter (µm)[d] | 0.06 | 0.26 | 0.09 | No data | No data | No data |
| Fiber size, median true length (µm)[d] | 0.55 | 2.53 | 1.16 | No data | No data | No data |
| Resistance to:<br>Acids<br><br><br><br>Bases | <br>Weak, undergoes fairly rapid attack<br><br>Very good | <br>Fair, slowly attacked<br><br>Good | <br>Good<br><br>Good | <br>Good<br><br>Good | <br>Very good<br><br>Very good | <br>Fair<br><br>Fair |
| Zeta potential (mV) | +13.6 to +54 | -20 to -40 | -32 | NA | NA | NA |
| Decomposition temperature (°C) | 600-850 | 600-900 | 400-900 | 950-1,040 | 950 | NA |

| | Chrysotile | Amosite | Crocidolite | Asbestiform Tremolite | Asbestiform Anthophyllite | Asbestiform Actinolite |
|---|---|---|---|---|---|---|
| [a] Badollet (1951).<br>[b] Hodgson (1986).<br>[c] Addison et al. (1966).<br>[d] Hwang (1983) | | | | | | |

## 2.2 Conditions of Use

TSCA § 3(4) defines the conditions of use as ''the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of.''

### 2.2.1 Data and Information Sources

In the scope documents EPA identified, based on reasonably available information, the conditions of use for the subject chemical. As further described in this document, EPA searched a number of available data sources (e.g., *Use and Market Profile for Asbestos*, EPA-HQ-OPPT-2016-0736-0085). Based on this search, EPA published a preliminary list of information and sources related to chemical conditions of use (see *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: Asbestos*) (Docket: EPA-HQ-OPPT-2016-0736-0005) (U.S. EPA, 2017b), prior to a February 2017 public meeting on scoping efforts for risk evaluation convened to solicit comment and input from the public. EPA also convened meetings with companies, industry groups, chemical users and other stakeholders to aid in identifying and verifying conditions of use. The information and input received from the public and stakeholder meetings was incorporated into this document to the extent appropriate, as indicated in Table 2-2. Thus, EPA believes the identified manufacture, processing, distribution, use and disposal activities identified in this document constitute the intended, known, and reasonably foreseen activities associated with the subject chemical, based on reasonably available information.

### 2.2.2 Identification of Conditions of Use

To determine the current conditions of use of asbestos and inversely, activities that do not qualify as conditions of use, EPA conducted extensive research and outreach. This included EPA's review of published literature and online databases including the most recent data available from EPA's Chemical Data Reporting program (CDR), Safety Data Sheets (SDSs), the United States Geological Survey's Mineral Commodities Summary and Minerals Yearbook, the U.S. International Trade Commission's Dataweb and government and commercial trade databases. EPA also reviewed company websites of potential manufacturers, importers, distributors, retailers, or other users of asbestos. EPA also received comments on the *Scope of the Risk Evaluation for Asbestos* (EPA-HQ-OPPT-2016-0736-0086) that were used to determine the conditions of use. In addition, prior to the June 2017 publication of the scope document, EPA convened meetings with companies, industry groups, chemical users, and other stakeholders to aid in identifying conditions of use and verifying conditions of use identified by EPA.

The Scope document (EPA-HQ-OPPT-2016-0736-0086) identified uses of asbestos and described them in terms of product categories. In an effort to understand the current asbestos product market, EPA referred to the *Regulatory Impact Analysis [RIA] of Controls on Asbestos and Asbestos Products (Final Report Volume III)*, which was conducted in support of the 1989 *Asbestos: Manufacture, Importation, Processing, and Distribution in Commerce Prohibitions; Final Rule* (40 CFR Part 763). The RIA explained that in 1981, asbestos products were distributed into 35 product categories (U.S. EPA, 1989). For scoping, EPA researched the 35 product categories included in the 1989 RIA, and based on the

results of this research, developed the following use categories that reflect current knowledge of uses as of June 2017 when the Scope document was published:

- Known Use – companies and manufacturing processes are identified
- Evidence of Use – web sites and/or Safety Data Sheets (SDS) indicate asbestos in products
- Reasonably Foreseen Use – indication by USGS that asbestos-containing products are imported to the United States

EPA has removed from the risk evaluation any activities that EPA has concluded do not constitute conditions of use – for example, because EPA has insufficient information to find certain activities are circumstances under which the chemical is actually "intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used or disposed of." EPA has also identified any conditions of use that EPA does not expect to include in the risk evaluation. As explained in the final rule for Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act, TSCA section 6(b)(4)(D) requires EPA to identify "the hazards, exposures, conditions of use and the potentially exposed or susceptible subpopulations that the Agency expects to consider in a risk evaluation," suggesting that EPA may exclude certain activities that EPA has determined to be conditions of use on a case-by-case basis (82 FR 33736, 33729; July 20, 2017). For example, EPA may exclude conditions of use that the Agency has sufficient basis to conclude would present only de minimis exposures or otherwise insignificant risks (such as use in a closed system that effectively precludes exposure or use as an intermediate).

The activities that EPA no longer believes are conditions of use or that were otherwise excluded during problem formulation are described in Section 2.2.2.1. The conditions of use included in the scope of the risk evaluation are summarized in Section 2.2.2.2.

#### 2.2.2.1 Categories Determined Not to be Conditions of Use During Problem Formulation

During problem formulation, the conditions of use of asbestos identified in the Scope document were further refined upon determination that EPA has insufficient information to find certain activities to be "conditions of use." After further investigation of the current conditions of use – circumstances under which the chemical is "intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of" – EPA determined there is a lack of sufficient evidence of the import, processing, or distribution of asbestos in adhesives and sealants, roof and non-roof coatings, and building materials other than asbestos cement products. EPA had originally identified an asbestos-containing adhesive for use as a mirror adhesive but later determined after contacting the supplier that it is no longer sold. EPA also identified during the scoping process a domestic company that appeared to manufacture and sell asbestos-containing roof and non-roof coatings, but after contacting the company, determined that the information available on their website was outdated and those products were no longer manufactured and sold in the United States.

Based on data available to EPA, general and some specified building materials and other unspecified activities have been removed from consideration from the original scope during problem formulation, as depicted in Table 2-2. EPA does not expect to consider or evaluate any such products or associated hazards or exposures in the applicable risk evaluation because the use of asbestos in these products is not intended, known, or reasonably foreseen in the United States. Therefore, the asbestos-containing products listed in Table 2-2 are not included in the Life Cycle Diagram, Figure 2-1.

**Table 2-2. Categories Determined Not to be Conditions of Use During Problem Formulation**

| Activity | Product Category | Example |
|---|---|---|
| No Known, Intended, or Reasonably Foreseen Use | Adhesives and Sealants | Mirror adhesive |
| | Roof and Non-Roof Coatings | Roofs/Foundations; Mastics |
| | Building Materials, Other | Articles not specified, including building materials other than asbestos cement products |

***Legacy Use – Excluded from Scope (and Problem Formulation) of the Risk Evaluation***

EPA interprets the mandates under section 6(a)-(b) to conduct risk evaluations and any corresponding risk management to focus on current and prospective uses for which manufacture, processing, or distribution in commerce is intended, known or reasonably foreseen, rather than reaching back to evaluate the risks associated with legacy uses, associated disposal, and legacy disposal, and interprets the definition of "conditions of use" in that context (TSCA section 6(b)(4)(B)). In other words, EPA interprets the risk evaluation process of section 6 to focus on the continuing flow of chemical substances from manufacture, processing and distribution in commerce into the use and disposal stages of their life cycle. Consistent with this rationale, EPA has excluded certain uses from the scope of the risk evaluation, as identified below.

During scoping, EPA identified uses including pre-existing materials currently in place within buildings (e.g., insulation materials, flooring, etc.) and also within pre-existing non-building equipment. Many asbestos products fall into this category. These materials were installed in the past, and there is no evidence to suggest that manufacturing, processing, or distribution for such activities is intended, known, or reasonably foreseen; EPA received no public comments providing information to indicate otherwise. Legacy asbestos-containing products excluded from the scope of the risk evaluation include:

- Asbestos arc chutes
- Asbestos pipeline wrap
- Asbestos separators in fuel cells and batteries
- Asbestos-reinforced plastics
- Beater-add gaskets
- Extruded sealant tape
- Filler for acetylene cylinders
- High-grade electrical paper
- Millboard
- Missile liner
- Roofing felt
- Vinyl-asbestos floor tile

Upon further investigation during problem formulation, EPA has determined that seven asbestos product categories (asbestos packings, asbestos protective clothing, automatic transmission friction components, clutch facings, asbestos-cement flat sheet, asbestos-cement shingles, and corrugated asbestos-cement sheet) that were listed as legacy uses in the Scope document fall under broader categories that EPA has identified as conditions of use (other gaskets and packing, woven products, automotive friction materials and asbestos cement products). Therefore, EPA has removed these seven product categories from the above list because it is reasonably foreseen that these products could be considered under the risk evaluation as specific products in broader categories of conditions of use.

The manufacture, processing, and distribution for a number of additional uses of asbestos were banned under TSCA in 1989 as part of the *Asbestos: Manufacture, Importation, Processing, and Distribution in Commerce Prohibitions; Final Rule* (40 CFR Part 763) (also known as Asbestos Ban and Phase-out Rule (Remanded), 1989). The uses of asbestos covered by the ban and thus excluded from the scope of the risk evaluation include:

- Corrugated paper
- Rollboard
- Commercial paper
- Specialty paper
- Flooring felt
- New uses[2]

Another legacy use not included in the scope of this evaluation is Libby Amphibole asbestos, which is a mixture of several mineral fibers such as winchite, richterite, and tremolite found in vermiculite ore mined near Libby, MT and extensively distributed throughout the United States during the 20th century. Vermiculite from Libby, MT had a range of commercial applications, the most common of which included packing material, attic and wall insulation, various garden and agricultural products, and various cement and building products. Although vermiculite contaminated with the Libby Amphibole remains in buildings as an insulating material it is no longer manufactured, processed or distributed for use in the United States and therefore is not considered a condition of use of asbestos for the purpose of risk evaluation under TSCA.

#### 2.2.2.2 Categories of Conditions of Use Included in the Scope of Risk Evaluation

Table 2-3 summarizes the conditions of use for asbestos that EPA expects to consider in the risk evaluation. Using the 2016 CDR, EPA identified industrial processing or use activities, industrial function categories and commercial and consumer use product categories. For risk evaluations, EPA intends to consider the conditions of use for each life cycle stage and assess relevant potential sources of release and human exposure associated with that life cycle stage (see Figure 2-1).

Reporting of asbestos in the 2016 Chemical Data Reporting (CDR) [3,4] period was limited (U.S. EPA, 2016b). Only two companies, both from the chlor-alkali industry, reported importing asbestos and the amounts cannot be publicly disclosed due to company claims of confidential business information (CBI).

Asbestos has not been mined or otherwise produced in the United States since 2002 (Flanagan, 2016); hence, mining is not included in the scope of the TSCA risk evaluation for asbestos. All asbestos used in this country is imported. According to the U.S. Geological Survey (USGS), the only form of asbestos

[2] Defined by 40 CFR 763.163 as "commercial uses of asbestos not identified in §763.165 the manufacture, importation or processing of which would be initiated for the first time after August 25, 1989."

[3] Manufacturers (including importers) are required to report under CDR if they meet certain production volume thresholds, generally ≥25,000 lbs of a chemical substance at any single site. Reporting is triggered if the annual reporting threshold is met during any of the calendar years since the last principal reporting year. In general, the reporting threshold remains 25,000 lbs per site. However, a reduced reporting threshold (2,500 lbs) now applies to some chemical substances, including asbestos, subject to certain TSCA actions (U.S. EPA, 2017a).

[4] For purposes of the CDR, manufacture means to manufacture, produce, or import for commercial purposes. Manufacture includes the extraction, for commercial purposes, of a component chemical substance from a previously existing chemical substance or complex combination of chemical substances. (40 CFR 711.3) (U.S. EPA, 2016c)

currently imported into the United States is chrysotile, all of which originated from Brazil in 2017 (USGS, 2018). USGS reports that in 2017, the United States imported approximately 300 metric tons of raw asbestos, the total of which they state is used in the chlor-alkali industry (USGS, 2018). In 2016, the United States imported approximately 702 metric tons of raw asbestos (USGS, 2018). Other import data presented in the USGS report are difficult to interpret with respect to volumes because most of the asbestos-containing products reported are described in terms of monetary value and not import volume. Also, the monetary value is associated with a product without reference to amount or type of asbestos present in that product. EPA continues to work with its federal partners such as USGS and Customs and Border Protection to better define import information on asbestos-containing products in support of conducting the risk evaluation.

Table 2-3 provides a listing of the conditions of use of asbestos intended, known, or reasonably foreseen to be considered under the TSCA risk evaluation for asbestos. The conditions of use identified in the Scope document have been refined as part of the problem formulation process. Table 2-3 reflects the updated list of conditions of use, identified by asbestos product category, and provides examples for how each product is used. Information provided in Table 2-3 is also reflected the Life Cycle Diagram, Figure 2-1.

**Table 2-3. Categories of Conditions of Use Included in the Scope of the Risk Evaluation**

| Activity | Product Category | Example |
|---|---|---|
| Known, Intended, or Reasonably Foreseen Use | Asbestos Diaphragms | Chlor-alkali Industry |
| | Sheet Gaskets | Chemical Manufacturing |
| | Oilfield Brake Blocks | Oil Industry |
| | Aftermarket Automotive Brakes/Linings | Passenger Vehicles |
| | Other Vehicle Friction Products | Non-passenger Vehicles |
| | Asbestos Cement Products | Cement pipe |
| | Other Gaskets and Packing | Equipment Seals |
| | Woven Products | Imported Textiles |

Most of the asbestos-containing products listed in the categories in Table 2-3 are primarily associated with industrial and commercial use. It is important to note that the import volume of products containing asbestos is not known.

#### 2.2.2.3 Overview of Conditions of Use and Life Cycle Diagram

The life cycle diagram provided in Figure 2-1 depicts the conditions of use that are within the scope of the risk evaluation during various life cycle stages including manufacturing, processing, distribution, use (industrial, commercial, consumer) and disposal. Additions or changes to the conditions of use based on additional information gathered or analyzed during problem formulation are described in Sections 2.2.2.1 and 2.2.2.2. The activities that EPA determined are out of scope during problem formulation are not included in the life cycle diagram.

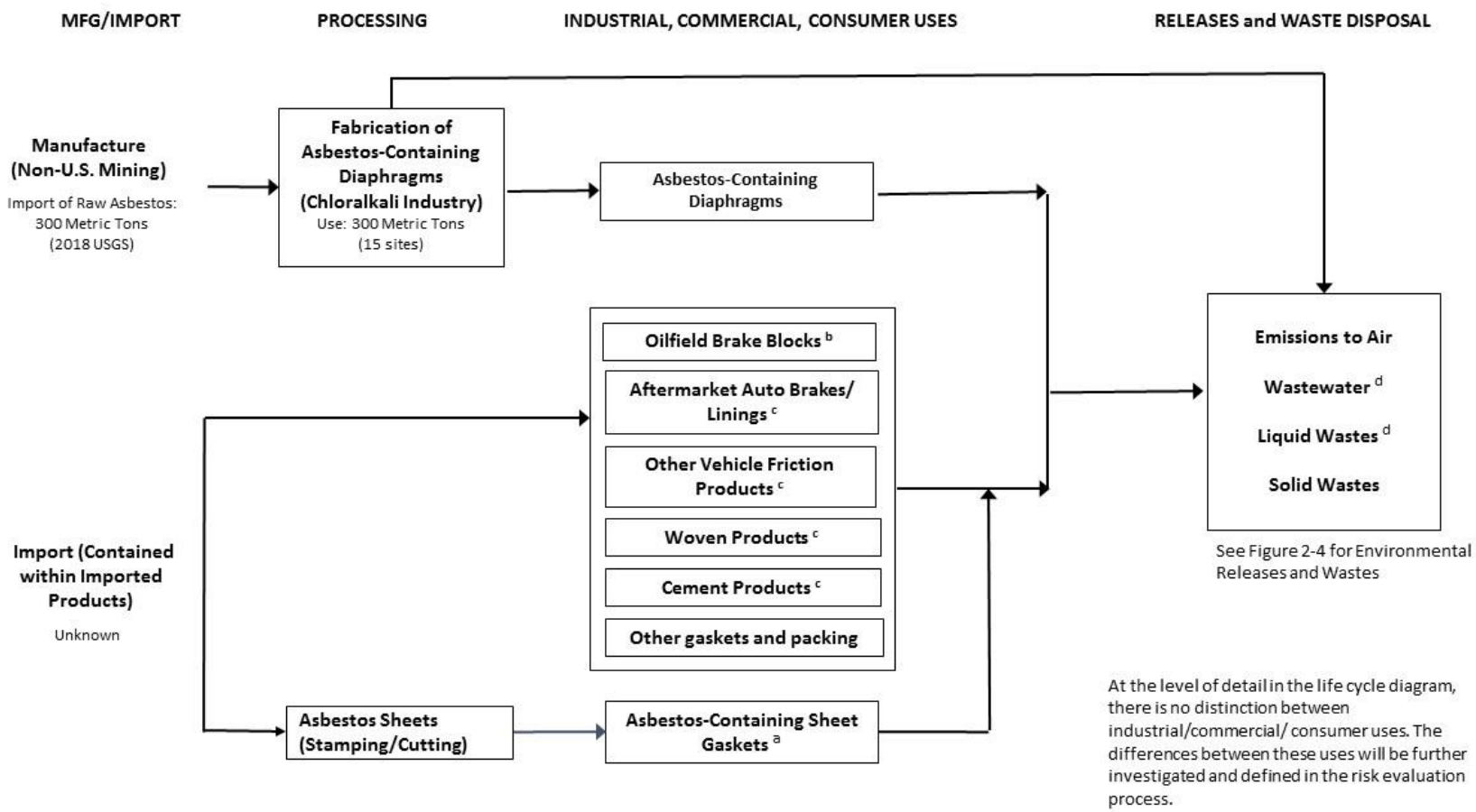
Use categories include the following: "industrial use" means use at a site at which one or more chemicals or mixtures are manufactured (including imported) or processed. "Commercial use" means the use of a chemical or a mixture containing a chemical (including as part of an article) in a commercial enterprise providing saleable goods or services. "Consumer use" means the use of a chemical or a

mixture containing a chemical (including as part of an article, such as furniture or clothing) when sold to or made available to consumers for their use (U.S. EPA, 2017a).

To understand conditions of use relative to one another and associated potential exposures under those conditions of use, the life cycle diagram includes the production volume associated with each stage of the life cycle, as reported in the 2016 CDR reporting (U.S. EPA, 2017a) when the volume was not claimed confidential business information (CBI). However, in the case of asbestos, reported USGS production volume was used since the CDR production volume was claimed CBI.

Descriptions of the industrial, commercial and consumer use categories included in the life cycle diagram are summarized below. The descriptions provide a brief overview of the use category; Appendix B contains more detailed descriptions (e.g., process descriptions, worker activities) for each manufacture, processing, distribution, use and disposal category.

Figure 2-1 depicts the life cycle diagram of asbestos from manufacture to the point of disposal. Activities related to distribution (e.g., loading, unloading) will be considered throughout the asbestos life cycle, rather than using a single distribution scenario.




## Figure 2-1. Asbestos Life Cycle Diagram

The life cycle diagram depicts the conditions of use that are within the scope of the risk evaluation during various life cycle stages including manufacturing, processing, use (industrial, commercial, consumer), distribution and disposal. The import volume shown is from 2018 USGS. Import volumes of asbestos-containing products are unknown. Activities related to distribution (e.g., loading, unloading, etc.) will be considered throughout the asbestos life cycle, rather than using a single distribution scenario.

[a] Sheet gaskets were identified during public comment period.

[b] Oilfield brake blocks identified via industry response during problem formulation.

[c] Data is very limited for these uses.

[d] Wastewater: combination of water and organic liquid, where the organic content is less than 50 percent. Liquid Wastes: combination of water and organic liquid, where the organic content is greater than 50 percent

EPA is aware of the use of raw imported chrysotile asbestos in the chlor-alkali industry, the use of imported asbestos-containing sheet gaskets in the manufacture of titanium dioxide, the use of imported asbestos-containing brake blocks in the oil industry, and other imported asbestos-containing products that could be used either in industrial or consumer settings.

***Diaphragms in Chlor-alkali Industry***

The chlor-alkali industry imports raw chrysotile asbestos for use in semipermeable diaphragms, which separate the anode from the cathode chemicals in the production of chlorine and sodium hydroxide (caustic soda) (USGS, 2017). During a meeting with EPA in January 2017, industry representatives stated that in the United States, there are three companies (Olin Corporation, Occidental Chemical and Axial/Westlake Corporation) who own a total of 15 chlor-alkali plants that continue to fabricate and use asbestos (chrysotile)-containing semipermeable diaphragms onsite.

EPA conducted a site visit of two chlor-alkali plants in March 2017 and observed the methods described at the January industry meeting. EPA also learned about the automated process wherein raw imported asbestos is processed and diaphragms are constructed. EPA continues to evaluate how representative the processes witnessed at these two facilities are of processes at other plants when evaluating this use in the analysis phase of the risk evaluation. EPA held a conference call with Axial/Westlake on April 11, 2017 to discuss their use of asbestos diaphragms at their Plaquemine, LA plant (EPA-HQ-OPPT-2016-0736-0070). EPA also had follow-up meetings with Occidental Chemical on September 6, 2017, (EPA-HQ-OPPT-2016-0736-0116) and Olin Chemical on September 14, 2017 (EPA-HQ-OPPT-2016-0736-0117) to better understand the use, processes (including personal protective equipment and engineering controls used) and disposal methods followed for asbestos diaphragms.

***Sheet Gaskets***

During the public comment period, one chemical production company, Chemours, notified EPA of their current use of imported gaskets from China (Comment ID (EPA-HQ-OPPT-2016-0736-0067). These sheet gaskets are composed of 80% (minimum) chrysotile asbestos, encapsulated in Styrene Butadiene Rubber, and used to create tight chemical containment seals during the production of titanium dioxide. On October 30, 2017, EPA met with both the commenter, Chemours, and their gasket supplier, Branham Corporation, who provided EPA with additional information on the fabrication and use of the gaskets (EPA-HQ-OPPT-2016-0736-0119). Branham imports rubberized sheets of the asbestos-containing material from a manufacturer in China and then fabricates (by cutting to specific sizes) the gaskets from the sheet material. Chemours informed EPA during the meeting that asbestos-containing gaskets are optimal because they are resistant to cyclical high temperatures and immense pressure. During the manufacture of titanium dioxide, temperatures can exceed 1850 degrees Fahrenheit and pressures can be greater than 50 pounds per square inch.

***Brake Blocks in Oilfields***

During problem formulation, EPA contacted a domestic brake blocks manufacturing company to confirm that asbestos brake blocks are still used in oilfield equipment within the United States (https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0736-0118 EPA-HQ-OPPT-2016-0736-0118). Although the company no longer fabricates brake blocks using asbestos, the company did confirm that they import asbestos-containing brake blocks on behalf of some clients for use in the oilfield industry. It is unclear how widespread the continued use of asbestos brake blocks is for use in oilfield equipment, but EPA understands from interactions with industry that the use of asbestos brake blocks has decreased significantly over time and continues to decline. EPA continues to investigate the use of this product.

***Asbestos Containing Products for Commercial and Consumer Use***

EPA found limited evidence of asbestos-containing products currently used in the United States. In the scope document, certain asbestos-containing products, such as cement products, aftermarket brake linings, other vehicle friction materials, and other gaskets and packing were identified in the *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: Asbestos* (Docket: EPA-HQ-OPPT-2016-0736-0005) (U.S. EPA, 2017b) . During problem formulation, EPA consulted with USGS staff on what uses of asbestos they consider to be ongoing based on their professional judgement after reviewing government and commercial trade databases. USGS believes that the asbestos-containing products that continue to be imported include raw chrysotile asbestos (for use in chlor-alkali diaphragms), asbestos brake linings (automotive brakes/linings, other vehicle friction products), knitted fabrics (woven products), asbestos rubber sheets (i.e., sheet gaskets) and asbestos cement products. USGS and EPA believe that other asbestos imports listed by harmonized tariff schedule (HTS) code in government and commercial trade databases are likely misreported and are not ongoing current conditions of use.

## 2.3 Exposures

For TSCA exposure assessments, EPA expects to evaluate exposures and releases to the environment resulting from the conditions of use applicable to asbestos. Post-release pathways and routes will be described to characterize the relationship between the conditions of use of the chemical and the exposure to human receptors, including potentially exposed or susceptible subpopulations and ecological receptors. EPA will take into account, where relevant, the duration, intensity (concentration), frequency and number of exposures in characterizing exposures to asbestos.

### 2.3.1 Fate and Transport

Environmental fate includes both transport and transformation processes. Environmental transport is the movement of the chemical within and between environmental media. Transformation occurs through the degradation or reaction of the chemical with other species in the environment. Hence, knowledge of the environmental fate of the chemical informs the determination of the specific exposure pathways and potential human and ecological receptors EPA expects to consider in the risk evaluation. EPA has identified and considered environmental fate data as reported in several assessments in developing the scope and problem formulation for asbestos (WHO, 2014; IARC, 2012; ATSDR, 2001).

Asbestos fibers are largely chemically and biologically inert under environmental conditions. They may undergo minor physical changes, such as changes in fiber length or leaching of surface minerals, but do not degrade, react or dissolve to any appreciable extent in the environment (IARC, 2012; ATSDR, 2001). Asbestos fibers can be found in soils, sediments, lofted in air and windblown dust, surface water, ground water and biota (IARC, 2012; ATSDR, 2001). Small asbestos fibers (<1 µm) remain suspended in air and water for a significant period of time and may be transported over long distances (ATSDR, 2001). Chrysotile asbestos forms stable suspensions in water and degrades to some extent in acidic conditions, however the silicate structure remains intact (IARC, 2012). Asbestos fibers will eventually settle to sediments and soil, and movement therein may occur via erosion, runoff or mechanical resuspension (wind-blown dust, vehicle traffic, etc.) (WHO, 2014).

Asbestos may be released to the environment through industrial or commercial activities, such as processing raw asbestos, fabricating/processing asbestos containing products, or the lofting of friable asbestos during use, disturbance and disposal of asbestos containing products. Systematic literature review is currently underway to determine if any new information may inform the development of the risk evaluation.

### 2.3.2 Releases to the Environment

Releases to the environment from conditions of use (e.g., industrial and commercial processes, commercial or consumer uses resulting in down-the-drain releases) are one component of potential exposure and may be derived from reported data that are obtained through direct measurement, and estimations based on empirical data and/or assumptions and models.

A source of information that EPA considered in evaluating exposure are data reported under the Toxics Release Inventory (TRI) program. Under the Emergency Planning and Community Right-to-Know Act (EPCRA) Section 313, asbestos (friable) is a TRI-reportable substance effective January 1, 1987.

EPA's TRI data contains information about asbestos releases to air and water and disposal to land from industrial facilities in covered sectors in the United States. For TRI reporting, facilities in covered sectors are required to report releases or other waste management of only the friable form of asbestos, under the general CASRN 1332-21-4. TRI interprets "friable" under EPCRA Section 313, referring to the physical characteristic of being able to be crumbled, pulverized or reducible to a powder with hand pressure, and "asbestos" to include the six types of asbestos as defined under Title II of TSCA.[5] Facilities are required to report if they are in a covered industrial code and manufacture (including import) or process more than 25,000 pounds of friable asbestos, or if they otherwise use more than 10,000 pounds of friable asbestos.

Table 2-4 provides production-related waste management data for friable asbestos reported by industrial facilities in covered sectors to the TRI program for 2015. In 2015, 36 facilities reported a total of approximately 25 million pounds of friable asbestos waste managed. Of this total, zero pounds were recovered for energy, approximately 188,000 pounds were treated, and nearly 25 million pounds were disposed of or otherwise released into the environment. It was determined during problem formulation that the 875 pounds of recycled material reported to TRI for 2015 was in error (error correction pending).

**Table 2-4. Summary of Asbestos TRI Production-Related Waste Managed in 2015 (lbs)**

| Number of Facilities | Recycling | Energy Recovery | Treatment | Releases [a,b,c] | Total Production Related Waste |
|---|---|---|---|---|---|
| 36 | 875 | 0 | 188,437 | 25,360,853 | 25,550,164 |

Data source: U.S. EPA (2017d).
[a] Terminology used in these columns may not match the more detailed data element names used in the TRI public data and analysis access points.
[b] Does not include releases due to one-time event not associated with production such as remedial actions or earthquakes.
[c] Counts all releases including release quantities transferred and release quantities disposed of by a receiving facility reporting to TRI.

Table 2-5 provides a summary of asbestos TRI releases to the environment in 2015. There were zero pounds of friable asbestos reported as released to water via surface water discharges, and a total of 314

[5] According to 53FR4519 (VII)C(5), "The listing for asbestos is qualified by the term "friable." This term refers to a physical characteristic of asbestos. EPA interprets "friable" as being crumbled, pulverized, or reducible to a powder with hand pressure. Again, only manufacturing, processing, or use of asbestos in the friable form triggers reporting. Similarly, supplier notification applies only to distribution of friable asbestos."

pounds of air releases from collective fugitive and stack air emissions. The vast majority of friable asbestos was disposed of to landfills from both Resource Conservation and Recovery Act (RCRA) Subtitle C landfills and to landfills other than RCRA Subtitle C.

**Table 2-5. Summary of Asbestos TRI Releases to the Environment in 2015 (lbs)**

| | Number of Facilities | Air Releases | | Water Releases | Land Disposal | | | Other Releases [a] | Total On- and Off-Site Disposal or Other Releases [b, c] |
|---|---|---|---|---|---|---|---|---|---|
| | | Stack Air Releases [d] | Fugitive Air Releases [e] | | Class I Under-ground Injection | RCRA Subtitle C Landfills | All other Land Disposal [a] | | |
| Subtotal | | 106 | 208 | | 0 | 9,718,957 | 15,849,020 | | |
| Totals | 36 | 314 | | 0 | 25,567,977 | | | 0 | 25,568,292 |

Data source: U.S. EPA (2017d).
[a] Terminology used in these columns may not match the more detailed data element names used in the TRI public data and analysis access points.
[b] These release quantities do include releases due to one-time events not associated with production such as remedial actions or earthquakes.
[c] Counts release quantities once at final disposition, accounting for transfers to other TRI reporting facilities that ultimately dispose of the chemical waste.
[d] Point source (stack) air emissions are releases to air that occur through confined air streams, such as stacks, ducts or pipes.
[e] Fugitive air emissions are emissions that do not occur through a confined air stream, which may include equipment leaks, releases from building ventilation systems, and evaporative losses from surface impoundments and spills.

While production-related waste managed shown in Table 2-4 excludes any quantities reported as catastrophic or one-time releases (TRI section 8 data), release quantities shown in Table 2-5 include both production-related and non-routine quantities (TRI section 5 and 6 data) for 2015. As a result, release quantities may differ slightly and may further reflect differences in TRI calculation methods for reported release range estimates (U.S. EPA, 2017d).

From TRI data available using TRI Explorer, Table 2-6 shows that there has been a relatively large increase in total on-site and off-site disposal or other releases of friable asbestos since 2009 [EPA-HQ-OPPT-2016-0736-0005 (U.S. EPA, 2017b)]. From 2009 to 2015, total on-site and off-site disposal or other releases of friable asbestos have risen from 8.8 million pounds to nearly 25.6 million pounds, respectively. As previously noted, the vast majority of the total on-site and off-site disposal or other releases of friable asbestos are released to land. Release quantities to other media sources such as air are of much smaller magnitude. It is important to note that quantities released from surface water discharges have been zero pounds since 2009. The industry accounting for the highest release quantities of friable asbestos is the hazardous waste treatment and disposal sector, followed by the petroleum and other chemical and electric sectors.

**Table 2-6. Total On- and Off-site Disposal or Other Releases of Friable Asbestos (lbs) (2009-2015), based on TRI Data**

| Year | Total On- and Off-site Disposal or Other Releases (lbs) |
|---|---|
| 2009 | 8,757,577 |
| 2010 | 13,015,169 |
| 2011 | 12,492,732 |
| 2012 | 16,018,091 |

| Year | Total On- and Off-site Disposal or Other Releases (lbs) |
|---|---|
| 2013 | 16,641,975 |
| 2014 | 17,521,650 |
| 2015 | 25,568,291 |

Other sources of information provide evidence of releases of asbestos, including EPA effluent guidelines (EGs) promulgated under the Clean Water Act (CWA), National Emission Standards for Hazardous Air Pollutants (NESHAPs) promulgated under the Clean Air Act (CAA); or other EPA standards and regulations that set legal limits on the amount of asbestos that can be emitted to a particular media.

In addition to TRI data, EPA has also received release information from industry that will be used in the risk evaluation (see Section 2.6.1.3).

### 2.3.3 Presence in the Environment and Biota

Monitoring studies or a collection of relevant and reliable monitoring studies provide(s) information that can be used in an exposure assessment. Monitoring data were identified in EPA's data search for asbestos.

Presence of asbestos fibers in the air is highly variable, although there typically is a 10-fold higher concentration of asbestos in cities (0.0001 fibers/ml) than in rural areas (0.00001 fibers/ml) (ATSDR, 2001).

In 2001, the U.S. drinking water supplies generally had asbestos concentrations <1 million fibers per liter (MFL), although some locations may contain 10-300 MFL (ATSDR, 2001).

Available data (although over 30 years old) indicate asbestos has been detected in many different freshwater fishes and mussels from bodies of water contaminated with asbestos (U.S. EPA, 1980b; Shugar, 1979).

Asbestos fibers have been measured in U.S. municipal sewage sludges, with asbestos fiber content up to 10% of ashed sludge by volume (ATSDR, 2001). Biosolids in the U.S. may be disposed of by land application, land filling, or incineration. However, in the most recent EPA biosolids review, asbestos was not detected (see Section 2.5.3.2).

### 2.3.4 Environmental Exposures

The manufacturing, processing, distribution, use, and disposal of asbestos can result in releases to the environment. EPA expects to consider exposures to the environment and ecological receptors that occur via the exposure pathways or media shown in the revised conceptual model, Figure 2-4, in conducting the risk evaluation for asbestos.

The physical chemical properties of asbestos indicate that fibers can settle over time into sediments from surface water. The larger the fiber, the faster it will settle.

Compliance monitoring data, available for 2006-2011 shows 214 systems (3.7% of 5,785 systems) had detects greater than the minimum reporting level (MRL) of 0.2 MFL but only 8 systems had detects of asbestos greater than the MCL of 7 MFL (https://www.epa.gov/dwsixyearreview/six-year-review-3-

compliance- monitoring-data-2006-2011). Data from 1998-2005 showed 268 systems (3.2% of 8278 systems) had detects ≥ the MRL of 0.2 MFL but only 14 (0.169%) systems had detects of asbestos greater than the MCL of 7 MFL (https://www.epa.gov/dwsixyearreview/six-year-review-2-drinking-water-standards).

A source of information that EPA expects to consider in evaluating surface water releases are data reported in EPA's Discharge Monitoring Report (DMR) Pollutant Loading Tool (https://cfpub.epa.gov/dmr/) to identify facilities that discharge asbestos to surface water. Information was obtained from the DMR Pollutant loading tool accessed on December 1, 2017. Facilities were identified using "EZ Search" which identifies facilities that submit Discharge Monitoring Reports (DMRs). Searches were conducted for the two most current (and complete) years in the tool: 2015 and 2016. Only one DMR facility was identified in 2014 and 2015 and this facility was a mining facility and may be related to legacy mining use runoff. Asbestos has not been mined or otherwise produced in the United States since 2002. EPA did not consider legacy releases or releases based on naturally occurring background levels in this assessment.

### 2.3.5 Human Exposures

EPA plans to analyze occupational, consumer and general population exposures. Subpopulations, including potentially exposed and susceptible subpopulations, within these exposed groups will also be considered.

The physical condition of asbestos is an important factor when considering the potential human pathways of exposure. Several of the asbestos-containing products identified as conditions of use of asbestos (refer to Section 2.2.2.2) are not friable as intact products; however, non-friable asbestos can be made friable due to physical and chemical wear and normal use of asbestos-containing products. Exposures to asbestos can potentially occur via all routes; however, EPA anticipates that the most likely exposure route is inhalation for all of the subpopulations considered (see discussion in Section 2.4.2).

#### 2.3.5.1 Occupational Exposures

Exposure pathways and exposure routes are listed for worker activities under the various conditions of use described in Section 2.2. In addition, occupational non-users (ONU), who do not directly handle asbestos but perform work in an area where the chemical is present are listed. Engineering controls and/or personal protective equipment may impact occupational exposure levels.

EPA considers inhalation of asbestos fibers to be the most likely asbestos exposure pathway for workers and occupational non-users during the conditions of use included in Sections 2.2.2.2 and 2.2.2.3. These include the fabrication of asbestos-containing diaphragms in the chlor-alkali industry, use of asbestos-containing gaskets in the production of titanium dioxide, and the use of asbestos containing brake blocks in the oil industry. Workers and occupational non-users may also be exposed to asbestos containing products (e.g., friction products, cement products, other gaskets and packing, woven products) that may become friable during use or handling. EPA will only evaluate the inhalation route of exposure (see Section 2.4.2 for discussion).

Workers and occupational non-users may be exposed to asbestos when performing activities associated with conditions of use described in Section 2.2.2.3 including, but not limited to:

- Unloading and transferring raw asbestos to and from storage containers to storage rooms, process equipment or glove boxes in the chlor-alkali industry;

- Using asbestos within process equipment (e.g., fabrication of diaphragms in the chlor-alkali industry);
- Cleaning and maintaining equipment in the chlor-alkali industry;
- Using imported and/or aftermarket asbestos-containing products (e.g., oilfield equipment maintenance);
- Processing and using imported sheet gaskets;
- Cutting cement pipes;
- Changing asbestos-containing automotive brakes;
- Handling, transporting and disposing waste containing asbestos in chlor-alkali plants and other industrial facilities handling asbestos.

Key data that inform occupational exposure assessment include: the OSHA Chemical Exposure Health Data (CEHD) and NIOSH Health Hazard Evaluation (HHE) program data. OSHA data are workplace monitoring data from OSHA inspections. The inspections can be random or targeted, or can be the result of a worker complaint. OSHA data can be obtained through the OSHA Integrated Management Information System (IMIS) at https://www.osha.gov/oshstats/index.html. Table Apx B-1 in Appendix B provides a summary of industry sectors with asbestos personal monitoring air samples obtained from OSHA inspections conducted between 2011 and 2016 (the data were received [October 25th, 2017] and are being evaluated). NIOSH HHEs are conducted at the request of employees, union officials, or employers and help inform potential hazards at the workplace. HHEs can be downloaded at https://www.cdc.gov/niosh/hhe/ . In addition, occupational monitoring information was received from companies in the chlor-alkali and sheet gasket industries; some of this data has been claimed CBI. EPA will review these data and evaluate their utility in the risk evaluation.

According to OSHA asbestos standards, the employee permissible exposure limit (PEL) is 0.1 fibers per cubic centimeter (f/cc) as an 8-hour, time-weighted average (TWA) and/or the excursion limit (1.0 f/cc as a 30-minute TWA) (Asbestos General Standard 29 CFR 1910). The NIOSH Recommended Exposure Limit (REL) (NIOSH, 2007) and the American Conference of Governmental Industrial Hygienists Threshold Limit Value (ACGIH TLV) (ACGIH, 1994) are also 0.1 f/cc (respirable fibers), with the REL duration of 100 minutes. Both the PEL and REL are based on phase contrast microscopy (PCM) (which would not include fibers with diameters less than approximately 0.25 µm).

#### 2.3.5.2 Consumer Exposures

Through further investigation of the list of products available for purchase on the internet as depicted in Section 3 of the *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: Asbestos* document EPA-HQ-OPPT-2016-0736-0005, (U.S. EPA, 2017b), EPA has determined that asbestos-containing consumer products are likely imported only, not produced in the United States, and are limited to aftermarket friction materials. Available data suggest woven products could also be imported and used by consumers in the United States.

Exposure routes for consumers using asbestos-containing products may include inhalation of particulates resulting from use, and there is the possibility that clothing contaminated from asbestos through product use or manipulation could result in exposures to asbestos. EPA will only evaluate the inhalation route of exposure (see Section 2.4.2 for discussion).

#### 2.3.5.3 General Population Exposures

Asbestos is a naturally occurring mineral and is therefore present in the environment. Thus, the general population may be exposed to low levels of naturally occurring asbestos (ATSDR, 2001). Asbestos fibers may potentially be released during processing or use of asbestos in industry and use of imported

asbestos containing products (see Section 2.3.2 and the public docket EPA-HQ-OPPT-2016-0736). As explained in Section 2.3.2, only friable asbestos above a specified threshold is required to be reported to the Toxics Release Inventory. Therefore, other sources of air releases will be consulted in the risk evaluation. For example, EPA will evaluate the data that has been submitted by the chlor-alkali and gasket industries as well as other sources of data.

#### 2.3.5.4 Potentially Exposed or Susceptible Subpopulations

TSCA requires the determination of whether a chemical substance presents an unreasonable risk to "a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation" by EPA. TSCA § 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." General population is "the total of individuals inhabiting an area or making up a whole group" and refers here to the U.S. general population (U.S. EPA, 2011).

As part of the Problem Formulation, EPA identified potentially exposed and susceptible subpopulations for further analysis during the development and refinement of the life cycle, conceptual models, exposure scenarios, and analysis plan. In this section, EPA addresses the potentially exposed or susceptible subpopulations identified as relevant based on greater exposure. EPA will address the subpopulations identified as relevant based on greater susceptibility in the hazard section.

EPA identifies the following as potentially exposed or susceptible subpopulations that EPA expects to consider in the risk evaluation due to their *greater exposure*:

- Workers and occupational non-users
- Consumers and bystanders associated with consumer use. Asbestos has been identified as being used in products available to consumers; however, only some individuals within the general population may use these products. Therefore, those who do use these products are a potentially exposed or susceptible subpopulation due to greater exposure.
- Other groups of individuals within the general population who may experience greater exposures due to their proximity to conditions of use identified in Section 2.2.2.2 that result in releases to the environment and subsequent exposures (e.g., individuals who live or work near manufacturing, processing, use or disposal sites).

In developing exposure scenarios, EPA will analyze available data to ascertain whether some human receptor groups may be exposed via exposure pathways that may be distinct to a particular subpopulation or life stage (e.g., children's crawling, mouthing or hand-to-mouth behaviors) and whether some human receptor groups may have higher exposure via identified pathways of exposure due to unique characteristics (e.g., activities, duration or location of exposure) when compared with the general population (U.S. EPA, 2006).

The population most likely to have high exposure to asbestos are workers who come into contact with asbestos while on the job (ATSDR, 2001). In the Scope document, fire fighters were also included as a potentially exposed or susceptible subpopulation. However, fire fighters will be exposed to materials that are predominately legacy uses, which will not be evaluated in the risk evaluation.

In summary, in the risk evaluation for asbestos, EPA plans to analyze the following potentially exposed groups of human receptors including: workers, occupational non-users, consumers, bystanders associated with consumer use, and other groups of individuals within the general population who may

experience greater exposure. EPA may also identify additional potentially exposed or susceptible subpopulations that will be considered, based on greater exposure.

## 2.4 Hazards (Effects)

For scoping, EPA conducted comprehensive searches for data on hazards of asbestos, as described in *Strategy for Conducting Literature Searches for Asbestos: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0736). Based on initial screening, EPA plans to analyze the hazards of asbestos identified in this scope document. However, when conducting the risk evaluation, the relevance of each hazard within the context of a specific exposure scenario will be judged for appropriateness. For example, hazards that occur only as a result of chronic exposures may not be applicable for acute exposure scenarios. This means that it is unlikely that every hazard will be analyzed for every exposure scenario.

### 2.4.1 Environmental Hazards

EPA identified the following sources of environmental hazard data for asbestos: 45 FR 79318, 1980 ATSDR (2001); U.S. EPA (2014c); U.S. EPA (2014b); WHO (2014); and IARC (2012). In addition, EPA conducted a literature search to identify additional environmental hazard data for asbestos as identified in the literature search conducted by the Agency for asbestos (*Asbestos (CASRN 1332-21-4) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0736). Only the *on-topic* references listed in the Ecological Hazard Literature Search Results were considered as potentially relevant data/information sources for the risk evaluation. Inclusion criteria were used to screen the results of the ECOTOX literature search (as explained in the *Strategy for Conducting Literature Searches for Asbestos: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0736). Data from the screened literature are summarized below (Table 2-7. Ecological Hazard Characterization of Chrysotile Asbestos (CASRN 12001-29-5) as ranges (min-max). EPA plans to review these data/information sources during risk evaluation using the data quality review evaluation metrics and the rating criteria described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018).

Data were available for aquatic organisms (vertebrates, invertebrates and plants) and terrestrial species (earthworms and plants). For problem formulation, a screening evaluation was conducted using aquatic toxicity studies characterizing the effects of chronic exposure of chrysotile asbestos to aquatic invertebrates and fish, presented in Table 2-7. Ecological Hazard Characterization of Chrysotile Asbestos (CASRN 12001-29-5) Preliminary review of these studies indicates that chronic exposure to waterborne chrysotile asbestos may result in reproductive, growth and sublethal effects to these taxa at a concentration range of $10^4$-$10^8$ fibers/L (i.e., 0.01-100 MFL). A comparison to available monitoring data (see Section 2.6.1.2) preliminarily indicates exposure concentrations may be within the same order of magnitude; hence, EPA will further evaluate this pathway.

**Table 2-7. Ecological Hazard Characterization of Chrysotile Asbestos (CASRN 12001-29-5)**

| Duration | Test Organism | Endpoint | Hazard Value[a] | Unit | Effect Endpoint(s) | References |
|---|---|---|---|---|---|---|
| **Aquatic Organisms** | | | | | | |
| Chronic | Fish | NOEC[b] | 0.01-1.5 | MFL[e] | Behavioral stress (aberrant swimming, loss of equilibrium); Egg development, hatchability, survival; Growth; Mortality | Belanger (1985); Belanger et al. (1990); Belanger et al. (1986c); Cairns et al. (1990) |
| | | LOEC[c] | 1-3 | | | |
| | | ChV[d] | 0.1-2.12 | | | |
| | Aquatic invertebrates | LOEC | 0.0001-100 | MFL | Reduction in siphoning activity; # of larvae released; Alterations of gill tissues; Fiber accumulation in tissues; Growth; Mortality | Belanger et al. (1986b); Belanger et al. (1986a) |
| | Aquatic Plant | LOEC | 0.5 | µg chrysotile/ frond | # of fronds; Root length; Chlorophyll content; Carotenoid content; Biomass of fronds; Protein content; Free sugar; Starch; Photosynthetic pigments; Lipid peroxidation; Cellular hydrogen peroxide levels; Catalase activity; Superoxide Dismutase | Trivedi et al. (2004); Trivedi et al. (2007) |
| **Terrestrial Organisms** | | | | | | |
| Chronic | Terrestrial Plant | ChV | No observed effects | N/A[f] | Growth | Miller et al. (1980) |

[a]Values in the tables are presented as reported by the study authors.
[b]NOEC, No Observable Effect Concentration
[c]LOEC, Lowest Observable Effect Concentration
[d]ChV, Chronic Value; Calculated using the geometric mean of LOEC and NOEC values [as described in U.S. EPA (2013)].
[e]MFL, Million Fibers/Liter
[f]N/A, Not applicable

For additional perspective on understanding the environmental hazard of asbestos materials, EPA/OPPT reviewed other, related documents on asbestos materials not considered under TSCA. For example, EPA Region 8 reviewed the same data identified above for the Libby Superfund Site ecological risk assessment (U.S. EPA, 2014b) and considered it relevant; thus suggesting the experiments/information reasonably describes the aquatic hazard of asbestos. However, Region 8 decided to perform *in situ* studies to specifically evaluate ecological receptor effects following exposure to Libby Amphibole Asbestos (LAA, or LA in the report). During the course of performing these experiments/exposures, Region 8 found them difficult to conduct and quantify, thus highlighting the difficulty of evaluating asbestos/asbestiform fibers in ecological receptors.

### 2.4.2 Human Health Hazards

Asbestos has an existing EPA IRIS Assessment and an ATSDR Toxicological Profile; hence, many of the hazards of asbestos have been previously compiled and reviewed. EPA relied heavily on these comprehensive reviews in preparing the scope and problem formulation documents. EPA expects to use these documents as a starting point for identifying key and supporting studies to inform the human health hazard assessment, including dose-response analysis. EPA also expects to consider other studies that have been published since these reviews, as identified in the literature search conducted by the Agency for asbestos (*Asbestos (CASRN 1332-21-4) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0736). The preponderance of information in these assessments

is based on inhalation exposures to human populations. Only inhalation exposures in humans will be evaluated in the risk evaluation of asbestos. The relevant studies will be evaluated using the data quality criteria in the *Application of Systemic Review in TSCA Risk Evaluations* document (U.S. EPA, 2018).

During scoping and problem formulation EPA reviewed the existing EPA IRIS health assessments to ascertain the established health hazards and any known toxicity values. EPA had previously, in the IRIS assessment on asbestos (1988), identified asbestos as a carcinogen causing both lung cancer and mesothelioma from inhalation exposures and derived a unit risk to address both cancers. No toxicity values or unit risks have yet been estimated for other cancers that have been identified by the International Agency for Research on Cancer (IARC) and other government agencies. Given the well-established carcinogenicity of asbestos for lung cancer and mesothelioma, EPA has decided to limit the scope of its systematic review to these two specific cancers with the goal of updating, or reaffirming, the existing unit risk. Asbestos may cause non-cancer health effects, with quantitative evidence coming from the EPA Toxicological Review of Libby Amphibole Asbestos (U.S. EPA, 2014c). At a Target Risk of 1 cancer per 1,000,000 people (1E-6), the existing EPA general asbestos toxicity value appears to be the clear risk driver compared to the only existing EPA non-cancer toxicity value (RfC) for Libby Amphibole Asbestos (U.S. EPA, 2014c). Because cancer is expected to be the risk driver, in conducting further analysis for the risk evaluation of asbestos, EPA will limit the scope of the risk evaluation to lung cancer and mesothelioma in humans. No clear association was found for drinking water asbestos exposure and cancer (NTP, 2016; IARC, 2012), and dermal exposures may cause non-cancerous skin lesions. Since neither oral nor dermal exposures are expected to contribute to the risks of lung cancer and mesothelioma, which are the basis of the 1988 cancer unit risk, exposures from the oral and dermal routes will not be assessed. These hazards will be evaluated based on the specific exposure scenarios identified for workers, consumers and the general population where applicable.

#### 2.4.2.1 Cancer Hazard

Many authorities have established that there are causal associations between asbestos exposures and lung cancer and mesotheliomas (NTP, 2016; IARC, 2012; ATSDR, 2001; U.S. EPA, 1988b; IARC, 1987, 1977). EPA also noted in the scope that there is a causal association between exposure to asbestos and cancer of the larynx and cancer of the ovary (IARC, 2012), and that there is also suggestive evidence of a positive association between asbestos and cancer of the pharynx (IARC, 2012; NRC, 2006), stomach (IARC, 2012; ATSDR, 2001) and colorectum (NTP, 2016; IARC, 2012; NRC, 2006; ATSDR, 2001; NRC, 1983; U.S. EPA, 1980a). In addition, the scope document reported increases in lung cancer mortality reported in both workers and residents exposed to various asbestos fiber types as well as fiber mixtures (IARC, 2012). Mesotheliomas, tumors arising from the thin membranes that line the chest (thoracic) and abdominal cavities and surround internal organs, are relatively rare in the general population, but are often observed in populations of asbestos workers. All types of asbestos fibers have been reported to cause mesothelioma (IARC, 2012).

During problem formulation, EPA reviewed the existing EPA IRIS health assessments (U.S. EPA, 2014c, 1988b) to ascertain the established health hazards and any known toxicity values. EPA had previously (U.S. EPA, 1988b, 1986) identified asbestos as a carcinogen causing both lung cancer and mesothelioma and derived a unit risk to address both cancers. The U.S. Institute of Medicine (NRC, 2006) and the International Agency for Research on Cancer (IARC, 2012) have evaluated the evidence for causation of cancers of the pharynx, larynx, esophagus, stomach, colon, and rectum, and IARC has evaluated the evidence for cancer of the ovary. Both the U.S. Institute of Medicine and IARC concluded that asbestos causes cancer of the larynx and IARC concluded that asbestos causes cancer of the ovary. No toxicity values or unit risks have yet been estimated for these other cancers.

#### 2.4.2.2 Potentially Exposed or Susceptible Subpopulations

TSCA requires that the determination of whether a chemical substance presents an unreasonable risk include consideration of unreasonable risk to "a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation" by EPA. TSCA § 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." In developing the hazard assessment, EPA will analyze available data to ascertain whether some human receptor groups may have greater susceptibility than the general population to asbestos.

## 2.5 Conceptual Models

EPA risk assessment guidance (U.S. EPA, 2014a, 1998), defines Problem Formulation as the part of the risk assessment framework that identifies the factors to be considered in the assessment. It draws from the regulatory, decision-making and policy context of the assessment and informs the assessment's technical approach.

A conceptual model describes the actual or predicted relationships between the chemical substance and receptors, either human or environmental. These conceptual models are integrated depictions of the conditions of use, exposures (pathways and routes), hazards and receptors. The initial conceptual models describing the scope of the assessment for asbestos have been refined during problem formulation. The changes to the conceptual models in this problem formulation are described along with the rationales.

In this section EPA outlines those pathways that will be included and further analyzed in the risk evaluation; will be included but will not be further analyzed in risk evaluation; and will not be included in the TSCA risk evaluation and the underlying rationale for these decisions.

EPA determined as part of problem formulation that it is not necessary to conduct further analysis on certain exposure pathways that were identified in the asbestos scope document and that remain in the risk evaluation. Each risk evaluation will be "fit-for-purpose," meaning not all conditions of use will warrant the same level of evaluation and the Agency may be able to reach some conclusions without extensive or quantitative risk evaluations (82 FR 33726, 33734, 33739).

As part of this problem formulation, EPA also identified exposure pathways under other environmental statutes, administered by EPA, which adequately assess and effectively manage exposures and for which long-standing regulatory and analytical processes already exist, i.e., the Clean Air Act (CAA), the Safe Drinking Water Act (SDWA), the Clean Water Act (CWA) and the Resource Conservation and Recovery Act (RCRA). OPPT worked closely with the offices within EPA that administer and implement the regulatory programs under these statutes. In some cases, EPA has determined that chemicals present in various media pathways (i.e., air, water, land) fall under the jurisdiction of existing regulatory programs and associated analytical processes carried out under other EPA-administered statutes and have been assessed and effectively managed under those programs. EPA believes that the TSCA risk evaluation should focus on those exposure pathways associated with TSCA uses that are not subject to the regulatory regimes discussed above because these pathways are likely to represent the greatest areas of concern to EPA. As a result, EPA does not expect to include in the risk evaluation certain exposure pathways identified in the asbestos scope document.

### 2.5.1 Conceptual Model for Industrial and Commercial Activities and Uses: Potential Exposures and Hazards

The revised conceptual model (Figure 2-2) describes the pathways of exposure from industrial and commercial activities and uses of asbestos EPA plans to include in the risk evaluation.

The population most likely to have high exposure to asbestos are workers who come into contact with asbestos while on the job (ATSDR, 2001). As described in Section 2.2.2.2, EPA has confirmed the ongoing industrial and commercial uses of asbestos in the chlor-alkali industry, brake blocks in oil industry, and use of sheet gaskets in titanium dioxide production. These uses, as well as uses in other products (brakes and other friction products, other gaskets, woven products, and cement products) will continue to be investigated during the risk evaluation. All of these uses will be included in the risk evaluation, as indicated in Figure 2-2.

EPA anticipates inhalation of asbestos fibers as being the most likely exposure route for workers and occupational non-users. As discussed in Section 2.4.2, given the well-established carcinogenicity of asbestos for lung cancer and mesothelioma, EPA will only evaluate these two specific cancers in the risk evaluation (and associated systematic review) with the goal of updating, or reaffirming, the existing unit risk.

In the Scope document, worker exposures via oral and dermal pathways were identified as potential routes of exposure. However, since neither oral nor dermal exposures are expected to contribute to the risks of lung cancer and mesothelioma, exposures from those routes (pathways) will not be included in the risk evaluation.

Workers may be exposed via direct contact with dry or friable asbestos during waste handling, treatment and disposal. This could occur during disposal of asbestos containing articles or wastes. When data and information are available to support the analysis, EPA also considers the effect that engineering controls and/or personal protective equipment have on occupational exposure levels.

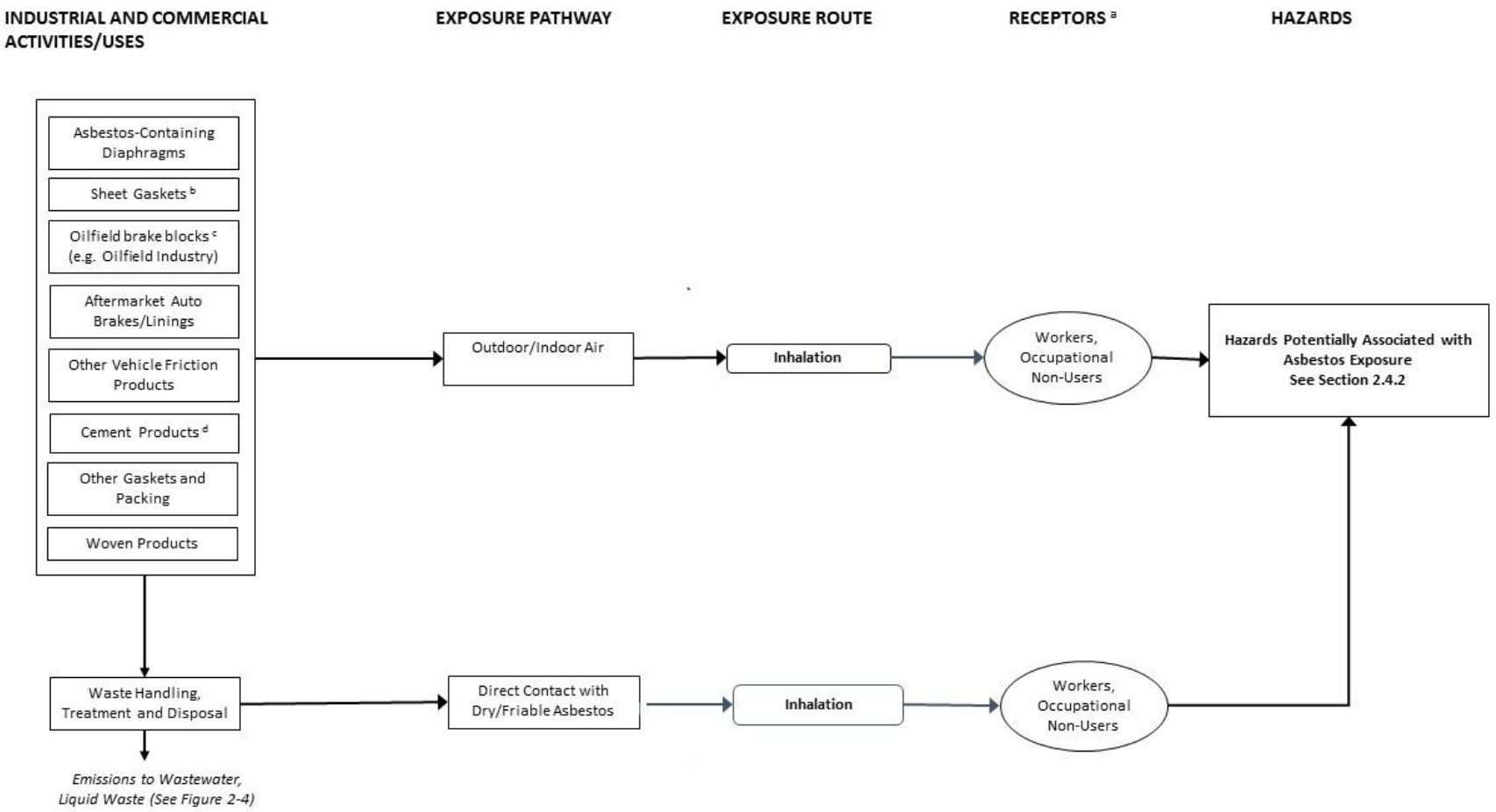



**Figure 2-2. Asbestos Conceptual Model for Industrial and Commercial Activities and Uses: Potential Exposures and Hazards**
The conceptual model presents the exposure pathways, exposure routes and hazards to human receptors from industrial and commercial activities and uses of asbestos.

[a] Receptors include potentially exposed or susceptible subpopulations.
[b] Sheet gaskets were identified during public comment period.
[c] Oilfield brake blocks identified via industry response during problem formulation.
[d] Asbestos cement products identified during problem formulation.

### 2.5.2 Conceptual Model for Consumer Activities and Uses: Potential Exposures and Hazards

Figure 2-3 presents the conceptual model for human populations from potential consumer uses of asbestos. There are very few asbestos-containing products with ongoing uses that were identified and confirmed during problem formulation. EPA identified the import of asbestos-containing automotive brakes and linings and woven products as the only known, intended, or reasonably foreseen asbestos-containing products that may have consumer exposure. These uses are included in Figure 2-3. Consumer exposures will be difficult to evaluate since the quantities of these products that still might be imported into the United States is not known.

Scenarios where consumers could be exposed and may be considered during risk evaluation include: changing asbestos-containing brakes or brake linings or cutting or using asbestos-containing woven products, and handling of asbestos waste that may result from these activities.

EPA anticipates inhalation of asbestos fibers as being the most likely exposure route for consumers. As discussed in Section 2.4.2, given the well-established carcinogenicity of asbestos for lung cancer and mesothelioma, EPA will only evaluate these two specific cancers in the risk evaluation (and associated systematic review) with the goal of updating, or reaffirming, the existing unit risk.

In the Scope document, consumer exposures via oral and dermal pathways were identified as potential routes of exposure. However, since neither oral nor dermal exposures are expected to contribute to the risks of lung cancer and mesothelioma, exposures from those routes (pathways) will not be included in the risk evaluation.

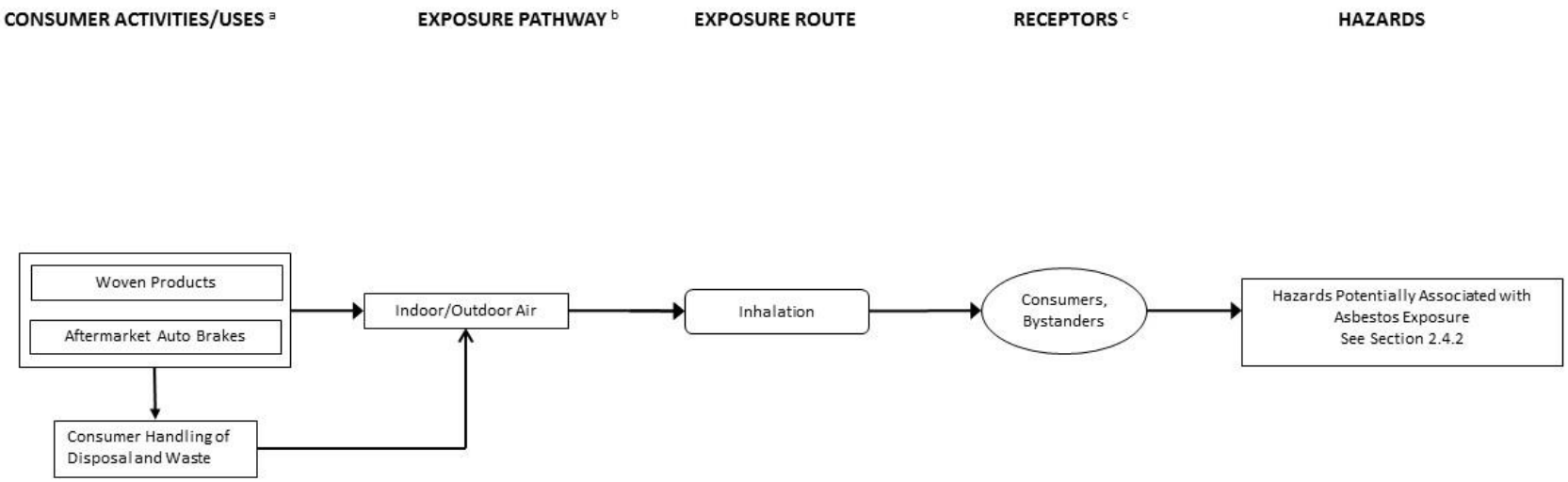



**Figure 2-3. Asbestos Conceptual Model for Consumer Activities and Uses: Potential Exposures and Hazards**

[a] Products may be used in both commercial and consumer applications.

[b] Products may be used during indoor and outdoor activities.

[c] Receptors include potentially exposed and susceptible subpopulations.

### 2.5.3 Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards

The revised conceptual model (Figure 2-4) illustrates the expected exposure pathways to human and ecological receptors from environmental releases and waste stream associated with industrial and commercial activities for asbestos. The pathway that EPA plans to include and analyze further in risk evaluation is described in Section 2.5.3.1 and shown in the conceptual model. The pathways that EPA plans to include but not further analyze in risk evaluation are described in Section 2.5.3.2 and the pathways that EPA does not expect to include in risk evaluation are described in Section 2.5.3.3.

#### 2.5.3.1 Pathways That EPA Expects to Include and Further Analyze in Risk Evaluation

EPA plans to further analyze environmental releases from water pathways to aquatic species exposed via contaminated surface water.

No releases to water have been reported to TRI for asbestos (Table 2-4). However, data submitted to EPA from the chlor-alkali industry indicate that water releases may occur from these industries. Based on data submitted to EPA from the chlor-alkali industry, who uses all of the raw asbestos imported into the United States to fabricate asbestos-containing diaphragms, asbestos containing wastes generated in their processes are disposed of according to NESHAP regulations established in 40 CFR 61.150. Asbestos is not regulated as a hazardous waste under RCRA. Asbestos-containing diaphragms used in the chlor-alkali processes may be reused at some of the plants. At the end of the diaphragms' life, water is used to clean and remove the diaphragm from its frame. The wet diaphragm is bagged and landfilled according to NESHAP regulations. Waste water from the washing of the diaphragm and frame is sent to on-site waste water treatment; which may lead to eventual releases to water.

Asbestos-containing gaskets are used in the production of rutile/chlorine based titanium dioxide (TiO2). Based on data submitted to EPA from the asbestos sheet gasket importer/processor, scrap pieces from the gasket cutting process are double bagged and transported to landfills. EPA has been informed that users of asbestos-containing gaskets dispose of spent gaskets primarily via incineration (3 onsite and 1 offsite facility) and RCRA Subtitle C landfill (1 facility). No water releases are anticipated.

Preliminary review of environmental studies indicates that chronic exposure to waterborne chrysotile asbestos may result in reproductive, growth and sublethal effects. Compliance monitoring data, available for 2006-2011 shows 214 systems (or 3.7% of 5,785 systems) with asbestos fiber concentrations greater than the minimum reporting level (MRL) of 0.2 MFL, with asbestos concentrations in 8 systems greater than the MCL of 7 MFL (https://www.epa.gov/dwsixyearreview/six-year-review-3-compliance- monitoring-data-2006-2011). Data from 1998-2005 showed 268 systems (or 3.237% of 8278 systems) had asbestos fiber concentrations greater than or equal to the MRL of 0.2 MFL, with asbestos concentrations in 14 (0.169%) systems greater than the MCL of 7 MFL (https://www.epa.gov/dwsixyearreview/six-year-review-2-drinking-water-standards).

As further explained in Section 2.5.3.2, EPA has not developed CWA section 304(a) recommended water quality criteria for the protection of aquatic life for asbestos and there are no national recommended criteria for this use available for adoption into state water quality standards and available for use in NPDES permits. As a result, this pathway will undergo aquatic life risk evaluation under TSCA (see Section 2.5.3.1).

Therefore, EPA plans to evaluate risks to aquatic species from exposures to asbestos in surface waters.

#### 2.5.3.2 Pathways That EPA Expects to Include in Risk Evaluation but Not Further Analyze

As noted in Section 2.5.3.1 above, there are possible releases from conditions of use (i.e., chlor-alkali plants) to water. Once in water, it will eventually settle into sediments (or possibly biosolids from wastewater treatment plants).

EPA does not expect to perform a full analysis of exposures to asbestos fibers to sediment-dwelling organisms. EPA is still reviewing literature sources identified in the original search that suggest that the asbestos exposure levels in sediments is low and perhaps outdated. Finally, the most important concern for asbestos exposures are via inhalation to humans.

However, EPA does not expect to further analyze general population exposures to asbestos fibers, via inhalation due to lofting of dried asbestos, during or after the land application of biosolids. EPA has identified literature which indicates that asbestos has been detected in biosolids from municipal wastewater treatment. However, it is expected that the concentration of asbestos fibers in biosolids due to current uses of asbestos will be low, and thus the subsequent re-suspension of the asbestos fibers into air following biosolid land application, although possible, will result in exceedingly low airborne concentrations.

#### 2.5.3.3 Pathways That EPA Does Not Expect to Include in the Risk Evaluation

Exposures to receptors (i.e. general population, terrestrial species) may occur from industrial and/or commercial uses, industrial releases to air, water or land, and other conditions of use. As described in Section 2.5, EPA does not expect to include in the risk evaluation pathways under programs of other environmental statutes, administered by EPA, which adequately assess and effectively manage exposures and for which long-standing regulatory and analytical processes already exist. These pathways are described below.

**Air Pathway**

The Clean Air Act (CAA) contains a list of hazardous air pollutants (HAP) and provides EPA with the authority to add to that list pollutants that present, or may present, a threat of adverse human health effects or adverse environmental effects. For stationary source categories emitting HAP, the CAA requires issuance of technology-based standards and, if necessary additions or revisions to address developments in practices, processes, and control technologies, and to ensure the standards adequately protect public health and the environment. The CAA thereby provides EPA with comprehensive authority to regulate emissions to ambient air of any hazardous air pollutant.

Asbestos is a HAP. Because stationary source releases of asbestos to ambient air are adequately assessed and any risks effectively managed when under the jurisdiction of the CAA, EPA does not plan to evaluate emission pathways to ambient air from commercial and industrial stationary sources or associated inhalation exposure of the general population or terrestrial species in this TSCA evaluation.

**Drinking Water Pathway**

EPA has regular analytical processes to identify and evaluate drinking water contaminants of potential regulatory concern for public water systems under the Safe Drinking Water Act (SDWA). Under SDWA, EPA must also review and revise "as appropriate" existing drinking water regulations every 6 years.

EPA has promulgated National Primary Drinking Water Regulations (NPDWRs) for asbestos under the Safe Drinking Water Act. EPA has set an enforceable Maximum Contaminant Level (MCL) as close as

feasible to a health based, non-enforceable Maximum Contaminant Level Goal (MCLG). Feasibility refers to both the ability to treat water to meet the MCL and the ability to monitor water quality at the MCL, SDWA Section 1412(b)(4)(D), and public water systems are required to monitor for the regulated chemical based on a standardized monitoring schedule to ensure compliance with the MCL. The MCL for asbestos in water is 7 million fibers/liter, or 7 MFL.

Hence, because the drinking water exposure pathway for asbestos is currently addressed in the SDWA regulatory analytical process for public water systems, EPA does not expect to include this pathway in the risk evaluation for asbestos under TSCA.

**Ambient Water Pathways**

EPA develops recommended water quality criteria under section 304(a) of the CWA for pollutants in surface water that are protective of aquatic life or human health designated uses. EPA develops and publishes water quality criteria based on priorities of states and others that reflect the latest scientific knowledge. A subset of these chemicals are identified as "priority pollutants" (103 human health and 27 aquatic life). The CWA requires states adopt numeric criteria for priority pollutants for which EPA has published recommended criteria under section 304(a), the discharge or presence of which in the affected waters could reasonably be expected to interfere with designated uses adopted by the state. When states adopt criteria that EPA approves as part of state's regulatory water quality standards, exposure is considered when state permit writers determine if permit limits are needed and at what level for a specific discharger of a pollutant to ensure protection of the designated uses of the receiving water. Once state adopt criteria as water quality standards, the CWA requires that National Pollutant Discharge Elimination System (NPDES) discharge permits include effluent limits as stringent as necessary to meet standards. CWA section 301(b)(1)(C). This is the process used under the CWA to address risk to human health and aquatic life from exposure to a pollutant in ambient waters.

EPA has identified asbestos as a priority pollutant and EPA has developed recommended water quality criteria for protection of human health for asbestos which are available for adoption into state water quality standards for the protection of human health and are available for use by NPDES permitting authorities in deriving effluent limits to meet state narrative criteria. As such, EPA does not expect to include this pathway in the risk evaluation under TSCA. EPA's Office of Water and Office of Pollution Prevention and Toxics will continue to work together providing understanding and analysis of the CWA water quality criteria development process and to exchange information related to toxicity of chemicals undergoing risk evaluation under TSCA. EPA may update its CWA section 304(a) water quality criteria for asbestos in the future under the CWA.

EPA has not developed CWA section 304(a) recommended water quality criteria for the protection of aquatic life for asbestos, so there are no national recommended criteria for this use available for adoption into state water quality standards and available for use in NPDES permits. As a result, this pathway will undergo aquatic life risk evaluation under TSCA (see Section 2.5.3.1). EPA may publish CWA section 304(a) aquatic life criteria for asbestos in the future if it is identified as a priority under the CWA.

**Disposal Pathways**

Asbestos is not regulated as a RCRA hazardous waste under RCRA Subtitle C. The general RCRA standard in RCRA section 3004(a) for the technical criteria that govern the management (treatment, storage, and disposal) of hazardous waste are those "necessary to protect human health and the environment." Subtitle C controls cover not only hazardous wastes that are landfilled, but also hazardous wastes that are incinerated (subject to joint control under RCRA Subtitle C and the Clean Air Act

(CAA) hazardous waste combustion MACT) or injected into UIC Class I hazardous waste wells (subject to joint control under Subtitle C and the Safe Drinking Water Act (SDWA)).

EPA does not expect to include emissions to ambient air from municipal and industrial waste incineration and energy recovery units in the risk evaluation, as they are regulated under section 129 of the Clean Air Act. An incinerator burning hazardous waste must achieve a destruction and removal efficiency (DRE) of 99.99% for each principal organic hazardous constituent. Furthermore, RCRA provisions for site-specific risk assessments and the Hazardous Waste Combustor maximum achievable control technology (MACT) rule provisions for a Residual Risk and Technology Review together cover risks for RCRA-regulated hazardous wastes and CAA HAPs. Emissions to ambient air from municipal and industrial waste incineration and energy recovery units will not be included in the risk evaluation, as they are regulated under section 129 of the Clean Air Act. CAA section 129 also requires EPA to review and, if necessary, add provisions to ensure the standards adequately protect public health and the environment. Thus, the asbestos combustion by-products from incineration treatment of asbestos wastes (less than 188,437 lbs identified in Table 2-4 under "treatment" which includes incineration, as well as other treatment methods) would be subject to the aforementioned regulations.

EPA does not expect to include on-site releases to land that go to underground injection in its risk evaluation. TRI reporting in 2015 indicated zero pounds of asbestos were released to underground injection to a Class I well. Therefore, disposal of asbestos via underground injection will not result in environmental and general population exposures.

EPA does not expect to include on-site releases to land that go to RCRA Subtitle C hazardous waste landfills or RCRA Subtitle D municipal solid waste (MSW) landfills or exposures of the general population (including susceptible populations) or terrestrial species from such releases in the TSCA risk evaluation. Based on 2015 reporting to TRI, approximately 38% of the land disposals of asbestos occur in Subtitle C landfills (9.7 million lbs) as opposed to all other land disposal (15.8 million pounds). Design standards for Subtitle C landfills require double liner, double leachate collection and removal systems, leak detection system, run on, runoff, and wind dispersal controls, and a construction quality assurance program. They are also subject to closure and post-closure care requirements including installing and maintaining a final cover, continuing operation of the leachate collection and removal system until leachate is no longer detected, maintaining and monitoring the leak detection and groundwater monitoring system. Bulk liquids may not be disposed in Subtitle C landfills. Subtitle C landfill operators are required to implement an analysis and testing program to ensure adequate knowledge of waste being managed, and to train personnel on routine and emergency operations at the facility. Hazardous waste being disposed in Subtitle C landfills must also meet RCRA waste treatment standards before disposal. In addition, landfills have special requirements for handling and securing the asbestos-containing waste regulated under NESHAP to prevent releases of asbestos into the air. NESHAP requires that regulated asbestos-containing waste material be sealed in a leak-tight container while wet, labeled, and disposed of properly in a landfill qualified to receive asbestos waste. Landfills have special requirements for handling and securing the asbestos containing waste to prevent releases of asbestos into the air. Transportation vehicles that move the waste from the point of generation to the asbestos landfill have special labeling requirements and waste shipment recordkeeping requirements. Finally, asbestos is a fiber that is not likely to be leached out of a landfill. Given these controls, general population exposure to asbestos in groundwater from Subtitle C landfill leachate is not expected to be a significant pathway.

While permitted and managed by the individual states, municipal solid waste (MSW) landfills are required by federal regulations to implement some of the same requirements as Subtitle C landfills. MSW landfills generally must have a liner system with leachate collection and conduct groundwater

monitoring and corrective action when releases are detected. MSW landfills are also subject to closure and post-closure care requirements, and must have financial assurance for funding of any needed corrective actions. MSW landfills have also been designed to allow for the small amounts of hazardous waste generated by households and very small quantity waste generators (less than 220 lbs per month). EPA does not expect to include on-site releases to land from RCRA Subtitle C hazardous waste landfills or RCRA Subtitle D municipal solid waste landfills or exposures of the general population (including susceptible populations) or terrestrial species in this TSCA evaluation.

Industrial-non-hazardous and construction/demolition waste landfills are primarily regulated under state regulatory programs. States must also implement limited federal regulatory requirements for siting, groundwater monitoring, and corrective action, and a prohibition on open dumping and disposal of bulk liquids. States may establish additional requirements such as for liners, post-closure care and financial assurance, but are not required to do so. Therefore, EPA does not expect to include this pathway in the risk evaluation.

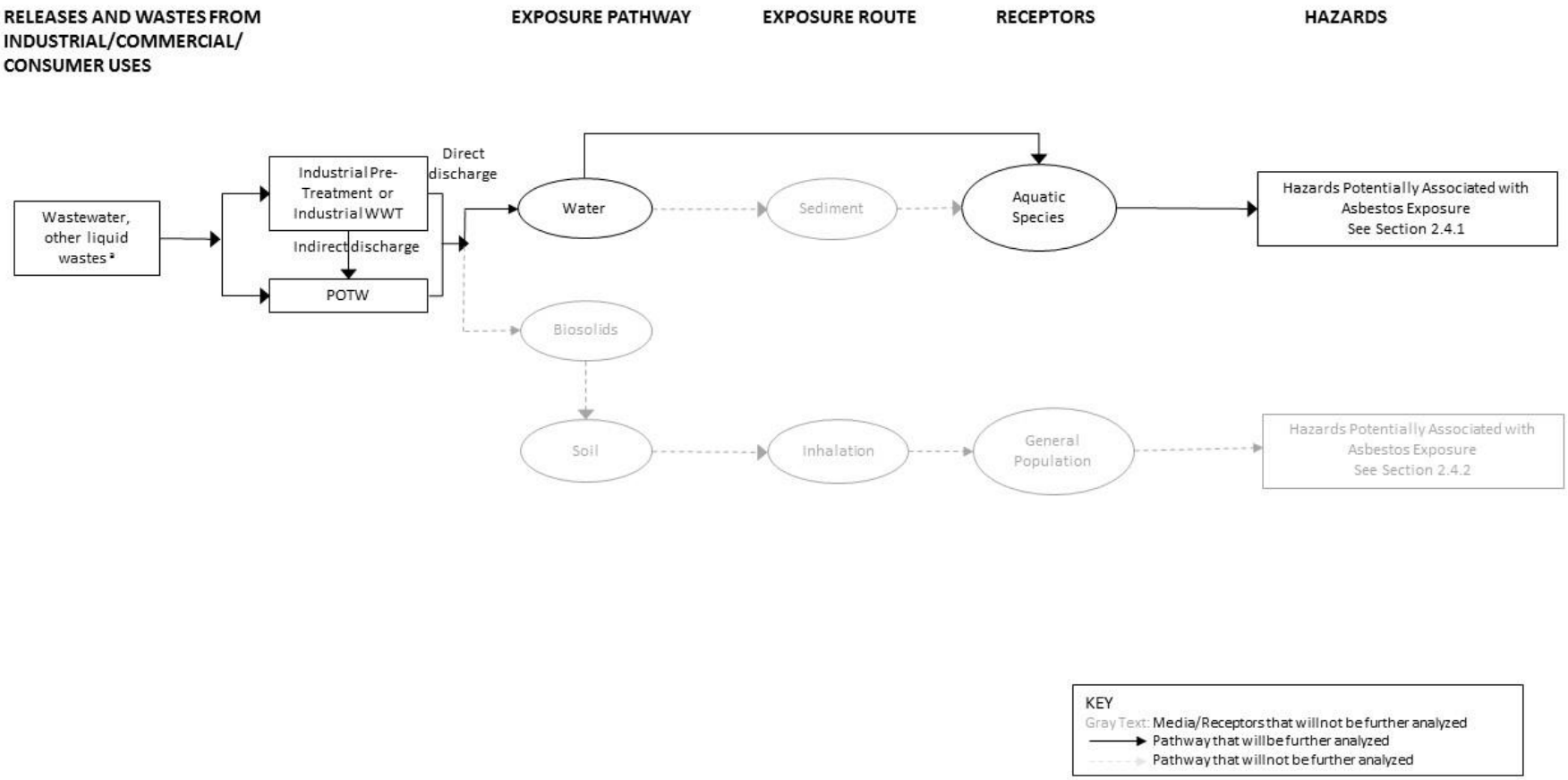



**Figure 2-4. Asbestos Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards**

[a] Industrial wastewater or liquid wastes may be treated on-site and then released to surface water (direct discharge), or pre-treated and released to POTW (indirect discharge). For consumer uses, such wastes may be released directly to POTW (i.e. down the drain).

## 2.6 Analysis Plan

The analysis plan presented here elaborates on the initial analysis plan that was published in the *Scope of the Risk Evaluation for Asbestos* (U.S. EPA, 2017c).

The analysis plan is based on the conditions of use of asbestos, as described in Section 2.2 of this problem formulation. EPA is implementing systematic review approaches to identify, select, assess, integrate and summarize the findings of studies supporting the TSCA risk evaluation. The analytical approaches and considerations in the analysis plan are used to frame the scope of the systematic review activities for that assessment. The supplemental document, *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018), provides additional information about criteria and methods that have been and will be applied to the first 10 chemical risk evaluations.

While EPA has conducted a comprehensive search for reasonably available information from public sources as described in the *Scope of the Risk Evaluation for Asbestos* (U.S. EPA, 2017c), EPA encourages submission of additional existing data, such as full study reports or workplace monitoring from industry sources, that may be relevant for refining conditions of use, exposures, hazards and potentially exposed or susceptible subpopulations during the risk evaluation. EPA will continue to consider new information submitted by the public.

During risk evaluation, EPA will rely on the comprehensive literature results (see *Asbestos (CASRN 1332-21-4) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0736) or supplemental literature searches to address specific questions. Further, EPA may consider any relevant confidential business information (CBI) in the risk evaluation in a manner that protects the confidentiality of the information from public disclosure. The analysis plan is based on EPA's knowledge of asbestos to date which includes partial, but not complete review of identified literature. Should additional data or approaches become available, EPA may refine its analysis plan based on this information.

### 2.6.1 Exposure

Based on their physical-chemical properties, expected sources, and transport and transformation within the outdoor and indoor environment chemical substances are more likely to be present in some media and less likely to be present in others. Media-specific levels will vary based on the chemical substance of interest. For most chemical substances level(s) can be characterized through a combination of available monitoring data and modeling approaches.

#### 2.6.1.1 Environmental Fate and Environmental Releases

In the scope document, there was a section in the analysis plan pertaining to environmental fate. Most questions originally posed were determined to be not relevant for asbestos, a naturally occurring and solid material, during problem formulation.

As described in Section 2.5, EPA does not expect to further analyze certain releases to environmental media. However, for purposes of developing estimates of occupational exposure, EPA may use release related data collected under selected data sources such as the Toxics Release Inventory (TRI) and National Emissions Inventory (NEI) programs.

EPA expects to consider and analyze releases to environmental media as follows:

1) Review reasonably available published literature or information on processes associated with the conditions of use to evaluate the types of releases and wastes generated from ongoing uses.

- EPA has received and continues to receive measured data from some of the industries, and these data will be reviewed and used in the risk evaluation, where appropriate. These documents can be found at:

  September 6, 2017, Asbestos Use Outreach Meeting Between EPA, Occidental Chemical Corporation and the American Chemistry Council (ACC)
  https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0736-0116

  September 14, 2017, Asbestos Use Outreach Meeting Between EPA, Olin Chemical and the American Chemistry Council (ACC)
  https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0736-0117

  October 20, 2017, Asbestos Use Outreach Teleconference Between EPA and American Friction
  https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0736-0118

  October 30, 2017, Asbestos Use Outreach Meeting Between EPA, Chemours, Branham Corp. and the American Chemistry Council (ACC)
  https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0736-0119

2) Review reasonably available release data on asbestos, including measured or estimated release data (e.g., data collected under the TRI and National Emissions Inventory [NEI] programs and Office of Water, and Office of Land and Emergency Management, etc.).
   - The Office of Water provided OPPT with surface water data and a preliminary review shows some samples in receiving waters have reported asbestos concentrations ranging from 1-14 million fibers per liter (MFL).
   - Review site specific treatment information for possible development of site specific release model.
   - Review the release assessment approaches developed for 1988 Asbestos Ban and Phase-Out rule and, if possible, make any needed modifications or updates to models and exposure parameters used in ABPO.

#### 2.6.1.2 Environmental Exposures

EPA expects to consider the following in developing its Environmental Exposure Assessment of asbestos:

1) Review reasonably available environmental and biological monitoring data for release water (ecological receptors only).
   - Based on the discussions in Sections 2.2 through 2.5, EPA will be focusing on the possible presence of asbestos in water for aquatic organisms.
2) Review reasonably available information on releases near industrial point sources (e.g. asbestos releases from chlor-alkali manufacture) compare with available monitoring data. Available exposure models will be evaluated and considered alongside available monitoring data to characterize environmental exposures to water for ecological receptors. The following sources of data could be consulted:
   - Some information has been evaluated (OW six-year review as cited above) and others (listed below) will be further analyzed.

- STORET (USGS/EPS) for chemicals in surface water and sediment: https://www.epa.gov/waterdata/storage-and-retrieval-and-water-quality-exchange#portal

3) Review 1989 Asbestos Ban and Phase Out (ABPO) support documents (i.e. exposure assessment, risk assessment documents) to inform approaches for air modeling and general population exposures for asbestos-containing products. Evaluate more recent modeling approaches for and review secondary sources of data (e.g., ATSDR).
4) Evaluate the weight of evidence of environmental occurrence data and modeled estimates.
5) Continue to map or group each condition(s) of use to environmental assessment scenario(s).

#### 2.6.1.3 Occupational Exposures

EPA expects to consider and analyze both worker and occupational non-user exposures as follows:

1) Review reasonably available worker exposure monitoring data for specific condition(s) of use (i.e., personal and area samples from chlor-alkali industry, users of asbestos-containing sheet gaskets, OSHA, NIOSH and other data received by EPA and found in published literature).
    - Information provided during meetings with the chlor-alkali industry, written correspondence from the American Chemistry Council (ACC), site visits to chlor-alkali plants will be reviewed and used by EPA in exposure scenarios;
    - Information provided by chemical industry representatives along with an importer/supplier of asbestos-containing sheet gaskets who further fabricate the sheet gaskets for use in equipment for the manufacture of titanium dioxide will be used by EPA in exposure scenarios.
    - Identify additional information on imported asbestos brake blocks used in the oil industry to define exposure scenarios.
    - Received personal monitoring and area sampling from OSHA.
2) Review process information, including use of personal protective equipment and engineering controls, from the chlor-alkali industry and users of asbestos-containing sheet gaskets (an effort currently underway), to better characterize work practices and exposures in occupational settings.
    - Review information on PPE use received from chlor-alkali industry;
    - Review information on PPE use received from gasket fabricators
    - Obtain PPE and exposure data for workers from use of oil brake blocks.
3) For conditions of use where information is limited or not available, review existing exposure models that may be applicable.
    - Review 1988 Asbestos Ban and Phase Out (ABPO) rule support documents to inform approaches for workplace exposure modeling.
    - Evaluate current models and exposure assessment approaches for workplace air modeling (e.g., AERMOD, EFAST).
    - EPA is continuing to review the literature to identify exposure scenarios corresponding to some of the conditions of use, such as other gaskets and packing and woven products. EPA will continue to look for reasonably available information to understand those conditions of use which may inform exposure scenarios. EPA may also need to further research applicable models that may be used to estimate releases for certain conditions of use.
4) Incorporate applicable engineering controls and/or personal protective equipment into exposure scenarios, as appropriate.
5) Evaluate the weight of the evidence of occupational exposure data.

6) Use the Table provided in Appendix C, which maps and groups each condition of use to occupational exposure assessment scenario(s), to develop, adapt, or apply exposure models or empirical data to the risk evaluation.

#### 2.6.1.4 Consumer Exposures

As noted in Section 2.2, the consumer products being considered are imported asbestos-containing woven products and imported asbestos brakes/linings. EPA expects to consider and analyze both consumers using a consumer product and bystanders who are nearby as follows:

1) Define exposure scenarios for consumers by considering sources of exposure (consumer products), exposure pathways, exposure settings, exposure routes, and populations exposed. Considerations for constructing exposure scenarios for consumers include:
    - Given that the consumer exposure scenarios are limited to 2 categories of uses and that very little information has been identified to date on the extent of the uses, EPA will attempt to communicate with identified importers of asbestos-containing products (automotive brakes and woven products) to determine current status of import and use
    - Identify reasonably available data on consumer products or products available for consumer use including the content of asbestos in products
    - Identify information characterizing the use patterns of consumer products containing asbestos including how the product is used, the amount of product used, frequency and duration of use, and room of use
    - Identify the associated exposure setting and route of exposure for consumers
    - Review reasonably available population- or subpopulation-specific exposure factors and activity patterns to determine if potentially exposed or susceptible subpopulations need be further refined. Populations who may be exposed to products, including potentially exposed and susceptible subpopulations such as children or women of child bearing age, consumers and bystanders of uses of existing asbestos products including subsets of consumers who may use commercially available asbestos-containing products more frequently. For exposure pathways where data are not available, review existing indoor and outdoor exposure models that may be applicable in estimating exposure levels. Determine the applicability of the identified models for use in a quantitative exposure assessment.
2) Use the Table provided in Appendix C, which maps and groups each condition of use to consumer exposure assessment scenario(s), to develop, adapt, or apply exposure models or empirical data to the risk evaluation.
3) Evaluate the weight of evidence of consumer exposure data.

### 2.6.2 Hazards (Effects)

#### 2.6.2.1 Environmental Hazards

EPA expects to consider and analyze environmental hazards of asbestos as follows:

1) Review reasonably available environmental hazard data.
    - Environmental hazard studies were identified using the literature search strategies laid out in the "*Strategy for Conducting Literature Searches for Asbestos: Supplemental Document to the TSCA Scope Document (CASRN 1332-21-4)*". Section 2.4.1 provides a summary of the appropriate environmental hazard data.
    - As discussed in Section 2.5.3.1, only aquatic ecological receptors were identified as being evaluated further for this risk evaluation.
2) Conduct hazard identification (the qualitative process of identifying acute and chronic endpoints) and concentration-response assessment (the quantitative relationship between hazard and exposure) for all identified environmental hazard endpoints.
    - There are aquatic (aqueous-only) studies identified, which assess the aquatic hazard of chronic (13-86 days) exposure to chrysotile asbestos. The chronic hazard to fish and aquatic invertebrates exposed to asbestos is possible at concentrations ranging from $10^4$-$10^8$ fibers/L.
3) Derive aquatic concentrations of concern (COC) for acute and, where possible, chronic endpoints.

    The aquatic environmental hazard studies may be used to derive acute and chronic concentrations of concern (COC) for mortality, behavioral, developmental and reproductive or other endpoints determined to be detrimental to environmental populations. Depending on the robustness of the evaluated data for a particular organism (e.g. aquatic invertebrates), environmental hazard values (e.g. ECx/LCx/NOEC/LOEC, etc.) may be derived and used to further understand the hazard characteristics of asbestos to aquatic species.
4) Evaluate the weight-of-evidence of the environmental hazard data.
    - In the risk evaluation, each study will be evaluated based on its overall study confidence. An analysis of the acute and chronic toxicity values derived from the studies may then be used to determine a reliable range of acute and chronic toxicity thresholds to characterize the hazard of asbestos to environmental organisms. EPA expects to consider and evaluate the weight-of-evidence (WOE) of the aquatic (aqueous-only) environmental hazard data by comparing and contrasting different aquatic endpoints in the literature and U.S. EPA WOE guidance document (U.S. EPA, 2016d).
5) Consider the route(s) of exposure, available environmental monitoring data and available approaches to integrate exposure and hazard assessments.
    - The chronic hazard to fish and aquatic invertebrates exposed to asbestos is possible at concentrations ranging from $10^4$- $10^8$ fibers/L; which is equivalent to 0.01 to 100 MFL (million fibers/Liter). The Office of Water provided OPPT with surface water data and a preliminary review shows some samples in receiving waters have reported asbestos concentrations ranging from 1-14 MFL.

#### 2.6.2.2 Human Health Hazards

Given the well-established carcinogenicity of asbestos for lung cancer and mesothelioma, EPA decided to limit the scope of its systematic review to these two specific cancers with the goal of updating, or reaffirming, the existing cancer unit risk (U.S. EPA, 1988b).

EPA expects to consider and analyze human health hazards as follows:

1) Included human health studies will be reviewed using the evaluation strategies laid out in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018).
    - Studies will be evaluated using specific data evaluation criteria.
    - Study results will be extracted and presented in evidence tables by cancer endpoint.
2) Evaluate the weight of the scientific evidence of human health hazard data.
    - EPA will rely on the weight of the scientific evidence when evaluating and integrating human health hazard data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.
    - Assess dose-response information to refine quantitative unit risk for lung cancer and mesothelioma. Review the appropriate human data identified to update, or reaffirm, the 1988 quantitative estimate of the unit risk of asbestos-related lung cancer and mesothelioma by the inhalation route.
3) In evaluating reasonably available data, EPA will determine whether particular human receptor groups may have greater susceptibility to the chemical's hazard(s) than the general population.

### 2.6.3 Risk Characterization

Risk characterization is an integral component of the risk assessment process for both ecological and human health risks. EPA will derive the risk characterization in accordance with EPA's *Risk Characterization Handbook* (U.S. EPA, 2000). As defined in EPA's Risk Characterization Policy, "the risk characterization integrates information from the preceding components of the risk evaluation and synthesizes an overall conclusion about risk that is complete, informative and useful for decision makers." Risk characterization is considered to be a conscious and deliberate process to bring all important considerations about risk, not only the likelihood of the risk but also the strengths and limitations of the assessment, and a description of how others have assessed the risk into an integrated picture.

Risk characterization at EPA assumes different levels of complexity depending on the nature of the risk assessment being characterized. The level of information contained in each risk characterization varies according to the type of assessment for which the characterization is written. Regardless of the level of complexity or information, the risk characterization for TSCA risk evaluations will be prepared in a manner that is transparent, clear, consistent, and reasonable (TCCR) (U.S. EPA, 2000). EPA will also present information in this section consistent with approaches described in the Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act (82 FR 33726). For instance, in the risk characterization summary, EPA will further carry out the obligations under TSCA section 26; for example, by identifying and assessing uncertainty and variability in each step of the risk evaluation, discussing considerations of data quality such as the reliability, relevance and whether the methods utilized were reasonable and consistent, explaining any assumptions used, and discussing information generated from independent peer review. EPA will also be guided by EPA's Information Quality Guidelines (U.S. EPA, 2002) as it provides guidance for presenting risk information. Consistent with those guidelines, in the risk characterization, EPA will also identify: (1) Each population addressed by an estimate of applicable risk effects; (2) the expected risk or central estimate of risk for the potentially exposed or susceptible subpopulations affected; (3) each appropriate upper-bound or lower bound estimate of risk; (4) each significant uncertainty identified in the process of the assessment of risk effects and the studies that would assist in resolving the uncertainty; and (5) peer reviewed studies known to the

Agency that support, are directly relevant to, or fail to support any estimate of risk effects and the methodology used to reconcile inconsistencies in the scientific information.

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# APPENDICES

# Appendix A REGULATORY HISTORY

## A-1 Federal Laws and Regulations

The federal laws and regulations applicable to asbestos are listed along with the regulating agencies below. States also regulate asbestos through state laws and regulations, which are also listed within this section.

**Toxics Substances Control Act (TSCA), 1976**
15 U.S.C. §2601 et seq
The Toxic Substances Control Act of 1976 provides EPA with authority to require reporting, record-keeping and testing requirements, and restrictions relating to chemical substances and/or mixtures. Certain substances are generally excluded from TSCA, including, among others, food, drugs, cosmetics and pesticides.

TSCA addresses the production, importation, use and disposal of specific chemicals including polychlorinated biphenyls (PCBs), asbestos, radon and lead-based paint. The Frank R. Lautenberg Chemical Safety for the 21st Century Act updated TSCA in 2016 https://www.epa.gov/laws-regulations/summary-toxic-substances-control-act.

**Asbestos Hazard Emergency Response Act (AHERA), 1986**
TSCA Subchapter II: Asbestos Hazard Emergency Response 15 U.S.C. §2641-2656

- Defines asbestos as the asbestiform varieties of— chrysotile (serpentine), crocidolite (riebeckite), amosite (cummingtonite-grunerite), anthophyllite, tremolite or actinolite.
- Requires local education agencies (i.e., school districts) to inspect school buildings for asbestos and submit asbestos management plans to appropriate state; management plans must be publicly available and inspectors must be trained and accredited.
- Tasked EPA to develop an asbestos Model Accreditation Plan (MAP) for states to establish training requirements for asbestos professionals who do work in school buildings and also public and commercial buildings.

**Asbestos-Containing Materials in Schools Rule (per AHERA), 1987**
40 CFR Part 763, Subpart E

- Requires local education agencies to use trained and accredited asbestos professionals to identify and manage asbestos-containing building material and perform asbestos response actions (abatements) in school buildings.

**1989 Asbestos: Manufacture, Importation, Processing, and Distribution in Commerce Prohibitions; Final Rule** (also known as Asbestos Ban and Phase-out Rule (Remanded), 1989)
40 CFR Part 763, Subpart I
Docket ID: OPTS-62048E; FRL-3269-8

- EPA issued a final rule under Section 6 of Toxic Substances Control Act (TSCA) banning most asbestos-containing products.
- In 1991, this rule was vacated and remanded by the Fifth Circuit Court of Appeals. As a result, most of the original ban on the manufacture, importation, processing or distribution in commerce for the majority of the asbestos-containing products originally covered in the 1989

final rule was overturned. The following products remain banned by rule under the Toxic Substances Control Act (TSCA):

- Corrugated paper
- Rollboard
- Commercial paper
- Specialty paper
- Flooring felt

In addition, the regulation continues to ban the use of asbestos in products that have not historically contained asbestos, otherwise referred to as "new uses" of asbestos (Defined by 40 CFR 763.163 as "commercial uses of asbestos not identified in §763.165 the manufacture, importation or processing of which would be initiated for the first time after August 25, 1989.").

**Other EPA Regulations:**

*Asbestos Worker Protection Rule, 2000*
40 CFR Part 763, Subpart G

- Extends OSHA standards to public employees in states that do not have an OSHA approved worker protection plan (about half the country).

*Asbestos Information Act, 1988*
15 U.S.C. §2607(f)

- Helped to provide transparency and identify the companies making certain types of asbestos-containing products by requiring manufacturers to report production to the EPA.

*Asbestos School Hazard Abatement Act (ASHAA)*, 1984 and *Asbestos School Hazard Abatement Reauthorization Act (ASHARA)*, 1990
20 U.S.C. 4011 et seq. and Docket ID: OPTS-62048E; FRL-3269-8

- Provided funding for and established an asbestos abatement loan and grant program for school districts and ASHARA further tasked EPA to update the MAP asbestos worker training requirements.

*Emergency Planning and Community Right-to-Know Act (EPCRA)*, 1986
42 U.S.C. Chapter 116

- Under Section 313, Toxics Release Inventory (TRI), requires reporting of environmental releases of friable asbestos at a concentration level of 0.1%.
- Friable asbestos is designated as a hazardous substance subject to an Emergency Release Notification at 40 CFR §355.40 with a reportable quantity of 1 pound.

*Clean Air Act*, 1970
42 U.S.C. §7401 et seq.

- Asbestos is identified as a Hazardous Air Pollutant.

*Asbestos National Emission Standard for Hazardous Air Pollutants (NESHAP)*, 1973
40 CFR Part 61, Subpart M of the Clean Air Act

- Specifies demolition and renovation work practices involving asbestos in buildings and other facilities (but excluding residences with 4 or fewer dwelling units single family homes).
- Requires building owner/operator notify appropriate state agency of potential asbestos hazard prior to demolition/renovation.

- Banned spray-applied surfacing asbestos-containing material for fireproofing/insulating purposes in certain applications.
- Requires that asbestos-containing waste material from regulated activities be sealed in a leak-tight container while wet, labeled, and disposed of properly in a landfill qualified to receive asbestos waste.

*Clean Water Act (CWA)*, 1972
33 U.S.C. §1251 et seq
- Toxic pollutant subject to effluent limitations per Section 1317.

*Safe Drinking Water Act (SDWA)*, 1974
42 U.S.C. §300f
- Asbestos Maximum Contaminant Level Goals (MCLG) 7 million fibers/L (longer than 10um).

*Resource Conservation and Recovery Act (RCRA)*, 1976
42 U.S.C. §6901 et seq.
40 CFR 239-282
- Asbestos is subject to solid waste regulation when discarded; NOT considered a hazardous waste.

*Comprehensive Environmental Response, Compensation and Liability Act (CERCLA)*, 1980
42 U.S.C. §9601 et seq.
40 CFR Part 302.4 - Designation of Hazardous Substances and Reportable Quantities
- 13 Superfund sites containing asbestos, nine of which are on the National Priorities List (NPL)
- Reportable quantity of friable asbestos is one pound.

**Other Federal Agencies:**
Occupational Safety and Health Administration (OSHA):
Public Law 91-596 Occupational Safety and Health Act, 1970
Employee permissible exposure limit (PEL) is 0.1 fibers per cubic centimeter (f/cc) as an 8-hour, time-weighted average (TWA) and/or the excursion limit (1.0 f/cc as a 30-minute TWA).
- Asbestos General Standard 29 CFR 1910
- Asbestos Shipyard Standard 29 CFR 1915
- Asbestos Construction Standard 29 CFR 1926

Consumer Product Safety Commission (CPSC): Banned several consumer products. Federal Hazardous Substances Act (FHSA) 16 CFR 1500
Food and Drug Administration (FDA): Prohibits the use of asbestos-containing filters in pharmaceutical manufacturing, processing and packing. 21 CFR 211.72

Mine Safety and Health Administration (MSHA): follows OSHA's safety standards.
Surface Mines 30 CFR part 56, subpart D
Underground Mines 30 CFR part 57, subpart D

Department of Transportation

Prescribes the requirements for shipping manifests and transport vehicle placarding applicable to asbestos 40 CFR part 172.

Non-regulatory information of note:

- NIOSH conducts related research and monitors asbestos exposure through workplace activities in an effort to reduce illness and ensure worker health and safety.

## A-2 State Laws and Regulations

Pursuant to AHERA, states have adopted through state regulation the EPA's Model Accreditation Plan (MAP) for asbestos abatement professionals who do work in schools and public and commercial buildings. . Thirty-nine (39) states[6] have EPA-approved MAP programs and twelve (12) states[7] have also applied to and received a waiver from EPA to oversee implementation of the Asbestos-Containing Materials in Schools Rule pursuant to AHERA. States also implement regulations pursuant to the Asbestos NESHAP regulations or further delegate those oversight responsibilities to local municipal governments. While federal regulations set national asbestos safety standards, states have the authority to impose stricter regulations. As an example, many states extend asbestos federal regulations – such as asbestos remediation by trained and accredited professionals, demolition notification, and asbestos disposal – to ensure safety in single-family homes. Thirty (30) states[8] require firms hired to abate asbestos in single family homes to be licensed by the state. Nine (9) states[9] mandate a combination of notifications to the state, asbestos inspections, or proper removal of asbestos in single family homes. Some states have regulations completely independent of the federal regulations. For example, California and Washington regulate products containing asbestos. Both prohibit use of more than 0.1% of asbestos in brake pads and require laboratory testing and labeling.

Below is a list of state regulations that are independent of the federal AHERA and NESHAP requirements that states implement. This may not be an exhaustive list.

**California**

Asbestos is listed on California's Candidate Chemical List as a carcinogen. Under California's Propositions 65, businesses are required to warn Californians of the presence and danger of asbestos in products, home, workplace and environment.

***California Brake Friction Material Requirements (Effective 2017)***

*Division 4.5, California Code of Regulations, Title 22 Chapter 30*

Sale of any motor vehicle brake friction materials containing more than 0.1% asbestiform fibers by weight is prohibited. All brake pads for sale in the state of California must be laboratory tested, certified and labeled by the manufacturer.

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[6] Alabama, Alaska, Arkansas, California, Colorado, Connecticut, Delaware, Florida, Illinois, Indiana, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Montana, Nebraska, New Hampshire, New Jersey, New York, North Carolina, North Dakota, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, South Dakota, Texas, Utah, Vermont, Virginia, Washington, West Virginia, and Wisconsin.

[7] Connecticut, Colorado, Illinois, Kentucky, Louisiana, Massachusetts, Maine, New Hampshire, Oklahoma, Rhode Island, Texas, and Utah.

[8] California, Colorado, Connecticut, Delaware, Florida, Georgia, Hawaii, Iowa, Kansas, Maine, Maryland, Massachusetts, Michigan, Minnesota, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, North Dakota, Oregon, Pennsylvania, Utah, Vermont, Virginia, Washington, West Virginia, and Wisconsin.

[9] Colorado, Connecticut, Georgia, Maine, Massachusetts, New York, Oregon, Vermont, and West Virginia.

**Massachusetts**
*Massachusetts Toxics Use Reduction Act (TURA)*
Requires companies in Massachusetts to provide annual pollution reports and to evaluate and implement pollution prevention plans. Asbestos is included on the Complete List of TURA Chemicals - March 2016.

**Minnesota**
*Toxic Free Kids Act Minn. Stat. 2010 116.9401 – 116.9407*
Asbestos is included on the 2016 Minnesota Chemicals of High Concern List as a known carcinogen.

**New Jersey**
New Jersey *Right to Know Hazardous Substances*
The state of New Jersey identifies hazardous chemicals and products. Asbestos is listed as a known carcinogen and talc containing asbestos is identified on the Right to Know Hazardous Substances list.

**Rhode Island**
*Rhode Island Air Resources – Air Toxics Air Pollution Control Regulation No. 22*
Establishes acceptable ambient air levels for asbestos.

**Washington**
***Better Brakes Law (Effective 2015)*** *Chapter 70.285 RCW Brake Friction Material*
Prohibits the sale of brake pads containing more than 0.1% asbestiform fibers (by weight) in the state of Washington and requires manufacturer certification and package/product labelling.
*Requirement to Label Building Materials that Contain Asbestos Chapter 70.310 RCW*
Building materials that contain asbestos must be clearly labeled as such by manufacturers, wholesalers, and distributors.

## A-3 International Laws and Regulations

Asbestos is also regulated internationally. Nearly 60 nations have some sort of asbestos ban. The European Union (EU) will prohibit the use of asbestos in the chlor-alkali industry by 2025 (Regulation (EC) No 1907/2006 of the European Parliament and of the Council, 18 December 2006).

Canada has proposed a rule to ban asbestos and regulate asbestos-containing products (Prohibition of Asbestos and Asbestos Products Regulations).

In addition, the Rotterdam Convention is considering adding chrysotile to Annex III, and the World Health Organization (WHO) has a global campaign to eliminate asbestos-related diseases (WHO Resolution 60.26).

# Appendix B PROCESS, RELEASE AND OCCUPATIONAL EXPOSURE INFORMATION

This appendix provides information and data found in preliminary data gathering for asbestos.

## B-1 Process Information

Process-related information potentially relevant to the risk evaluation may include process diagrams, descriptions and equipment. Such information may inform potential release sources and worker exposure activities for consideration.

### B-1-1 Manufacture and Import

#### B-1-1-1 Manufacturing

As a naturally occurring mineral, asbestos is manufactured by mining, but asbestos has not been mined (or manufactured) in the United States since 2002 (USGS, 2016).

#### B-1-1-2 Import

All asbestos used in this country is imported. According to the U.S. Geological Survey (USGS), the only form of asbestos currently imported into the United States is chrysotile, all of which originated from Brazil in 2017 (USGS, 2018). USGS reports that in 2017, the United States imported approximately 300 metric tons of raw asbestos, the total of which they state is used in the chlor-alkali industry (USGS, 2018). In 2016, the United States imported approximately 702 metric tons of raw asbestos (USGS, 2017). According to chlor-alkali industry information, chrysotile asbestos used in the fabrication of diaphragms is imported in sealed containers, with the asbestos in 40-50 kg sealed bags made of dust-proof, woven plastic. Typically, they indicated that 20 bags are placed on a pallet at the point of shipment and the pallet is covered completely by a heavyweight wrap – durable and similar in thickness to a drum liner. The pallets are placed in a shipping container, which gets sealed with a heavy-duty bolt-type seal. At the port of entry, the shipping container is marked and transported to a chlor-alkali facility where the pallets and bags are removed.

### B-1-2 Processing

#### B-1-2-1 Chlor-Alkali Industry

Asbestos (raw chrysotile) is used in the chlor-alkali industry for the fabrication of semi-permeable diaphragms, which effectively separate the anode from the cathode chemicals in the production of chorine and sodium hydroxide (caustic soda) (USGS, 2017). The information in this section was described by industry representatives to EPA in a January 2017 meeting, provided to EPA by the American Chemistry Council (ACC) in written communication, or observed during March 2017 EPA visits to chlor-alkali plants. The information provided below is primarily based on information provided by either the chlor-alkali industry or ACC and is meant to represent typical practices.

Chlor-alkali industry representatives have stated that in the United States, there are three companies who own a total of 15 chlor-alkali plants that continue to fabricate and use asbestos-containing semi-permeable diaphragms onsite. From its entry into a port in the United States to its ultimate disposal, the management of asbestos in the chlor-alkali industry is typically managed in a closely controlled process. The ACC reports that engineering controls, personal protective equipment (PPE), employee training, medical surveillance and personal monitoring are all used to monitor and mitigate worker exposures.

After arriving at the plant, the shipping container is inspected and damaged containers are rejected. According to industry, where containers are damaged, port/warehouse remediation activities are managed in conformance with OSHA's asbestos standard for general industry (29 CFR 1910.1001). Once the container is opened, the bags are inspected. If broken bags or loose asbestos is evident, the area is controlled to prevent accidental exposure, the bags are repaired, and the area is barricaded and treated as an area requiring cleanup. Plastic-wrapped pallets are labeled per OSHA's hazard communication and asbestos standards. Any loose asbestos from punctured bags inside the container is cleaned up using high-efficiency particulate air-filtered (HEPA-filtered) vacuum cleaners or wetted with water and cleaned up before unloading proceeds. Damaged bags are placed in appropriately labeled, heavy-duty plastic bags or appropriately repaired. Individuals not involved in cleanup are prohibited from entering the area until cleanup is complete. When moving the asbestos bags into storage locations, care is taken to ensure that bags are not punctured, and personnel moving the bags wear specific PPE, including respirators and protective clothing. Storage areas are isolated, enclosed and labeled. They are secure and inspected on a regular basis. Any area or surface with evidence of asbestos is HEPA-vacuumed or wetted and cleaned up by employees wearing PPE.

To create these asbestos-containing diaphragm cells, sealed bags of asbestos are placed inside a glove box (at some plants) before being opened. They are then opened and the asbestos is transferred to a mixing tank via a closed system maintained under vacuum. At other plants, this process is fully automated and enclosed; where asbestos bags are placed into a machine, opened and transferred to mixing tanks. Empty bags are placed into closed and labeled waste containers, either through a port in the glove box or during the automated process. The raw asbestos used to create a diaphragm is mixed with a liquid solution of weak caustic soda and salt. A resultant chrysotile asbestos slurry is created and asbestos is no longer likely to become airborne. Modifiers (e.g., Halar®, Teflon®) are added to the slurry and then co-deposited in the diaphragm and heated. The modifiers fuse to the asbestos. The amount of asbestos used for each are added to the slurry, which is then co-deposited in the diaphragm and heated. The modifiers fuse to the asbestos. The amount of asbestos used for each diaphragm is in the range of 50-250 lbs (depending on cell size) and a typical plant will use about 5-25 tons of raw asbestos per year. Industry representatives stated during meetings with EPA that a standard-sized manufacturing cell will have a surface area of 70 $m^2$ and each cell will typically have 20 chrysotile asbestos diaphragms within it, although cell size can vary.

The chlor-alkali chemical production process involves the separation of the sodium and chloride atoms of salt in saltwater (brine) via electricity to produce sodium hydroxide (caustic soda), hydrogen and chlorine. Specifically, brine is passed through an electric current and sodium hydroxide, hydrogen and chlorine are formed. This reaction occurs in an electrolytic cell. The cell contains two compartments separated by a semi-permeable diaphragm, which is made mostly of chrysotile asbestos. The diaphragm prevents the reaction of the caustic soda with the chlorine and allows for the separation of both materials for further processing.

The cell will typically operate for 1-3 years before it must be replaced due to a loss of conductivity. Many factors can determine the life of a cell, including the brine quality and the size of the cell. In plants where the diaphragm is replaced but the cell is reused, the asbestos is hydro-blasted out (remaining in a wet state) in a cleaning bay. The excess water used during this process is filtered prior to discharge to the facility's wastewater collection and treatment system. The filtered waste is to be sealed into containers that are sent to a landfill that accepts asbestos-containing waste per federal and state asbestos disposal regulations.

### B-1-3 Uses

#### B-1-3-1 Oil Industry

At least one company in the United States sells asbestos-containing brake blocks in the oil industry. The brake of a drawworks hoisting machine is an essential component of a rotary drilling rig, as the machine is used to hoist or lower thousands of pounds of weight in large operations. At least one U.S. company imports and distributes non-metallic, asbestos-woven brake blocks used in the drawworks of drilling rigs. According to product specification sheets, asbestos-containing brake blocks are most often used on large drilling drawworks and contain wire in the backing only for added strength, and they are more resistant than full-metallic blocks, with good flexibility and a favorable coefficient of friction block. The asbestos allows for heat dissipation and the woven structure provides firmness and controlled density of the brake block. Workers in the oilfield industry operate a drilling rig's brakes in an outdoor environment, and must periodically replace spent brake blocks.

#### B-1-3-2 Use of Sheet Gaskets in Titanium Dioxide Production

In the *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: Asbestos* public document [Docket: EPA-HQ-OPPT-2016-0736; (U.S. EPA, 2017b)], Table 1 depicts a "List of Asbestos-Containing Products Currently Available for Purchase on the internet." On page 11 of the preliminary information document, EPA lists useful types of information. During the public comment period, one chemical production company notified EPA of the current use of imported gaskets from China (Comment ID EPA-HQ-OPPT-2016-0736-0067). According to the comment, these sheet gaskets are composed of 80% (minimum) chrysotile asbestos, fully encapsulated in Styrene Butadiene Rubber, and used to create tight chemical containment seals during the production of titanium dioxide. EPA learned through stakeholder meetings that these sheet gaskets are imported, processed, then distributed in the United States.

#### B-1-3-3 Commercial Uses

Chrysotile asbestos has several unique properties, including low electrical conductivity, high tensile strength, high friction coefficient and high heat resistance (Virta, 2011). These properties make asbestos ideal for use in friction materials (brakes), insulation (sound, heat and electrical) and building materials (cement pipes, roofing compounds, adhesives, flooring) over the past century. However, due to health concerns and consumer preference, most products used commercially in the United States are now asbestos-free. Although most domestically manufactured products are asbestos-free, it is possible that imported asbestos-containing products could go into aftermarket sales and be used commercially (e.g., a mechanic installing new brakes or construction worker installing cement pipes). Most available products used commercially contain non-friable asbestos but can become friable during processing and use.

#### B-1-3-4 Consumer Uses

Remaining asbestos-containing products available for consumer use in the United States include a limited number of imported woven products and imported aftermarket friction products (USGS, 2017). These same products could also be used commercially. EPA staff conducted an online search using various search terms to determine any currently available asbestos-containing products in the United States. The products found were either advertised as containing asbestos or the associated Safety Data Sheet (SDS) listed asbestos as a product constituent. Additionally, the EPA reviewed databases (EPA CPCat, U.S. Department of Health and Human Services [DHHS] Household Products Database and

DeLima Associates Consumer Product Information Database [CPID]) that list manufacturers/distributers/retailers of asbestos-containing products. Some companies found are no longer in business or have been rebranded and absorbed by another company. In researching these companies' products and their SDSs, EPA found little evidence of continued asbestos use. Consumer activities using these products would likely be limited to small-scale do-it-yourself projects.

### B-1-4 Disposal

Asbestos NESHAP minimizes asbestos release during renovation/demolition by requiring NESHAP-regulated asbestos-containing waste material be sealed in a leak-tight container while wet, labeled and disposed of properly in a landfill qualified to receive asbestos waste.

https://www.epa.gov/asbestos/asbestos-national-emissions-standard-hazardous-air-pollutants-neshap#was.

Transport and Disposal of Asbestos Waste (Appendix D to Subpart E of 40 CFR Part 763)

Landfills have special requirements for handling and securing the asbestos-containing waste regulated under NESHAP to prevent releases of asbestos into the air. Transportation vehicles that move the waste from the point of generation to the asbestos landfill have special labeling requirements and waste shipment recordkeeping requirements(U.S. EPA, 2016a)(U.S. EPA, 2016a)(U.S. EPA, 2016a). Specific waste management practices are controlled at the state level.

## B-2 Occupational Exposure Data

Data that inform occupational exposure assessment and which EPA expects to consider as part of the occupational exposure assessment are the Occupational Safety and Health Administration (OSHA) Chemical Exposure Health Data (CEHD), which are monitoring data collected during OSHA inspections. According to OSHA asbestos standards, the employee permissible exposure limit (PEL) is 0.1 fibers per cubic centimeter (f/cc) as an 8-hour, time-weighted average (TWA) and/or the excursion limit (1.0 f/cc as a 30-minute TWA) (Asbestos General Standard 29 CFR 1910).

A preliminary summary of OSHA's monitoring data from 2011 to 2016 is presented in Table_Apx B-1. These data represent actual exposure levels of asbestos at specific workplaces encompassing several industry sectors and conditions of use.

**Table_Apx B-1. Summary of Industry Sectors with Asbestos Personal Monitoring Air Samples Obtained from OSHA Inspections Conducted Between 2011 and 2016**

| North American Industrial Classification System (NAICS) | NAICS Description |
|---|---|
| 22 | Utilities |
| 23 | Construction |
| 31 | Manufacturing |
| 32 | Manufacturing |
| 33 | Manufacturing |
| 42 | Wholesale trade |

| North American Industrial Classification System (NAICS) | NAICS Description |
|---|---|
| 44 | Retail trade |
| 45 | Retail trade |
| 48 | Transportation and warehousing |
| 49 | Transportation and warehousing |
| 52 | Finance and insurance |
| 53 | Real estate rental and leasing |
| 54 | Professional, scientific and technical services |
| 56 | Administrative and support and waste management and remediation services |
| 61 | Educational services |
| 62 | Health care and social assistance |
| 71 | Arts, entertainment and recreation |
| 72 | Accommodation and food services |
| 92 | Public administration |

# Appendix C SUPPORTING TABLE FOR INDUSTRIAL, COMMERCIAL AND CONSUMER ACTIVITIES AND USES FOR CONCEPTUAL MODELS

This appendix provides the rationale for inclusion and exclusion of exposure pathways for industrial, commercial and consumer activities.

**Table_Appendix C-1. Preliminary Rationale for Inclusion and Exclusion of Exposure Pathways for Industrial, Commercial and Consumer Activities**

| Product Category (or Category) | Use Example (or Subcategory) | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population[1] | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|
| Asbestos Diaphragms | Chlor-alkali Industry | Manufacture of Asbestos Diaphragms | Air | Inhalation | Workers, ONU | Yes | This is the only known use of imported raw asbestos in the U.S. today, and inhalation is the most important exposure route. |
| | | | | Oral | Workers, ONU | No | Since neither oral nor dermal exposures are expected to contribute to the risks of lung cancer and mesothelioma, which are the focus of the risk evaluation, exposures from the oral and dermal routes will not be assessed. |
| | | | | Dermal | | | |
| | | | Solid Contact | Dermal | Workers | | |
| | | Chlor-Alkali Industry Use of Asbestos Diaphragms | Air | Inhalation | Workers, ONU | Yes | This is the only known use of imported raw asbestos in the U.S. today; inhalation exposure will be evaluated. |
| | | | | Oral | Workers, ONU | No | Since neither oral nor dermal exposures are expected to contribute to the risks of lung cancer and mesothelioma, which are the focus of the risk evaluation, exposures from the oral and dermal routes will not be assessed. |
| | | | | Dermal | | | |
| | | | Solid Contact | Dermal | Workers | | |
| Sheet Gaskets | Chemical Manufacturing | Processing/Cutting Sheet Gaskets | Air | Inhalation | Workers, ONU | Yes | Asbestos-containing sheet gaskets are cut/processed; inhalation – will be further evaluated. |
| | | | | Oral | Workers, ONU | No | Since neither oral nor dermal exposures are expected to contribute to the risks of |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | Dermal | | | lung cancer and mesothelioma, which are the focus of the risk evaluation, exposures from the oral and dermal routes will not be assessed. |
| | | Installing and Replacing Sheet Gaskets | Air | Inhalation | Workers, ONU | Yes | The work process described in Comment ID EPA-HQ-OPPT-2016-0736-0067 should be further evaluated. |
| | | | | Oral | Workers, ONU | No | Since neither oral nor dermal exposures are expected to contribute to the risks of lung cancer and mesothelioma, which are the focus of the risk evaluation, exposures from the oral and dermal routes will not be assessed |
| | | | | Dermal | | | |
| | | | Solid Contact | Dermal | Workers | | |
| Industrial Friction Products | Brake Blocks in Oil Industry | Oilfield Well Production | Air | Inhalation | Workers, ONU | Yes | The process of replacing asbestos-containing brake blocks will likely generate friable airborne asbestos and will be further evaluated. |
| | | | | Oral | Workers, ONU | No | Since neither oral nor dermal exposures are expected to contribute to the risks of lung cancer and mesothelioma, which are the focus of the risk evaluation, exposures from the oral and dermal routes will not be assessed. |
| | | | | Dermal | | | |
| | | | Solid Contact | Dermal | Workers | | |
| Aftermarket Automotive Brakes | Passenger and Non-passenger Vehicles | Commercial Brake Servicing and Consumer | Air | Inhalation | Workers, ONU, Consumer | Yes | The process of replacing asbestos-containing brakes will likely generate friable airborne asbestos and will be further evaluated. |
| | | | | Oral | Workers, ONU, Consumer | No | Since neither oral nor dermal exposures are expected to contribute to the risks of lung cancer and mesothelioma, which are the focus of the risk evaluation, exposures from the oral and dermal routes will not be assessed. |
| | | | | Dermal | | | |
| | | | Solid Contact | Dermal | Workers | | |
| Cement Products | Cement pipe | Contracting and Masonry Work | Air | Inhalation | Workers, ONU | Yes | Based on data from USGS, it is possible that asbestos cement pipe is imported and used in the United States. Exposures to workers will be evaluated. |
| | | | | Oral | Workers, ONU | No | Since neither oral nor dermal exposures are expected to contribute to the risks of lung cancer and mesothelioma, which are the focus of the risk evaluation, exposures |
| | | | | Dermal | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | Solid Contact | Dermal | Workers | | from the oral and dermal routes will not be assessed. |
| Woven Products | Imported Textiles | Use of Heat-Resistant Woven Textiles | Air | Inhalation | Workers, ONU, Consumer | Yes | Based on conversations with USGS, knitted fabrics (woven products) containing asbestos continue to be imported into U.S. |
| | | | | Oral | Workers, ONU, Consumer | No | Since neither oral nor dermal exposures are expected to contribute to the risks of lung cancer and mesothelioma, which are the focus of the risk evaluation, exposures from the oral and dermal routes will not be assessed. |
| | | | | Dermal | | | |
| | | | Solid Contact | Dermal | Workers | | |
| Other gaskets and packing | Chemical Manufacturing | Installing and Replacing Gaskets | Air | Inhalation | Workers, ONU | Yes | The work process described in Comment ID EPA-HQ-OPPT-2016-0736-0067 will be further evaluated. |
| | | | | Oral | | No | Since neither oral nor dermal exposures are expected to contribute to the risks of lung cancer and mesothelioma, which are the focus of the risk evaluation, exposures from the oral and dermal routes will not be assessed. |
| | | | | Dermal | | | |
| | | | Solid Contact | Dermal | Workers | | |
| Waste Handling, Treatment and Disposal | Disposal of Asbestos Waste | Worker Handling of Wastes | Air | Inhalation | Workers, ONU | Yes | Disposal of asbestos containing articles/wastes are placed in plastic bags for disposal. |
| | | | Air | Oral | | No | Since neither oral nor dermal exposures are expected to contribute to the risks of lung cancer and mesothelioma, which are the focus of the risk evaluation, exposures from the oral and dermal routes will not be assessed. |
| | | | Air | Dermal | | | |
| | | | Solid Contact | Dermal | Workers | | |
| | | | Liquid Contact | Dermal | | | |

# Appendix D INCLUSION AND EXCLUSION CRITERIA FOR FULL TEXT SCREENING

Appendix D contains the eligibility criteria for various data streams informing the TSCA risk evaluation: environmental fate; engineering and occupational exposure; exposure to the general population and consumers; and human health hazard. The criteria are applied to the *on-topic* references that were identified following title and abstract screening of the comprehensive search results published on June 22, 2017.

Systematic reviews typically describe the study eligibility criteria in the form of PECO statements or a modified framework. PECO stands for Population, Exposure, Comparator and Outcome and the approach is used to formulate explicit and detailed criteria about those characteristics in the publication that should be present in order to be eligible for inclusion in the review. EPA/OPPT adopted the PECO approach to guide the inclusion/exclusion decisions during full text screening.

Inclusion and exclusion criteria were also used during the title and abstract screening, and documentation about the criteria can be found in the *Strategy for Conducting Literature Searches* document published in June 2017 along with each of the TSCA Scope documents. The list of *on-topic* references resulting from the title and abstract screening is undergoing full text screening using the criteria in the PECO statements. The overall objective of the screening process is to select the most relevant and highest quality evidence for the TSCA risk evaluation. As a general rule, EPA is excluding non-English data/information sources and will translate on a case by case basis.

The inclusion and exclusion criteria for ecotoxicological data have been documented in the ECOTOX SOPs. The criteria can be found at https://cfpub.epa.gov/ecotox/help.cfm?helptabs=tab4) and in the *Strategy for Conducting Literature Searches* document published along with each of the TSCA Scope documents.

Since full text screening commenced right after the publication of the TSCA Scope document, the criteria were set to be broad to capture relevant information that would support the initial scope. Thus, the inclusion and exclusion criteria for full text screening do not reflect the refinements to the conceptual model and analysis plan resulting from problem formulation. As part of the iterative process, EPA is in the process of refining the results of the full text screening to incorporate the changes in information/data needs to support the revised scope.

These refinements will include changes to the inclusion and exclusion criteria discussed in this appendix to better reflect the revised scope of the risk evaluation and will likely reduce the number of data/information sources that will undergo evaluation.

## D-1 Inclusion Criteria for Data Sources Reporting Environmental Fate Data

EPA/OPPT developed a generic Pathways and Processes, Exposure, Setting or Scenario, and Outcomes (PESO) statement to guide the full text screening of environmental fate data sources. Subsequent versions of the PESO statement may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the inclusion criteria in the PESO statement are eligible for inclusion, considered for evaluation, and possibly included in the environmental

fate assessment. On the other hand, data sources are excluded if they do not meet the criteria in the PESO statement.

Assessors seek information on various chemical-specific fate endpoints and associated fate processes, environmental media and exposure pathways as part of the process of developing the environmental fate assessment (Table_Apx D-1. Inclusion Criteria for Data Sources Reporting Environmental Fate Data). The PESO statement and information in Table_Apx D-2. Fate Endpoints and Associated Processes, Media and Exposure Pathways Considered in the Development of the Environmental Fate Assessment) will be used when screening the fate data sources to ensure complete coverage of the processes, pathways and data relevant to the fate of the chemical substance of interest.

Since full text screening commenced right after the publication of the TSCA Scope document, the criteria for fate data were set to be broad to capture relevant information that would support the initial scope. Thus, the inclusion and exclusion criteria for full text screening do not reflect the refinements to the conceptual model and analysis plan resulting from problem formulation. As part of the iterative process, EPA is in the process of refining the results of the full text screening to incorporate the changes in information/data needs to support the revised scope.

**Table_Apx D-1. Inclusion Criteria for Data Sources Reporting Environmental Fate Data**

| PESO Element | Evidence |
|---|---|
| **P**athways and **P**rocesses | • Fate will use transport, partitioning and degradation behavior across media to inform exposure pathways in conceptual models<br>• Exposure pathways included in the conceptual models:<br>- Water<br>- Air<br>• Processes associated with the target exposure pathways |
| **E**xposure | • Exposures of aquatic organisms to Asbestos<br>• Consumer exposure pathways of humans to Asbestos<br><br>(Chemical-specific population[s] of interest may be determined by toxicologists or by EPA policy decisions) |
| **S**etting or **S**cenario | • All aquatic ecological exposure scenarios for releases of Asbestos to the natural or built environment.<br>• Consumer exposure scenarios of humans to Asbestos<br><br>(Chemical-specific scenarios will be determined in conjunction with toxicologists and exposure assessors or by EPA policy decisions) |

| PESO Element | Evidence |
|---|---|
| **O**utcomes | • Fate properties which allow assessments of exposure pathways:<br>o Partitioning within and between environmental media (see Pathways) |

**Table_Apx D-2. Fate Endpoints and Associated Processes, Media and Exposure Pathways Considered in the Development of the Environmental Fate Assessment**

| Fate Data Endpoint | Associated Process(es) | Associated Media/Exposure Pathways | | | | |
|---|---|---|---|---|---|---|
| | | Surface water | Soil, Biosolids | Ground-water | Air | [Indoor environment, anthropogenic materials] |
| **First Tier Environmental Fate Data** | | | | | | |
| Particle Transport | Mobility | X | | | X | X |
| Suspension/Resuspension | Suspension/Resuspension, Mobility | X | | | | |
| Water and wastewater treatment removal | Wastewater treatment | X | | | | |

## D-2 Inclusion Criteria for Data Sources Reporting Engineering and Occupational Exposure Data

EPA/OPPT developed a generic RESO statement to guide the full text screening of engineering and occupational exposure literature (Table_Apx D-3. Inclusion Criteria for Data Sources Reporting Engineering and Occupational Exposure Data for Asbestos). RESO stands for Receptors, Exposure, Setting or Scenario, and Outcomes. Subsequent versions of the RESO statement may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the inclusion criteria specified in the RESO statement will be eligible for inclusion, considered for evaluation, and possibly included in the environmental release and occupational exposure assessments, while those that do not meet these criteria will be excluded.

The RESO statement should be used along with the engineering and occupational exposure data needs table (**Error! Reference source not found.**) when screening the literature.

Since full text screening commenced right after the publication of the TSCA Scope document, the criteria for engineering and occupational exposure data were set to be broad to capture relevant information that would support the initial scope. Thus, the inclusion and exclusion criteria for full text screening do not reflect the refinements to the conceptual model and analysis plan resulting from problem formulation. As part of the iterative process, EPA is in the process of refining the results of the full text screening to incorporate the changes in information/data needs to support the revised scope.

**Table_Apx D-3. Inclusion Criteria for Data Sources Reporting Engineering and Occupational Exposure Data for Asbestos**

| RESO Element | Evidence |
|---|---|
| **R**eceptors | • **Humans:**<br>Workers, including occupational non-users<br><br>• **Environment:**<br>Aquatic ecological receptors (release estimates input to Exposure)<br><br>Please refer to the conceptual models for more information about the ecological and human receptors included in the TSCA risk evaluation. |
| **E**xposure | • Worker exposure to and relevant environmental releases of asbestos<br>o Inhalation as indicated in the conceptual model<br>o Water and air indicated in the conceptual model<br><br>Please refer to the conceptual models for more information about the routes and media/pathways included in the TSCA risk evaluation. |
| **S**etting or **S**cenario | • Any occupational setting or scenario resulting in worker exposure and relevant environmental releases (includes all manufacturing, processing, use, disposal indicated in Table B-2 below except (state none excluded or list excluded uses) |
| **O**utcomes | • Quantitative estimates* of worker exposures and of relevant environmental releases from occupational settings<br>• General information and data related and relevant to the occupational estimates* |

* Metrics (e.g., mg/kg/day or mg/m$^3$ for worker exposures, kg/site/day for releases) are determined by toxicologists for worker exposures and by exposure assessors for releases; also, the Engineering Data Needs (Table_Apx D-4) provides a list of related and relevant general information.
TSCA=Toxic Substances Control Act

**Table_Apx D-4. Engineering, Environmental Release and Occupational Data Necessary to Develop the Environmental Release and Occupational Exposure Assessments**

| Objective Determined during Scoping | Type of Data |
|---|---|
| General Engineering Assessment (may apply for either or both Occupational Exposures and / or Environmental Releases) | 1. Description of the life cycle of the chemical(s) of interest, from manufacture to end-of-life (e.g., each manufacturing, processing, or use step), and material flow between the industrial and commercial life cycle stages. [Tags: Life cycle description, Life cycle diagram][a]<br>2. The total annual U.S. volume (lb/yr or kg/yr) of the chemical(s) of interest manufactured, imported, processed, and used; and the share of total annual manufacturing and import volume that is processed or used in each life cycle step. [Tags: Production volume, Import volume, Use volume, Percent PV] [a]<br>3. Description of processes, equipment, unit operations, and material flows and frequencies (lb/site-day or kg/site-day and days/yr; lb/site-batch and batches/yr) of the chemical(s) of interest during each industrial/ commercial life cycle step. Note: if available, include weight fractions of the chemicals (s) of interest and material flows of all associated primary chemicals (especially water). [Tags: Process description, Process material flow rate, Annual operating days, Annual batches, Weight fractions (for each of above, manufacture, import, processing, use)] [a]<br>4. Basic chemical properties relevant for assessing exposures and releases, e.g., molecular weight, normal boiling point, melting point, physical forms, and room temperature vapor pressure. [Tags: Molecular weight, Boiling point, Melting point, Physical form, Vapor pressure, Water solubility ] [a]<br>5. Number of sites that manufacture, process, or use the chemical(s) of interest for each industrial/ commercial life cycle step and site locations. [Tags: Numbers of sites (manufacture, import, processing, use), Site locations ] [a] |
| Occupational Exposures | 6. Description of worker activities with exposure potential during the manufacture, processing, or use of the chemical(s) of interest in each industrial/commercial life cycle stage. [Tags: Worker activities (manufacture, import, processing, use)] [a]<br>7. Potential routes of exposure (e.g., inhalation, dermal). [Tags: Routes of exposure (manufacture, import, processing, use)] [a]<br>8. Physical form of the chemical(s) of interest for each exposure route (e.g., liquid, vapor, mist) and activity. [Tags: Physical form during worker activities (manufacture, import, processing, use)] [a]<br>9. Breathing zone (personal sample) measurements of occupational exposures to the chemical(s) of interest, measured as time-weighted averages (TWAs), short-term exposures, or peak exposures in each occupational life cycle stage (or in a workplace scenario similar to an occupational life cycle stage). [Tags: PBZ measurements (manufacture, import, processing, use)] [a]<br>10. Area or stationary measurements of airborne concentrations of the chemical(s) of interest in each occupational setting and life cycle stage (or in a workplace scenario similar to the life cycle stage of interest). [Tags: Area measurements (manufacture, import, processing, use)] [a]<br>11. For solids, bulk and dust particle size characterization data. [Tags: PSD measurements (manufacture, import, processing, use)] [a]<br>12. Dermal exposure data. [Tags: Dermal measurements (manufacture, import, processing, use)]<br>13. Data needs associated with mathematical modeling (will be determined on a case-by-case basis). [Tags: Worker exposure modeling data needs (manufacture, import, processing, use)] [a]<br>14. Exposure duration (hr/day). [Tags: Worker exposure durations (manufacture, import, processing, use)] [a]<br>15. Exposure frequency (days/yr). [Tags: Worker exposure frequencies (manufacture, import, processing, use)] [a]<br>16. Number of workers who potentially handle or have exposure to the chemical(s) of interest in each occupational life cycle stage. [Tags: Numbers of workers exposed (manufacture, import, processing, use)] [a] |

| Objective Determined during Scoping | Type of Data |
|---|---|
| | 17. Personal protective equipment (PPE) types employed by the industries within scope. [Tags: Worker PPE (manufacture, import, processing, use)] [a]<br>18. Engineering controls employed to reduce occupational exposures in each occupational life cycle stage (or in a workplace scenario similar to the life cycle stage of interest), and associated data or estimates of exposure reductions. [Tags: Engineering controls (manufacture, import, processing, use), Engineering control effectiveness data] [a] |
| Environmental Releases | 19. Description of sources of potential environmental releases, including cleaning of residues from process equipment and transport containers, involved during the manufacture, processing, or use of the chemical(s) of interest in each life cycle stage. [Tags: Release sources (manufacture, import, processing, use)] [a]<br>20. Estimated mass (lb or kg) of the chemical(s) of interest released from industrial and commercial sites to each environmental medium (air, water, land) and treatment and disposal methods (POTW, incineration, landfill), including releases per site and aggregated over all sites (annual release rates, daily release rates) [Tags: Release rates (manufacture, import, processing, use)] [a]<br>21. Release or emission factors. [Tags: Emission factors (manufacture, import, processing, use)] [a]<br>22. Number of release days per year. [Tags: Release frequencies (manufacture, import, processing, use)] [a]<br>23. Data needs associated with mathematical modeling (will be determined on a case-by-case basis). [Tags: Release modeling data needs (manufacture, import, processing, use)] [a]<br>24. Waste treatment methods and pollution control devices employed by the industries within scope and associated data on release/emission reductions. [Tags: Treatment/ emission controls (manufacture, import, processing, use), Treatment/ emission controls removal/ effectiveness data] [a] |

**Notes:**

[a] These are the tags included in the full text screening form. The screener makes a selection from these specific tags, which describe more specific types of data or information.

**Abbreviations:**

hr=Hour
kg=Kilogram(s)
lb=Pound(s)
yr=Year
PV=Particle volume
PBZ= Personal Breathing Zone
POTW=Publicly owned treatment works
PPE=Personal projection equipment
PSD=Particle size distribution
TWA=Time-weighted average

## D-3 Inclusion Criteria for Data Sources Reporting Exposure Data on General Population, Consumers and Ecological Receptors

EPA/OPPT developed PECO statements to guide the full text screening of exposure data/information for human (i.e., general population, consumers, potentially exposure or susceptible subpopulations) and ecological receptors. Subsequent versions of the PECO statements may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the inclusion criteria in the PECO statement are eligible for inclusion, considered for evaluation, and possibly included in the exposure assessment. On the other hand, data sources are excluded if they do not meet the criteria in the PECO statement. The asbestos-specific PECO is provided in Table_Apx D-5.

Since full text screening commenced right after the publication of the TSCA Scope document, the criteria for exposure data were set to be broad to capture relevant information that would support the initial scope. Thus, the inclusion and exclusion criteria for full text screening do not reflect the refinements to the conceptual model and analysis plan resulting from problem formulation. As part of the iterative process, EPA is in the process of refining the results of the full text screening to incorporate the changes in information/data needs to support the revised scope.

**Asbestos Specific PECO Statement**

**Population:** Asbestos has been detected in indoor and outdoor air as well as in many different freshwater fishes and mussels from bodies of contaminated water. Potentially exposed populations include consumers and bystanders in the home using imported asbestos aftermarket brake pads and friction products (e.g., from do-it-yourself (DIY) replacement of asbestos aftermarket brake pads), and aquatic organisms which may become exposed from asbestos from surface water.

**Exposure:** Expected primary and lesser exposure sources, pathways, and routes are noted in the table below.

- The sources of asbestos are based on current marketed uses of asbestos only. The use profile of asbestos has changed. Currently asbestos can be found in only certain articles that are readily available for public purchase at common retailers. Asbestos is no longer mined in the U.S. and production of asbestos diaphragms are the only known importer of raw asbestos. Currently marketed articles include asbestos diaphragms, asbestos sheet gaskets, other gaskets (equipment seals), vehicle friction products (non-passenger vehicles), brake blocks for oil drilling, imported asbestos cement products and automotive brakes/linings. Legacy uses and associated/legacy disposals will be excluded from the scope of the risk evaluation. These include asbestos-containing materials remaining in older buildings or parts of older products for which manufacture, processing and distribution in commerce are not currently intended, known or reasonably foreseen.

The pathways of asbestos are based on detection of possible presence in certain environmental and biological media. Human-health-specific pathways include direct inhalation with articles containing asbestos only.

The route of asbestos exposure for humans is inhalation exposure for only currently marketed asbestos articles. Although many of the ongoing uses of asbestos articles are classified as non-friable, it can be made friable due to physical and chemical wear and normal use of asbestos-containing products. While exposures to asbestos can potentially occur via all routes, EPA anticipates that the most likely exposure route is inhalation for adults.

**Comparator** (Scenario): Is there range/variation across exposure scenarios to help inform a comparison of exposure to individuals or population groups (human or ecological)?

**Outcome:** Many authorities have established a causal association between asbestos exposure and lung cancer and mesotheliomas and will be used as endpoint for exposure analysis. EPA expects to consider the hazards of asbestos to aquatic organisms (including fish, aquatic invertebrates and aquatic plants) that are potentially exposed under acute and chronic exposure conditions.

**Table_Apx D-5. Inclusion Criteria for Data Sources Reporting Asbestos Exposure Data on General Population, Consumers and Ecological Receptors**

| PECO Element | Evidence |
|---|---|
| **P**opulation | **Human:** Consumers; bystanders experiencing indoor exposures in the home to current regulated uses of asbestos articles (e.g., changing aftermarket asbestos brake pads). Adults are likely to be the only population to work with these articles. |
| | **Ecological:** Aquatic organisms (fish, aquatic invertebrates, plants);. |
| **E**xposure | **Expected Exposure Sources, Pathways, Routes**<br>Source: Secondary ambient air exposure to industrial activities if applicable (chlor-alkali, sheet gasket manufacturing or commercial use, asbestos, brake blocks for oil well drilling), consumer uses of articles containing asbestos (aftermarket asbestos brakes/linings pads/shoes) that were not categorized as legacy. [Asbestos has not been produced in the US since 2002, but can still be imported. Legacy uses and legacy disposals are excluded from the problem formulation.]<br>Pathway: waste streams described in the problem formulation (e.g., surface water); indoor air from contact with asbestos articles (brakes);<br>Routes: inhalation (indoor) |
| **C**omparator (Scenario) | **Human:** Consider only replacement of asbestos aftermarket articles [asbestos brakes/linings and friction products (clutch facings and/or gaskets)] used for consumer use in their garage at home. Inhalation monitoring data for commercial auto worker (i.e., replacing brake pads) may be an applicable conservative surrogate data source for this exposure assuming consumer exposure factors are utilized.<br><br>The use of other asbestos articles may be more appropriate for occupational settings (use and processing of asbestos woven material, replacing sheet gaskets, workers replacing chloro- alkali diaphragms, replacement of brake blocks for oil well drilling, automotive workers engaged in replacement of auto gaskets, brake blocks for trucks, brake pads and shoes, clutch facings, and other asbestos friction products), which would likely be out of scope for ambient exposures to general population and consumers. However, reference material will also be collected and scenarios identified if considered applicable and reasonable. |
| | **Ecological:** Consider narrow use/source specific exposure scenarios for imported asbestos cement products, gasket manufacture, or chloro-alklali plants that release asbestos to surface water. |

| | |
|---|---|
| **O**utcomes for Exposure Concentration or Dose | **Human:** Chronic air, and water concentration estimates (fibers/$cm^3$ or fibers/L) |
| | **Ecological:** A narrow range of ecological receptors will be considered (range depending on available ecotoxicity data) using surface water concentrations from releases to specific current asbestos releases to surface water (see sources above and in the problem formulation). |

## D-4 Inclusion Criteria for Data Sources Reporting Human Health Hazards

EPA/OPPT developed an asbestos-specific PECO statement Table_Apx D-6 to guide the full text screening of the human health hazard literature. Subsequent versions of the PECOs may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the criteria specified in the PECO statement will be eligible for inclusion, considered for evaluation, and possibly included in the human health hazard assessment, while those that do not meet these criteria will be excluded according to the exclusion criteria.

In general, the PECO statements were based on (1) information accompanying the TSCA Scope document, and (2) preliminary review of the health effects literature from authoritative sources cited in the TSCA Scope documents. When applicable, these authoritative sources (e.g., IRIS assessments, EPA/OPPT's Work Plan Problem Formulations or risk assessments) will serve as starting points to identify PECO-relevant studies.

**Table_Apx D-6. Inclusion Criteria for Data Sources Reporting Human Health Hazards Related to Asbestos Exposure**

| PECO Element | Papers/Features Included | Papers/Features Excluded |
|---|---|---|
| | **Human Evidence Streams** [b] | |
| **Population** | • Any population<br>• The following study designs will be considered:<br>  ○ Controlled exposure, cohort, case-control, cross-sectional, case-crossover | • Non-human populations<br>• Study designs other than controlled exposure, cohort, case-control, cross-sectional, case-crossover |
| **Exposure** | • Exposure to TSCA-defined asbestos fiber types:<br>  ○ Chrysotile, Amosite, Anthophylite, Crocidolite, Tremolite, and Anthophylite (includes studies of mixed asbestos fiber types) [c]<br>• Exposure based on measured or estimated concentrations of asbestos and may be combined with estimates of duration of exposure, such as exposure biomonitoring data (e.g., lung tissue specimens), environmental or occupational-setting monitoring data (e.g., ambient air levels), job title or residence.<br>• Exposure identified as ***or presumed to be*** from inhalation routes | • Route of exposure ***not*** by inhalation, type (i.e., oral, dermal, intraperitoneal, or injection routes)<br>• Non-quantitative measures of exposure<br>• Less than 2 exposure groups present<br>• Not pertaining to one or more of the TSCA-defined asbestos fiber types [c] |

| PECO Element | Papers/Features Included | Papers/Features Excluded |
|---|---|---|
| | • Quantitative measures or estimates of exposure ***only***<br>• For categorical exposures, a minimum of 2 exposure groups (referent group + 1) | |
| **Comparator** | • An internal or external comparison population included, (i.e., non-exposed or exposed to lower levels).<br>• Exposure-response modeling results are presented in sufficient detail (e.g., relative risk models for lung cancer [i.e., SMR, RR, OR], additive models for mesothelioma, potency factors [KL, KM], or regression coefficients presented with variation) | • No comparison group<br>• No exposure-response modeling results |
| **Outcome** | • Health Endpoints [d, e]:<br>o Lung cancer<br>o Mesothelioma | • Not pertaining to lung cancer or mesothelioma health effects. |
| **General Considerations** | **Papers/Features Included** | **Papers/Features Excluded** |
| | • Written in English [f]<br>• Reports primary data [a]<br>• Full-text available<br>• Reports both asbestos exposure ***and*** a health outcome<br>• Publication date after 1986 [d] | • Not written in English [f]<br>• Reports secondary data (e.g., review papers) [a]<br>• No full-text available (e.g., only a study description/abstract, out-of-print text)<br>• Reports an asbestos-related exposure ***or*** a health outcome, but not both (e.g. incidence, prevalence report)<br>• Not published after 1986 [d] |

[a] Some of the studies that are excluded based on the PECO statement may be considered later during the systematic review process. For asbestos, EPA will evaluate studies related to susceptibility and may evaluate, toxicokinetics and physiologically based pharmacokinetic models after other data (e.g., human dose-response data) are reviewed. EPA may also review other data as needed (e.g., mechanistic data including genotoxicity, review papers).

[b] Animal and mechanistic data are excluded during the full text screening phase of the systematic review process but may be considered later (see footnote *a*).

[c] Papers reporting exposure to "asbestos" generally, not specific fiber type of asbestos, will be included for further consideration.

[d] EPA will review key and supporting studies in the IRIS assessment that were considered in the dose-response assessment for non-cancer and cancer endpoints as well as studies published after the IRIS assessment.

[e] EPA may screen for hazards other than those listed in the scope document if they were identified in the updated literature search that accompanied the scope document.

[f] EPA may translate studies as needed.

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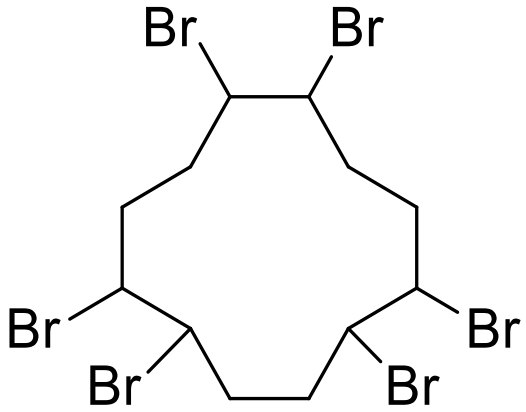
May 2018
Office of Chemical Safety and
Pollution Prevention

United States
Environmental Protection Agency

# Problem Formulation for Cyclic Aliphatic Bromides Cluster (HBCD)




| CASRN | NAME |
|---|---|
| 25637-99-4 | Hexabromocyclododecane |
| 3194-55-6 | 1,2,5,6,9,10-Hexabromocyclododecane |
| 3194-57-8 | 1,2,5,6-Tetrabromocyclooctane |

***May 2018***

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# ACKNOWLEDGEMENTS

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**Docket**
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**Disclaimer**
Reference herein to any specific commercial products, process or service by trade name, trademark, manufacturer or otherwise does not constitute or imply its endorsement, recommendation or favoring by the United States Government.

# ABBREVIATIONS

| | |
|---|---|
| °C | Degrees Celsius |
| atm | Atmosphere(s) |
| BAF | Bioaccumulation Factor |
| BCF | Bioconcentration Factor |
| C&D | Construction and Demolition |
| CAA | Clean Air Act |
| CASRN | Chemical Abstracts Service Registry Number |
| CBI | Confidential Business Information |
| CCL | Candidate Contaminant List |
| CDR | Chemical Data Reporting |
| $cm^3$ | Cubic Centimeter(s) |
| COC | Concentration of Concern |
| CPSC | Consumer Product Safety Commission |
| EC | European Commission |
| ECHA | European Chemicals Agency |
| EPA | Environmental Protection Agency |
| EPCRA | Emergency Planning and Community Right-to-Know Act |
| EPS | Expanded Polystyrene |
| EPS-IA | Expanded Polystyrene Industry Alliance |
| ESD | Emission Scenario Document |
| g | Gram(s) |
| HAP | Hazardous Air Pollutant |
| HBCD | Hexabromocyclododecane |
| HIPS | High Impact Polystyrene |
| HPV | High Production Volume |
| IRIS | Integrated Risk Information System |
| kg | Kilogram(s) |
| $K_{oa}$ | Octanol:Air Partition Coefficient |
| L | Liter(s) |
| lb | Pound |
| LCD | Liquid-Crystal Display |
| LOAEL | Lowest Observed Adverse Effect Level |
| LOEC | Lowest Observed Effect Concentration |
| Log $K_{oc}$ | Logarithmic Organic Carbon:Water Partition Coefficient |
| Log $K_{ow}$ | Logarithmic Octanol:Water Partition Coefficient |
| $m^3$ | Cubic Meter(s) |
| MATC | Maximum Acceptable Toxicant Concentration |
| µg | Microgram(s) |
| mmHg | Millimeter(s) of Mercury |
| MSW | Municipal Solid Waste |
| MSWLF | Municipal Solid Waste Landfills |
| NICNAS | National Industrial Chemicals Notification and Assessment Scheme |
| NIOSH | National Institute of Occupational Safety and Health |
| NOEC | No Observed Effect Concentration |
| OCSPP | Office of Chemical Safety and Pollution Prevention |
| OECD | Organisation for Economic Co-operation and Development |

| | |
|---|---|
| OPPT | Office of Pollution Prevention and Toxics |
| OSHA | Occupational Safety and Health Administration |
| PBPK | Physiologically Based Pharmacokinetic |
| PEC | Predicted Environmental Concentration |
| PESS | Potentially Exposed or Susceptible Subpopulation |
| POD | Point of Departure |
| POP | Persistent Organic Pollutant |
| POTW | Publicly Owned Treatment Works |
| ppm | Part(s) per Million |
| PQL | Practical Quantitation Limit |
| SDS | Safety Data Sheet |
| SIPS | Structural Insulated Panels |
| SNUR | Significant New Use Rule |
| TRI | Toxics Release Inventory |
| TSCA | Toxic Substances Control Act |
| TURA | Toxics Use Reduction Act |
| U.S. | United States |
| UNEP | United Nations Environment Programme |
| WEEE | Waste Electrical and Electronic Equipment |
| WSDE | Washington State Department of Ecology |
| WWTP | Wastewater Treatment Plant |
| XPS | Extruded Polystyrene |
| XPSA | Extruded Polystyrene Association |

# EXECUTIVE SUMMARY

TSCA § 6(b)(4) requires the United States Environmental Protection Agency (U.S. EPA) to establish a risk evaluation process. In performing risk evaluations for existing chemicals, EPA is directed to "determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of costs or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator under the conditions of use." In December of 2016, EPA published a list of 10 chemical substances that are the subject of the Agency's initial chemical risk evaluations (81 FR 91927), as required by TSCA § 6(b)(2)(A). The cyclic aliphatic bromide cluster (HBCD) was one of these chemicals.

TSCA § 6(b)(4)(D) requires that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use and potentially exposed or susceptible subpopulations that the Administrator expects to consider. In June 2017, EPA published the Scope of the Risk Evaluation for HBCD. As explained in the Scope Document, because there was insufficient time for EPA to provide an opportunity for comment on a draft of the scope, as EPA intends to do for further scope documents, EPA is publishing and taking public comment on a problem formulation document to refine the current scope, as an additional interim step prior to publication of the draft risk evaluation for HBCD. Comments received on this problem formulation document will inform development of the draft risk evaluation.

This problem formulation document refines the conditions of use, exposures and hazards presented in the scope of the risk evaluation for HBCD and presents refined conceptual models and analysis plans that describe how EPA expects to analyze the risk associated with the conditions of use of HBCD.

The cyclic aliphatic bromide cluster chemicals, including HBCD (Chemical Abstracts Service Registry Number [CASRN] 25637-99-4), 1,2,5,6,9,10-hexabromocyclododecane (1,2,5,6,9,10-HBCD; CASRN 3194-55-6 are flame retardants. Uses for 1,2,5,6-tetrabromocyclooctane have not been identified. For the purposes of this problem formulation document, the use of "HBCD" refers to either CASRN 25637-99-4 or 3194-55-6, or both.

The primary use of HBCD is as a flame retardant in expanded polystyrene (EPS) foam and extruded polystyrene (XPS) foam in the building and construction industry for thermal insulation boards and foam insulation panels. HBCD also has limited use in replacement parts for automobiles. Past uses of HBCD have included use in HIPS (high impact polystyrene) and textiles. Information gathered from research, industry and consumer product organizations, however, has led EPA to conclude that those past uses are not ongoing; there is no longer manufacture, processing or distribution of HBCD for HIPS or textiles; and therefore, those uses are not included in the scope of the risk evaluation of HBCD.

With the listing of HBCD as a persistent organic pollutant under the Stockholm Convention in 2013, industry began to phase out manufacture and use of HBCD. In recent years, domestic manufacture of HBCD has ceased. Some HBCD was imported in 2017 and EPA believes that a small amount of import of HBCD may be ongoing. Use of stockpiles and exportation from the United States was completed at the end of 2017, and is further discussed in Section 2.2.2 of the Problem Formulation. EPA concludes that the import and processing of HBCD for use in EPS and XPS in buildings may be ongoing.

The conditions of use of EPS and XPS building insulation are within the scope of the evaluation and are anticipated to continue to contribute to exposures in indoor environments. In indoor environments, there

may also be exposures resulting from legacy uses of HBCD in articles (textiles, electronics and electrical products) containing HBCD. These exposures are expected to decline over time as use of these articles is phased out. The time scales for this are dependent on the age of the products, their useful service lives and time lines for replacement.

While environmental exposures are expected to decline as importing and processing of the chemical are phased out, based on past production volumes (millions of pounds per year) and the only recent cessation of domestic manufacturing, reductions in environmental concentrations will occur gradually over a period of time for this persistent and bioaccumulative compound.

This document presents the potential exposures that may result from the conditions of use of HBCD. Exposures to workers, consumers and/or the general population may occur from industrial, commercial, and consumer uses of HBCD and releases to air, water or land. Workers and occupational non-users may be exposed to HBCD during conditions of use such as import, processing, distribution, repackaging and recycling. Consumers and bystanders may also be exposed to HBCD via inhalation of particulates, dermal contact with HBCD in articles and oral exposure via ingestion of settled dust. Exposures to the general population may occur from industrial releases related to the import, processing, distribution and use of HBCD. For HBCD, EPA considers workers, occupational non-users, consumers, and bystanders and certain other groups of individuals who may experience greater exposures than the general population due to proximity to conditions of use to be potentially exposed or susceptible subpopulations. EPA will evaluate whether groups of individuals within the general population may be exposed via pathways that are distinct from the general population due to unique characteristics (e.g., life stage, behaviors, activities, duration) that increase exposure, and whether groups of individuals have heightened susceptibility, and should therefore be considered potentially exposed or susceptible subpopulations for purposes of the risk evaluation.

For aquatic ecological receptors, sediment-dwelling benthic species are expected to be exposed to HBCD. Exposures to pelagic species are also expected from HBCD present in surface water. Trophic magnification may result in greater exposure following bioaccumulation. It is expected that aquatic and terrestrial species will be exposed to HBCD through the dietary exposure pathway. EPA will consider which aquatic and terrestrial species are related via the food chain.

HBCD has been the subject of several prior health hazard, ecological hazard and risk assessments. Human health hazards of HBCD have been reviewed previously and include toxicity following acute (e.g., potential neurological effects, clinical signs of toxicity, and death at high-doses), and chronic (liver toxicity, thyroid toxicity, reproductive/developmental toxicity, neurotoxicity, immunotoxicity) exposures, and sensitization/irritation, all of which EPA expects to evaluate in the scope of the TSCA risk evaluation. HBCD hazards to fish, aquatic plants, sediment invertebrates and terrestrial organisms have also previously been assessed. If additional hazard concerns are identified during the systematic review of the literature, these will also be considered. These hazards will be evaluated based on the specific exposure scenarios identified.

The revised conceptual models presented in this problem formulation identify conditions of use; exposure pathways (e.g., media); exposure routes (e.g., inhalation, dermal, oral); potentially exposed or susceptible subpopulations; and hazards EPA expects to consider in the risk evaluation. The initial conceptual models provided in the HBCD Scope Document (U.S. EPA, 2017d) were revised during problem formulation based on evaluation of reasonably available information for physical-chemical

properties, fate, exposures, hazards and conditions of use and based upon consideration of other statutory and regulatory authorities. In each problem formulation document for the first 10 chemical substances, EPA also refined the activities, hazards, and exposure pathways that will be included in and excluded from the risk evaluation.

EPA's overall objectives in the risk evaluation process are to conduct timely, relevant, high-quality, and scientifically credible risk evaluations within the statutory deadlines, and to evaluate the conditions of use that raise the greatest potential for risk. 82 FR 33726, 33728 (July 20, 2017).

# 1 INTRODUCTION

This document presents for comment the problem formulation of the risk evaluation to be conducted for HBCD under the Frank R. Lautenberg Chemical Safety for the 21st Century Act. The Frank R. Lautenberg Chemical Safety for the 21st Century Act amended the Toxic Substances Control Act (TSCA), the Nation's primary chemicals management law, on June 22, 2016. The new law includes statutory requirements and deadlines for actions related to conducting risk evaluations of existing chemicals.

In December of 2016, EPA published a list of 10 chemical substances that are the subject of the Agency's initial chemical risk evaluations (81 FR 91927), as required by TSCA § 6(b)(2)(A). These 10 chemical substances were drawn from the 2014 update of EPA's TSCA Work Plan for Chemical Assessments, a list of chemicals that EPA identified in 2012 and updated in 2014 (currently totaling 90 chemicals) for further assessment under TSCA. EPA's designation of the first 10 chemical substances constituted the initiation of the risk evaluation process for each of these chemical substances, pursuant to the requirements of TSCA § 6(b)(4).

TSCA § 6(b)(4)(D) requires that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use and potentially exposed or susceptible subpopulations that the Administrator expects to consider, within 6 months after the initiation of a risk evaluation. The scope documents for all first 10 chemical substances were issued on June 22, 2017. The first 10 problem formulation documents are a refinement of what was presented in the first 10 scope documents. TSCA § 6(b)(4)(D) does not distinguish between scoping and problem formulation, and requires EPA to issue scope documents that include information about the chemical substance, such as the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations that the Administrator expects to consider in the risk evaluation. In the future, EPA expects scoping and problem formulation to be completed prior to the issuance of scope documents and intends to issue scope documents that include problem formulation.

As explained in the scope document, because there was insufficient time for EPA to provide an opportunity for comment on a draft of the scope, as EPA intends to do for future scope documents, EPA is publishing and taking public comment on a problem formulation document to refine the current scope, as an additional interim step prior to publication of the draft risk evaluation for HBCD. Comments received on this problem formulation document will inform development of the draft risk evaluation.

The Agency defines problem formulation as the analytical phase of the risk assessment in which "the purpose for the assessment is articulated, the problem is defined and a plan for analyzing and characterizing risk is determined" [see Section 2.2 of the Framework for Human Health Risk Assessment to Inform Decision Making (U.S. EPA, 2014c)]. The outcome of problem formulation is a conceptual model(s) and an analysis plan. The conceptual model describes the linkages between stressors and adverse human health effects, including the stressor(s), exposure pathway(s), exposed life stage(s) and population(s), and endpoint(s) that will be addressed in the risk evaluation (U.S. EPA, 2014c). The analysis plan follows the development of the conceptual model(s) and is intended to describe the approach for conducting the risk evaluation, including its design, methods and key inputs and intended outputs as described in the EPA Human Health Risk Assessment Framework (U.S. EPA, 2014c). The problem formulation documents refine the initial conceptual models and analysis plans that were provided in the scope documents.

First, EPA has removed from the risk evaluation any activities and exposure pathways that EPA has concluded do not warrant inclusion in the risk evaluation. For example, for some activities which were listed as "conditions of use" in the scope document, EPA has insufficient information following the further investigations during problem formulation to find they are circumstances under which the chemical is "intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of." Other activities, for example, may have been determined to be legacy use, associated disposal, or legacy disposal during problem formulation. EPA does not expect to consider or evaluate any such activities or associated hazards or exposures in the applicable risk evaluation – that is to say, EPA does not expect to determine whether these activities, hazards or exposures present unreasonable risk.

Second, EPA also identified certain exposure pathways that are under the purview of regulatory programs and associated analytical processes carried out under other EPA-administered environmental statutes – namely, the Safe Drinking Water Act (SDWA), the Clean Water Act (CWA), and the Resource Conservation and Recovery Act (RCRA) – and which EPA does not expect to include in the risk evaluation.

As a general matter, EPA believes that certain programs under other Federal environmental laws adequately assess and effectively manage the risks for the covered exposure pathways. To use Agency resources efficiently under the TSCA program, to avoid duplicating efforts taken pursuant to other Agency programs, to maximize scientific and analytical efforts, and to meet the three-year statutory deadline, EPA is planning to exercise its discretion under TSCA 6(b)(4)(D) to focus its analytical efforts on exposures that are likely to present the greatest concern and consequently merit a risk evaluation under TSCA, by excluding, on a case-by-case basis, certain exposure pathways that fall under the jurisdiction of other EPA-administered statutes.[1] EPA does not expect to include any such excluded pathways as further explained below in the risk evaluation. The provisions of various EPA-administered environmental statutes and their implementing regulations represent the judgment of Congress and the Administrator, respectively, as to the degree of health and environmental risk reduction that is sufficient under the various environmental statutes.

Third, EPA identified any conditions of use, hazards, or exposure pathways which were included in the scope document and that EPA expects to include in the risk evaluation but which EPA does not expect to further analyze in the risk evaluation. EPA expects to be able to reach conclusions about particular conditions of use, hazards or exposure pathways without further analysis and therefore plans to conduct no further analysis on those conditions of use, hazards or exposure pathways in order to focus the Agency's resources on more extensive or quantitative analyses. Each risk evaluation will be "fit-for-purpose," meaning not all conditions of use will warrant the same level of evaluation and the Agency may be able to reach some conclusions without comprehensive or quantitative risk evaluations. 82 FR 33726, 33734, 33739 (July 20, 2017).

EPA received comments on the published scope document for HBCD and has considered the comments specific to HBCD in this problem formulation document. EPA is soliciting public comment on this problem formulation document and when the draft risk evaluation is issued, the Agency intends to

[1] As explained in the final rule for chemical risk evaluation procedures, "EPA may, on a case-by case basis, exclude certain activities that EPA has determined to be conditions of use in order to focus its analytical efforts on those exposures that are likely to present the greatest concern, and consequently merit an unreasonable risk determination". [82 FR 33726, 33729 (July 20, 2017)].

respond to comments that are submitted. In its draft risk evaluation, EPA may revise the conclusions and approaches contained in this problem formulation, including the conditions of use and pathways covered and the conceptual models and analysis plans, based on comments received.

## 1.1 Regulatory History

EPA conducted a search of existing domestic and international laws, regulations and assessments pertaining to HBCD. EPA compiled this summary from data available from federal, state, international and other government sources, as cited in Appendix A. EPA evaluated and considered the impact of these existing laws and regulations (e.g. regulations on landfill disposal, design and operations) in the problem formulation step to determine what, if any further analysis might be necessary as part of the risk evaluation. Consideration of the nexus between these existing regulations and TSCA uses may additionally be made as detailed/specific conditions of use and exposure scenarios are developed in conducting the analysis phase of the risk evaluation.

***Federal Laws and Regulations***

HBCD is subject to federal statutes or regulations, other than TSCA, that are implemented by other offices within EPA and/or other federal agencies/departments. A summary of federal laws, regulations and implementing authorities is provided in Appendix A.1.

***State Laws and Regulations***

HBCD is subject to state statutes or regulations implemented by state agencies or departments. A summary of state laws, regulations and implementing authorities is provided in Appendix A.2.

***Laws and Regulations in Other Countries and International Treaties or Agreements***

HBCD is subject to statutes or regulations in countries other than the United States and/or international treaties and/or agreements. A summary of these laws, regulations, treaties and/or agreements is provided in Appendix A.3.

## 1.2 Assessment History

EPA has identified assessments conducted by other EPA Programs and other organizations (see Table 1-1). Depending on the source, these assessments may include information on conditions of use, hazards, exposures and potentially exposed or susceptible subpopulations. Table 1-1 shows the assessments that have been conducted.

In addition to using this information, EPA intends to conduct a full review of the relevant data/information collected in the initial comprehensive search (see *HBCD (CASRN 25637-99-4, 3194-55-6, 3194-57-8) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0735) following the literature search and screening strategies documented in the *Strategy for Conducting Literature Searches for HBCD: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0735). This will ensure that EPA considers information that has been made available since these evaluations were conducted.

A Problem Formulation and Initial Assessment (PFIA) for the Cyclic Aliphatic Bromides Cluster was published in 2015 (U.S. EPA, 2015c); however, a draft risk assessment was not completed. As part of the scope, EPA developed an initial life cycle diagram and initial conceptual models for HBCD that re-considered reasonably available information.

**Table 1-1. Assessment History of HBCD**

| Authoring Organization | Assessment |
|---|---|
| **EPA assessments** | |
| EPA, Office of Chemical Safety and Pollution Prevention (OCSPP), Office of Pollution Prevention and Toxics (OPPT) | Initial Risk Based Prioritization of High Production Volume Chemicals. Chemical/Category: Hexabromocyclododecane (HBCD) (U.S. EPA, 2008) |
| EPA, OCSPP, OPPT | Hexabromocyclododecane (HBCD) Action Plan (U.S. EPA, 2010) |
| EPA, OCSPP, OPPT | Flame Retardant Alternatives for Hexabromocyclododecane (HBCD) (U.S. EPA, 2014a) |
| EPA, OCSPP, OPPT | Toxic Chemical Work Plan Problem Formulation and Initial Assessment for HBCD, Cyclic Aliphatic Bromides Cluster (U.S. EPA, 2015c) |
| **Other U.S.-based organizations** | |
| Consumer Product Safety Commission (CPSC) | CPSC Staff Exposure and Risk Assessment of Flame Retardant Chemicals in Residential Upholstered Furniture (CPSC, 2001) |
| National Research Council | National Academy of Sciences Report: Toxicological Risks of Selected Flame Retardant Chemicals (NRC, 2000) |
| **International** | |
| Organisation for Economic Co-operation and Development (OECD), Screening Information Data Set (SIDS) | OECD SIDS Initial Assessment Profile (SIAP) (OECD, 2007b) |
| European Commission (EC), European Chemicals Bureau | European Union Risk Assessment Report, Hexabromocyclododecane CASRN 25637-99-4. EINECS No: 247-148-4 (EINECS, 2008) |
| United Nations Environment Programme (UNEP); Stockholm Convention on Persistent Organic Pollutants (POPs) | Hexabromocyclododecane Draft Risk Profile (UNEP, 2010)<br><br>Hexabromocyclododecane Risk Management Evaluation (2011) (UNEP, 2011) |

| Authoring Organization | Assessment |
|---|---|
| Environment Canada and Health Canada | Draft Screening Assessment of Hexabromocyclododecane (Environment Canada, 2011) |
| Australian Government Department of Health, National Industrial Chemicals Notification and Assessment Scheme (NICNAS) | Priority Existing Chemical Assessment Report, Hexabromocyclododecane (NICNAS, 2012b) |

## 1.3 Data and Information Collection

EPA/OPPT generally applies a systematic review process and workflow that includes: (1) data collection; (2) data evaluation; and (3) data integration of the scientific data used in risk assessments developed under TSCA. Scientific analysis is often iterative in nature as new knowledge is obtained. Hence, EPA/OPPT expects that multiple refinements regarding data collection will occur during the process of risk evaluation. Additional information that may be considered and was not part of the comprehensive bibliographies will be documented in the Draft Risk Evaluation for HBCD.

***Data Collection: Data Search***

EPA/OPPT conducted chemical-specific searches for information on: physical and chemical properties; environmental fate and transport; conditions of use information; environmental and human exposures, including potentially exposed or susceptible subpopulations; and ecological hazard and human health hazard, including potentially exposed or susceptible subpopulations.

EPA/OPPT designed its initial data search to be broad enough to capture a comprehensive set of sources containing data and/or information potentially relevant to the risk evaluation. Generally, the search was not limited by date and was conducted on a wide range of data sources, including but not limited to: peer-reviewed literature and gray literature (e.g., publicly-available industry reports, trade association resources, government reports). When available, EPA/OPPT relied on the search strategies from recent assessments, such as EPA Integrated Risk Information System (IRIS) assessments and the National Toxicology Program's (NTP) *Report on Carcinogens*, to identify relevant references and supplemented these searches to identify relevant information published after the end date of the previous search to capture more recent literature. *Strategy for Conducting Literature Searches for HBCD: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0735) provides details about the data sources and search terms that were used in the literature search.

***Data Collection: Data Screening***

Following the data search, references were screened and categorized using selection criteria outlined in *Strategy for Conducting Literature Searches for HBCD: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0735, (U.S. EPA, 2017f)). Titles and abstracts were screened against the criteria as a first step with the goal of identifying a smaller subset of the relevant data to move into the subsequent data extraction and data evaluation steps. Prior to full-text review, EPA/OPPT anticipates refinements to the search and screening strategies, as informed by an evaluation of the performance of the initial title/abstract screening and categorization process.

The categorization scheme (or tagging structure) used for data screening varies by scientific discipline (i.e., physical and chemical properties; environmental fate and transport; chemical use/conditions of use

information; environmental exposures, human exposures, including potentially exposed or susceptible subpopulations identified by virtue of greater exposure; human health hazard, including potentially exposed or susceptible subpopulations identified by virtue of greater susceptibility; and ecological hazard). However, within each data set, there are two broad categories or data tags: (1) o*n-topic* references or (2) *off-topic* references. *On-topic* references are those that may contain data and/or information relevant to the risk evaluation. O*ff-topic* references are those that do not appear to contain data or information relevant to the risk evaluation. The supplemental document, *Strategy for Conducting Literature Searches for HBCD: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0735, (U.S. EPA, 2017f)) discusses the inclusion and exclusion criteria that EPA/OPPT used to categorize references as *on-topic* or *off-topic*.

Additional data screening using sub-categories (or sub-tags) was also performed to facilitate further sorting of data/information - for example, identifying references by source type (e.g., published peer-reviewed journal article, government report); data type (e.g., primary data, review article); human health hazard (e.g., liver toxicity, cancer, reproductive toxicity); or chemical-specific and use-specific data or information. These sub-categories are described in *Strategy for Conducting Literature Searches for HBCD: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0735, (U.S. EPA, 2017f)) and will be used to organize the different streams of data during the stages of data evaluation and data integration steps of systematic review.

Results of the initial search and categorization results can be found in the *HBCD (CASRN 25637-99-4, 3194-55-6, 3194-57-8) Bibliography: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0735). This document provides a comprehensive list (bibliography) of the sources of data identified by the initial search and the initial categorization for *on-topic* references and *off-topic* references. Because systematic review is an iterative process, EPA/OPPT expects that some references may move from the *on-topic* to the *off-topic* categories, and vice versa. Moreover, targeted supplemental searches may also be conducted to address specific needs for the analysis phase (e.g., to locate specific data needed for modeling); hence, additional *on-topic* references not initially identified in the initial search may be identified as the systematic review process proceeds.

## 1.4 Data Screening During Problem Formulation

EPA/OPPT is in the process of completing the full text screening of the *on-topic* references identified in the *HBCD (CASRN 25637-99-4, 3194-55-6, 3194-57-8) Bibliography: Supplemental File for the TSCA Scope Document*. The screening process at the full-text level is described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018). Appendix E provides the inclusion and exclusion criteria applied at the full text screening. The eligibility criteria are guided by the analytical considerations in the revised conceptual models and analysis plan, as discussed in the problem formulation document. Thus, it is expected that the number of data/information sources entering evaluation is reduced to those that are relevant to address the technical approach and issues described in the analysis plan of this document.

Following the screening process, the quality of the included data/information sources will be assessed using the evaluation strategies that are described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018).

# 2 PROBLEM FORMULATION

As required by TSCA, the scope of the risk evaluation identifies the conditions of use, hazards, exposures and potentially exposed or susceptible subpopulations that the Administrator expects to consider. To communicate and visually convey the relationships between these components, EPA included in the scope document a life cycle diagram and conceptual models that describe the actual or potential relationships between HBCD and human and ecological receptors. During the problem formulation, EPA revised the conceptual models based on further data gathering and analysis, as presented in this problem formulation document. An updated analysis plan is also included which identifies, to the extent feasible, the approaches and methods that EPA may use to assess exposures, effects (hazards) and risks under the conditions of use for HBCD.

## 2.1 Physical and Chemical Properties

Physical-chemical properties influence the environmental behavior and the toxic properties of a chemical, thereby informing the potential conditions of use, exposure pathways and routes and hazards that EPA intends to consider. For scope development, EPA considered the measured or estimated physical-chemical properties set forth in Table 2-1 and EPA found no additional information during problem formulation that would change these values.

HBCD is a white odorless non-volatile solid that is used as a flame retardant. Technical HBCD is often characterized as a mixture of mainly three diastereomers, which differ only in the spatial disposition of the atoms. Commercial-grade HBCD may contain some impurities, such as tetrabromocyclododecene or other isomeric HBCDs (UNEP, 2010), which are not separately included in this scope. The density of HBCD is greater than that of water (2.24 g/cm$^3$ at 20°C). It has low water solubility (66 µg/L at 20°C) and a log octanol:water partition coefficient (log $K_{ow}$) of 5.62.

**Table 2-1. Physical and Chemical Properties of HBCD**

| Property | Value [a] | References |
|---|---|---|
| Molecular formula | $C_{12}H_{18}Br_6$ | |
| Molecular weight | 641.7 g/mole | |
| Physical form | White solid; odorless | EINECS (2008) |
| Melting point | Ranges from approximately: 172-184°C to 201-205°C | EINECS (2008) |
| Boiling point | >190°C (decomposes) | EINECS (2008) |
| Density | 2.24 g/cm$^3$ | EINECS (2008) |
| Vapor pressure | 4.7E-07 mmHg at 21°C | EINECS (2008) |
| Vapor density | Not readily available | EINECS (2008) |
| Water solubility | 66 µg/L at 20°C | EINECS (2008) |
| Octanol:water partition coefficient (log $K_{ow}$) | 5.625 at 25°C | EINECS (2008) |
| Henry's Law constant | 7.4E-06 atm-m$^3$/mole (estimated) | U.S. EPA (2012b) |
| Flash point | Not readily available | EINECS (2008) |

| Property | Value [a] | References |
|---|---|---|
| Autoflammability | Decomposes at >190°C | EINECS (2008) |
| Viscosity | Not readily available | EINECS (2008) |
| Refractive index | Not readily available | EINECS (2008) |
| Dielectric constant | Not readily available | EINECS (2008) |
| [a] Measured unless otherwise noted. | | |

## 2.2 Conditions of Use

TSCA § 3(4) defines the conditions of use as ‘‘the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of.’’

### 2.2.1 Data and Information Sources

In the scope documents, EPA identified, based on reasonably available information, the conditions of use for the subject chemicals. EPA searched a number of available data sources (e.g., *Use and Market Profile for HBCD,* EPA-HQ-OPPT-2016-0735). Based on this search, EPA published a preliminary list of information and sources related to chemical conditions of use (see *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: HBCD,* EPA-HQ-OPPT-2016-0735-0003) prior to a February 2017 public meeting on scoping efforts for risk evaluation convened to solicit comment and input from the public. EPA also convened meetings with companies, industry groups, chemical users and other stakeholders to aid in identifying conditions of use and verifying conditions of use identified by EPA. The information and input received from the public, stakeholder meetings and the additional contacts was incorporated into this problem formulation to the extent appropriate. Thus, EPA believes the manufacture, processing, distribution, use and disposal activities constitute the intended, known, and reasonably foreseen activities associated with the subject chemical, based on reasonably available information.

### 2.2.2 Identification of Conditions of Use

To determine the conditions of use of HBCD and inversely, activities that do not qualify as conditions of use, EPA conducted extensive research and outreach. This included EPA’s review of published literature and online databases including the most recent data available from: U.S. Consumer Product Safety Commission (CPSC), CPSC staff exposure and risk assessment of flame retardant chemicals in residential upholstered furniture, 2001; National Institute of Health’s (NIH) Household Product Database; EPA’s Chemical/Product Categorical Data (CPcat) database; the most recent data available from EPA’s Chemical Data Reporting program (CDR); Safety Data Sheets (SDSs); European Chemical Agency (ECHA) reports; United Nations Environment Program (UNEP) reports. EPA also conducted online research by reviewing company websites of potential manufacturers, importers, distributors, retailers, or other users of HBCD and queried government and commercial trade databases. EPA also received comments (EPA-HQ-OPPT-2016-0735) on the *Scope of the Risk Evaluation for HBCD* (U.S. EPA, 2017e)that were used to determine the current conditions of use. In addition, EPA convened meetings and personal communications with companies, industry groups, chemical users, states, environmental groups, federal agencies, and other stakeholders to aid in identifying conditions of use and verifying conditions of use identified by EPA. Those meetings included a February 14, 2017 public meeting with such entities (EPA-HQ-OPPT-2016-0735) in addition to meeting with: Adhesives and

Sealants Council, American Chemistry Council, Alliance of Automobile Manufacturers, Association of Global Automakers, Motor and Equipment Manufacturers Association, Business and Institutional Furniture Manufacturer's Association, Consumer Specialty Products Association, Duke University Faculty, Design Chain, Eagle Performance Products, Ecology Center, EPS Industry Alliance, Green Policy Institute, Motor & Equipment Manufacturers Association, National Council of Textile Organizations, Plastics Industry Association, XPS Association, and others.

EPA has removed from the risk evaluation any activities that EPA concluded do not constitute conditions of use – for example, because EPA has insufficient information to find certain activities are circumstances under which the chemical is actually "intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of." EPA has also identified any conditions of use that EPA does not expect to include in the risk evaluation. As explained in the final rule for Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act, TSCA section 6(b)(4)(D) requires EPA to identify "the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations the Administrator expects to consider" in a risk evaluation, suggesting that EPA may exclude certain activities that EPA has determined to be conditions of use on a case-by-case basis. (82 FR 33736, 33729; July 20, 2017). For example, EPA may exclude conditions of use that the Agency has sufficient basis to conclude would present only de minimis exposures or otherwise insignificant risks (such as use in a closed system that effectively precludes exposure or use as an intermediate).

The activities that EPA no longer believes are conditions of use or were otherwise excluded during problem formulation are described in Section 2.2.2.1. The conditions of use included in the scope of the risk evaluation are summarized in Section 2.2.2.2.

#### 2.2.2.1 Categories and Subcategories Determined not to be Conditions of Use or Otherwise Excluded During Problem Formulation

**Domestic Manufacture of HBCD**

Domestic manufacture of HBCD has ceased. Domestic manufacture of HBCD is not intended, known, or reasonably foreseen and is therefore not considered a condition of use under which EPA will evaluate HBCD.

U.S. manufacturers have indicated complete replacement of HBCD in their product lines (U.S. EPA, 2017g) and that use of stockpiles and exportation was completed in 2017. Communication with Chemtura (Lanxess Solutions, US) indicates that the company has not manufactured HBCD since 2015, and that there are currently no U.S. manufacturers of the chemical (LANXESS, 2017b). The company does not intend to manufacture, import, or export HBCD in the future and has no existing stockpiles (LANXESS, 2017a). Albemarle Corporation, another historic manufacturer of HBCD, indicated that they stopped manufacturing HBCD flame retardants around 2016 and do not intend to resume the manufacture of HBCD-based flame retardants. In 2017, Albemarle exported its entire inventory of approximately 57 metric tons (MT) of HBCD to Mexico and Turkey for use in construction (EPS/XPS) applications (Albemarle, 2017b). Albemarle does not intend to import HBCD in the future (Albemarle, 2017a).

**Domestic Manufacture of EPS Resin and XPS Masterbatch**
In the past, the process for making insulation with HBCD included an intermediate step of resin manufacture. A small group of EPS and XPS resin manufacturers purchased HBCD (domestically manufactured or imported) and combined it with polystyrene and other ingredients to produce resin. Separate facilities used the resin to make foam insulation products for construction. Domestic manufacturers of EPS and XPS resin have phased out the use of HBCD due to international bans and the availability of alternative flame retardants. The EPS Industry Alliance (EPS-IA) which represents all major North American manufacturers (including Canada and Mexico) of EPS resin, reports that its members have phased out of the use of HBCD in the production of EPS resins (Public comment, EPA-HQ-OPPT-2016-0735-0026). Similar to the EPS resin industry, major producers of XPS masterbatch have fully transitioned out of using HBCD (XPSA, 2017a) .

**Use in High Impact Polystyrene (HIPS)**
Use of HBCD in High Impact Polystyrene (HIPs) appears to have ceased and EPA does not believe this use is intended, known, or reasonably foreseen. Therefore, use of HBCD in HIPS is not considered a condition of use under which EPA will evaluate HBCD.

HBCD was used as a flame retardant in HIPS in electronic components. The most recent information showing use, in both the United States and Europe, of HBCD as a flame retardant in HIPS for electrical and electronic appliances, such as audio-visual equipment, refrigerator lining and some wire and cable applications was based on a 2009 data source (ECHA, 2009b; Morose, 2006a). Use in television sets at that time was the predominant application of HIPS (Weil and Levchik, 2009). EPA's recent research and outreach did not yield data showing current use of HBCD in HIPS for electrical and electronic appliances (Design Chain Associates, 2017).

The Australian Department of Health and Aging reported in 2012 that minimal amounts of HBCD were imported into Australia already incorporated into various articles, such as inkjet printers, projectors, scanners, ventilation units for offices, compact fluorescent lights and liquid-crystal display (LCD) digital audiovisual systems (NICNAS, 2012a). Similar current uses of HBCD in electronic articles or import of those articles into the U.S. have not been found.

The use of HBCD in electronic equipment is legacy and therefore disposal of HBCD containing HIPS is also considered legacy (associated disposal). Electronic products (which may or may not contain HBCD) can be recycled and HIPS materials constitute more than half the plastic materials recovered from household electronics (Borchardt, 2006). However, no information was identified that confirms use of HBCD in recycled HIPS for the purposes of flame retardancy. EPA, therefore, does not believe that this use is intended, known, or reasonably foreseen and is not a condition of use for HBCD. Nor is there information that the recycling (i.e., processing) of HIPS containing HBCD is done to retrieve the HBCD or to otherwise use the flame retardant properties of HBCD. Therefore, EPA believes the manufacturing, processing, or distribution in commerce for use of HBCD as a flame retardant in HIPS is not intended, known, or reasonably foreseen and is not a condition of use of HBCD.

**Use in Textiles**
In the United States, HBCD was historically used as a flame retardant in the back coating of textiles. Use in this application was quite small; in 2005, manufacturers reported only 1% of HBCD was used in textiles in the United States and only for commercial, not consumer use (U.S. EPA, 2012e).

Use in Consumer Textiles: EPA found that a small amount of HBCD was being used in consumer textiles, i.e., floor mats, headliners and possibly other interior fabrics in motor vehicles made or imported to the United States in 2011 (U.S. EPA, 2012e). Based on this information and the CDR reporting in 2005, EPA finalized a SNUR in 2015 (U.S. EPA, 2015b) which requires persons who intend to manufacture (including import) or process HBCD for use in consumer textiles (other than for use in motor vehicles) to notify EPA at least 90 days before commencing that activity. EPA has received no notifications since the rule became effective in late 2012, and therefore does not expect HBCD to be used in such consumer textiles. Articles containing HBCD that were manufactured prior to the effective date of the SNUR might continue to be in service.

Information from industry indicates that HBCD is no longer used in textiles in motor vehicles (Alliance of Automobile Manufacturers, 2018) and EPA does not believe the use is intended, known, or reasonably foreseen. Therefore, use in textiles in motor vehicles is not a condition of use under which EPA will evaluate HBCD.

From June 2012 to March 2017, the use of HBCD in children's clothing and blankets was self-reported 44 times by manufacturers and retailers to Washington State under state law (Public comment, EPA-HQ-OPPT-2016-0735-0022). The forty-four reports are associated with consumer textiles which are expected to have been covered by the SNUR (U.S. EPA, 2015b); and therefore may reflect textiles produced prior to 2015. The textile products were reported with practical quantitation levels (PQL) of less than 100 parts per million (ppm). EPA further assessed the data and concluded that none of the products appear to contain intentionally-added HBCD.

Information gathered from research, industry and consumer product organizations has led EPA to believe that HBCD is no longer used in consumer textiles. Current use in consumer textiles has not been confirmed and EPA does not believe it is known, intended, or reasonably foreseen. Therefore, use in consumer textiles is not a condition of use under which EPA will evaluate HBCD.

Use in Commercial Textiles: EPA received information in 2011 from a group of textile formulators that the end uses of HBCD-containing textiles are for military, institutional and aviation applications, such as durable carpet tiles for hospitals or prisons (U.S. EPA, 2012e; Friddle, 2011). By 2017, HBCD use in these textile applications appeared to be phasing out (Friddle, 2017). The U.S. Department of Defense found no direct use of HBCD (Underwood, 2017). According to the National Council of Textile Organizations, HBCD has not been used in textiles for more than a decade (Poole, 2017). Current use in commercial textiles could not been confirmed, but EPA concludes that based on the information above, HBCD use in these textiles is not intended, known, or reasonably foreseen. Therefore, use in commercial textiles is not a condition of use under which EPA will evaluate HBCD.

**Use in Adhesives**

Use of HBCD in adhesives was one of several minor uses included in the HBCD Scope Document, however further research could not confirm current use in adhesives. During Problem Formulation, EPA found that the Henkel company manufactured a pressure sensitive adhesive containing HBCD for use in flexible air duct core under the product name Aquence AV 7584 Black, according to the company's website and product Safety Data Sheet (Henkel Corp, 2017). However, as of January 2018 (Pierson, 2018), EPA has learned that the company will no longer use HBCD in their product line and does not have a current supply of HBCD to draw from. EPA could find no evidence of ongoing manufacture,

processing or distribution of adhesives using HBCD. Therefore, adhesives are not included as a condition of use for which EPA will evaluate HBCD.

**Use in Automotive Sector**
Use of HBCD in the automotive sector was not reported in the 2012/2016 CDR or 2006 IUR datasets.

EPA received a public comment from the Global Automakers Association stating that "our members have not identified any ongoing uses [of HBCD] in the manufacture of new vehicles. However, [HBCD] has been and currently is being used in the manufacture of replacement parts only – replacement parts designed prior to the date of the publication of the EPA HBCD Scoping Document" (Public comment, EPA-HQ-OPPT-2016-0735-0027).

The Motor and Equipment Manufacturers Association reports that HBCD "is not used during the manufacturing process of any automotive components. Information from our members submitted in 2015 also indicated it had nearly phased out completely the use of HBCD. Our data indicates HBCD is phased out" (Public comment, EPA-HQ-OPPT-2016-0735-0014).

In a public comment on the Use Document, however, the Alliance of Automotive Manufacturers wrote: "Our members have indicated to us that this chemical is not used during the auto manufacturing process. HBCD has been aggressively phased out by the auto industry over the past several years. However, the chemical may still be used by some automakers as a flame retardant in coatings of certain components (e.g., dashboards and headliners) and in solder paste in interior components (e.g., circuits). This chemical may also be present in adhesives and foams." (Public comment, EPA-HQ-OPPT-2016-0735-0015). Specifics on these uses by non-member companies could not be verified.

Based on the information provided above, EPA concludes that use of HBCD in the manufacture of new automobiles is not occurring (U.S. EPA, 2017c, 2012d, 2006b). Therefore, the use of HBCD in manufacture of new automobiles is not intended, known, or reasonably foreseen and therefore is not a condition of use under which EPA will evaluate HBCD. Automotive replacement parts, however, are considered a condition of use and will be included within the scope of the risk evaluation based on the information provided above.

**Other Uses**
In order to determine whether other uses exist and to what extent, EPA reviewed state databases, product testing results and information from foreign countries, in addition to the literature search and contacts with industry groups.

Detections of HBCD in children's products reported by industry to Washington State Department of Ecology (WSDE) include three products listed as "toy/games variety pack" and one entry for a baby car/booster seat. The HBCD was found in surface coatings and polymers. One toy product and the car seat were reported to have practical quantitation limits (PQLs) of "equal to or greater than 100 but less than 5000 ppm." As this data is self-reported to the WSDE state database, more specific information regarding the contaminant test methodologies, tested components, or prevalence of HBCD in the products information could not be verified. The WSDE tested for flame retardants in a set of 169 general and consumer products purchased between August 2012 and August 2013 from local stores in the south Puget Sound area and online retailers. HBCD was detected in two of the products: in the polystyrene of a child's bean bag chair at a concentration of 0.06%, and in the plastic of a protective work glove at

4.4% (WSDE, 2014). WSDE noted in a 2015 report to the Washington state legislature that these test results showed HBCD at percent levels but concluded: "TBBPA and HBCD were not detected in children's products and furniture at levels consistent with use as a flame retardant in products tested by Ecology" (https://fortress.wa.gov/ecy/publications/documents/1404047.pdf). EPA followed up with the supplier of the Carbon X brand of work glove that WSDE had tested in 2012-2013. The company provided documentation that HBCD is not used in four varieties of the Carbon X work glove (Mechanix Wear, 2018). EPA concludes that other uses are not intended, known, or reasonably foreseen and are not considered conditions of use under which EPA will evaluate HBCD.

EPA has concluded that legacy uses of HBCD include adhesives, textiles (including upholstery fabric, floor mats and headliners in automobiles, and commercial uses) and electronics and electrical products.

EPA has concluded that the following are not conditions of use: coatings, solder, children's products including toys and car seats; furniture (such as bean bag chairs).

Beyond the uses identified in the Scope of the Risk Evaluation for HBCD, EPA has received no additional information identifying additional current conditions of use for HBCD from public comment and stakeholder meetings.

**Table 2-2. Categories and Subcategories Determined not to be Conditions of Use or Otherwise Excluded During Problem Formulation**

| Life Cycle Stage | Category[a] | Subcategory[b] | References |
|---|---|---|---|
| Manufacture | Domestic manufacture | Domestic manufacture | U.S. EPA (2016b) |
| Processing | Processing as a reactant/ intermediate | Intermediate for all other basic inorganic chemical manufacturing | U.S. EPA (2016b) |
| | Processing - incorporated into formulation, mixture or reaction product | Flame retardants used in plastic material and resin manufacturing (e.g., manufacture of EPS resin beads) | Use Document, EPA-HQ-OPPT-2016-0735-0003; EINECS (2008); Market Profile, EPA-HQ-OPPT-2016-0735. |
| | Processing - incorporated into formulation, mixture or reaction product | Flame retardants used in paints and coatings manufacturing (e.g., micronisation and formulation of polymer-based dispersions for textile coatings). | Use Document, EPA-HQ-OPPT-2016-0735-0003; Market Profile, EPA-HQ-OPPT-2016-0735; EINECS (2008) |
| | Processing - incorporated into formulation, mixture or reaction product | Flame retardants used in adhesive manufacturing (e.g., manufacture of solder paste and other adhesives) | Public Comment, EPA-HQ-OPPT-2016-0735-0008; Public Comment, EPA-HQ-OPPT-2016-0735-0015 |
| | Incorporated into article | Flame retardants used in plastics product manufacturing | Use Document, EPA-HQ-OPPT-2016-0735-0003; Market Profile, EPA-HQ- |

| Life Cycle Stage | Category[a] | Subcategory[b] | References |
|---|---|---|---|
| | | (manufacture of HIPS; manufacture of electronics articles)[d] | OPPT-2016-0735; U.S. EPA (2014b) |
| | Incorporated into article | Flame retardants used in textiles, apparel and leather manufacturing (e.g., coatings used at textile and fabric finishing mills, fabric coating mills and carpet and rug mills)[d] | Use Document, EPA-HQ-OPPT-2016-0735-0003; U.S. EPA (2014b) |
| | Incorporated into article | Flame retardants used in transportation equipment manufacturing (e.g., manufacture of interior components in automobiles, including fabrics, coatings, solder paste, adhesives and foams) [d] | Use Document, EPA-HQ-OPPT-2016-0735-0003; Market Profile, EPA-HQ-OPPT-2016-0735; Public Comment, EPA-HQ-OPPT-2016-0735-0015 |
| Processing | Recycling | Recycling of Products and Articles Containing HBCD for applications that do not have intentional flame retardancy | |
| Commercial/consumer Use | Electrical and electronic products | Plastic articles (soft) (e.g., wire and cable) | Use Document, EPA-HQ-OPPT-2016-0735-0003; Market Profile, EPA-HQ-OPPT-2016-0735; U.S. EPA (2016b) |
| | | Plastic articles (hard) (e.g., distribution boxes, audio-visual equipment; refrigerator lining; computers; Inkjet printers/scanners) | Use Document, EPA-HQ-OPPT-2016-0735-0003; Market Profile, EPA-HQ-OPPT-2016-0735; U.S. EPA (2016b) |
| | Adhesives | Adhesives (e.g., ductwork) | (Henkel Corp, 2017), (Pierson, 2018). |
| | Floor coverings | Fabrics, textiles and apparel (e.g., carpets and rugs) | Use Document, EPA-HQ-OPPT-2016-0735-0003 |
| | Furniture and furnishings | Fabrics, textiles and apparel: Furniture and furnishings, including furniture coverings (e.g., institutional furniture) | Use Document, EPA-HQ-OPPT-2016-0735-0003; |

| Life Cycle Stage | Category[a] | Subcategory[b] | References |
|---|---|---|---|
| | Fabric, textile and leather products [d] | Fabrics, textiles and apparel (e.g., interior fabrics for automobiles) | Use Document, EPA-HQ-OPPT-2016-0735-0003; Market Profile, EPA-HQ-OPPT-2016-0735 |
| | Fabric, textile and leather products [d] | Textile finishing and impregnating/surface treatment products (e.g., other textile products) | Use Document, EPA-HQ-OPPT-2016-0735-0003; Public Comment, EPA-HQ-OPPT-2016-0735-0022; Public Comment, EPA-HQ-OPPT-2016-0735-0008; |
| Commercial/consumer Use | Other uses[e] | Other (e.g., toys and games, car seats, toys and toy vehicles) | Use Document, EPA-HQ-OPPT-2016-0735-0003; Market Profile, EPA-HQ-OPPT-2016-0735; Public Comment, EPA-HQ-OPPT-2016-0735-0022; Public Comment, EPA-HQ-OPPT-2016-0735-0008; Public Comment, EPA-HQ-OPPT-2016-0735-0015; EPA-HQ-OPPT-2016-0735-0015; WSDE (2017). |

**Note**: This table presents categories and subcategories of activities that are based on the 2016 CDR industrial function category and industrial sector descriptions and the OECD product and article category descriptions for the HBCD uses identified. Clarification on the subcategories of use from the listed data sources are provided in parentheses.

[a] These categories of activities appear in the Life Cycle Diagram, reflect CDR codes and broadly represent activities in industrial and/or consumer settings.

[b] These subcategories reflect more specific uses of HBCD.

[c] 2015 SNUR; (U.S. EPA, 2015a), EPA requires 90-day notification before manufacture or processing of HBCD in consumer textiles, except those used in motor vehicles.

[d] Historically have been used.

[e] Other uses in EPA's Market Report 2017 (U.S. EPA, 2017g) were identified from foreign studies and product testing results, reporting by manufacturers to the state of Washington, and other sources. For the uses in other countries, it is uncertain whether similar U.S. products contain HBCD. In some of the articles, HBCD is present but may not have been intentionally used.

#### 2.2.2.2 Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation

Table 2-3 summarizes each life cycle stage and the corresponding categories and subcategories of conditions of use for HBCD that EPA expects to consider in the risk evaluation. Using the 2016 CDR, EPA identified industrial processing or use activities, industrial function categories and commercial use product categories. EPA identified the subcategories by supplementing CDR data with other published literature and information obtained through stakeholder consultations. For risk evaluations, EPA intends to consider each life cycle stage (and corresponding use categories and subcategories) and assess relevant potential sources of release and human exposure associated with that life cycle stage.

**Automotive Replacement Parts**
EPA received a public comment from the Global Automakers Association stating that HBCD is no longer used in new automobile manufacturing and is only present in replacement parts manufactured prior to date of the EPA HBCD Scoping Document (Public comment, EPA-HQ-OPPT-2016-0735-0027). Major automobile manufacturers have phased out use of HBCD in U.S. production but continue to use it in a few replacement parts, according to information provided to EPA by the Alliance of Automotive Manufacturers since publication of the HBCD Scope Document. Manufacturers identified three replacement parts containing HBCD, these are absorbers (front roof rail energy) and two types of insulator panels (Alliance of Automobile Manufacturers, 2018). EPA assumes that HBCD in these replacement parts is incorporated into EPS and XPS based on CDR reporting that showed the vast majority of use of HBCD was for EPS and XPS. For the risk evaluation, EPA will try to obtain more specific information on the three replacement parts, including whether they are domestically manufactured or imported, what materials incorporate the HBCD, and volumes used.

**Expanded Polystyrene (EPS) and Extruded Polystyrene (XPS) Foam**
"Building/Construction Materials" include products containing HBCD as a flame retardant primarily in XPS and EPS foam insulation products that are used for the construction of residential, public, commercial or other structures (UNEP, 2010; Weil and Levchik, 2009).

Use in EPS and XPS foam had accounted for 95% of all HBCD applications in the past decade (U.S. EPA, 2014a; UNEP, 2010). Based on information from market reports (U.S. EPA, 2017g), HBCD is used primarily in construction materials, which may include structural insulated panels (SIPS). The building and construction industry uses EPS and XPS foam thermal insulation boards and laminates for sheathing products. EPS foam prevents freezing, provides a stable fill material and creates high-strength composites in construction applications. XPS foam board is used mainly for roofing applications and architectural molding. HBCD is used in both types of foams because it is highly effective at levels less than 1% and, therefore, maintains the insulation properties of EPS and XPS foam (Morose, 2006a). EPS foam boards contain approximately 0.5% HBCD by weight in the final product and XPS foam boards contain 0.5-1% HBCD by weight (Public comment, EPA-HQ-OPPT-2016-0735-0017) (XPSA, 2017b; U.S. EPA, 2014a; Morose, 2006b).

According to the EPS-IA, an estimated 80-85% of EPS rigid foam insulation manufactured in the United States is molded from EPS resins supplied by EPS-IA member companies, none of which use HBCD (EPS Industry Alliance, 2017).

The XPS Association (XPSA) stated that its members, which are the major producers of XPS resin, supply the resin for more than 95% of the XPS foam insulation products manufactured for the North American market and that the remaining small percentage is probably made using imported resin (XPSA, 2017a). An intermediate step in manufacture of XPS foam insulation, compounding of masterbatch, in which HBCD, resins, and other chemicals are processed is described in Appendix B.

Some companies reuse EPS and XPS insulation. See discussion below in Recycling of EPS and XPS foam.

EPA is including the use of HBCD in XPS and EPS insulation using imported HBCD in the risk evaluation. There is a potential for import of HBCD for use in the manufacture of EPS and XPS foam insulation. Taking into account the high percentage of HBCD production volume dedicated to these two

uses in previous years and the fact that smaller EPS and XPS manufacturers may be currently using imported HBCD resin, EPA is including the processing and use of HBCD in XPS and EPS insulation and import of HBCD resin in the risk evaluation.

**Recycling of EPS and XPS foam**

To date, little is known by EPA about the recycling of EPS and XPS products containing HBCD. Schlummer et al. (Schlummer et al., 2017) notes that EPS and XPS foam in construction insulation materials are rarely recycled for numerous reasons, including that insulation waste is typically not separated from mixed waste stream and most insulation containing HBCD is still in place. Schlummer et al. (Schlummer et al., 2017) describe technologies available only on a small scale to separate HBCD from insulation panels and recycle polystyrene.

Reuse and recycling is available in the United States for consumers through removal of insulation during re-roofing projects. Two companies were identified that directly reuse (e.g., reuse without reforming) and recycle (e.g., melting and inserting into the manufacturing process) XPS and EPS foam insulation.

- Green Insulation Group: http://www.greeninsulationgroup.com/products/
- Nationwide Foam Recycling: http://nationwidefoam.com/what-you-can-recycle.cfm

Nationwide Foam Recycling, which is owned by Conigliaro Industries, Inc., indicate that their plant recycles all EPS insulation and reuses all XPS insulation (U.S. EPA, 2017g). Once processed, their recycled EPS roofing insulation is taken to polystyrene product manufacturers, notably picture frame manufacturers, mostly in China but also in domestic markets. The company also delivers recycled roofing material to other local EPS recycling plants that may use different processes. Nationwide Foam Recycling processes 90,000 pounds/year of EPS standard packaging and 10,000 pounds/year of EPS roofing material and estimated that 10-20% of EPS roofing material is recycled nationally. The company also reuses XPS roofing material due the special equipment needed to recycle XPS and indicated that XPS is rarely recycled in the United States. It was estimated that the majority (>50%) of XPS roofing material is sent to landfills or waste energy plants. Processing estimates for XPS material were not provided by the company.

**Disposal of Existing HBCD Products**

Despite industry indicating that production of HBCD products is declining, there is a large of amount of HBCD products still in use, particularly in construction materials. Eventually, buildings constructed with HBCD-containing products will be either demolished or remodeled and the HBCD containing products will need to be removed and either reused, disposed of or recycled.

**Summary of Conditions of Use Included in the Risk Evaluation**

Based on the information described in this section, EPA plans to analyze HBCD importation; incorporation into formulation, mixture or reaction product (e.g. compounding of masterbatch XPS); incorporation into articles (e.g. manufacture of EPS and XPS and the manufacture of structural insulated panels from EPS and XPS); disposal; recycling; and the industrial, commercial and consumer use of EPS and XPS in construction materials (e.g. insulation boards).

**Table 2-3. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation**

| Life Cycle Stage | Category[a] | Subcategory[b] | References |
|---|---|---|---|
| Manufacture | Import | Import | U.S. EPA (2016b) |
| Processing | Processing - incorporated into formulation, mixture or reaction product | Flame retardants used in custom compounding of resin (e.g., compounding in XPS masterbatch) | EINECS (2008) |
| | Incorporated into article | Flame retardants used in plastics product manufacturing (manufacture of XPS and EPS foam; manufacture of structural insulated panels (SIPS) and automobile replacement parts from XPS and EPS foam) | Use Document, EPA-HQ-OPPT-2016-0735-0003; Market Profile, EPA-HQ-OPPT-2016-0735; U.S. EPA (2014a) (Alliance of Automobile Manufacturers, 2018). |
| | Recycling | Recycling of XPS and EPS foam, resin, panels containing HBCD | Use Document, EPA-HQ-OPPT-2016-0735-0003 |
| Distribution | Distribution | Distribution | |
| Commercial/consumer Use | Building/construction materials | Plastic articles (hard): construction and building materials covering large surface areas (e.g., EPS/XPS foam insulation in residential, public and commercial buildings, and other structures) | Use Document, EPA-HQ-OPPT-2016-0735-0003; U.S. EPA (2016b); U.S. EPA (2014a) |
| | Other | Automobile replacement parts | (Alliance of Automobile Manufacturers, 2018) |
| Disposal | Disposal | Other land disposal (e.g. Construction and Demolition Waste) | EINECS (2008) |

**Note**: This table presents categories and subcategories of conditions of use that are based on the 2016 CDR industrial function category and industrial sector descriptions and the OECD product and article category descriptions for the HBCD uses identified. Clarification on the subcategories of use from the listed data sources are provided in parentheses.

[a] These categories of conditions of use appear in the Life Cycle Diagram, reflect CDR codes and broadly represent conditions of use of HBCD in industrial and/or consumer settings.

[b] These subcategories reflect more specific uses of HBCD.

### 2.2.2.3 Overview of Conditions of Use and Lifecycle Diagram

The life cycle diagram provided in Figure 2-1 depicts the conditions of use that are considered within the scope of the risk evaluation during various life cycle stages including manufacturing, processing, use (industrial, commercial, and consumer), distribution and disposal. Additions or changes to the conditions of use based on additional information gathered or analyzed during problem formulation are described in Sections 2.2.2.1 and 2.2.2.2. The activities that EPA determined are out of scope during problem formulation are not included in the life cycle diagram. The information is grouped according to Chemical Data Reporting (CDR) processing codes and use categories (including functional use codes for industrial uses and product categories for industrial, commercial and consumer uses), in combination with other data sources (e.g., published literature and consultation with stakeholders) to provide an overview of conditions of use. EPA notes that some subcategories of use may be grouped under multiple CDR categories.

Use categories include the following: "industrial use" means use at a site at which one or more chemicals or mixtures are manufactured (including imported) or processed. "Commercial use" means the use of a chemical or a mixture containing a chemical (including as part of an article) in a commercial enterprise providing saleable goods or services. "Consumer use" means the use of a chemical or a mixture containing a chemical (including as part of an article, such as furniture or clothing) when sold to or made available to consumers for their use (U.S. EPA, 2016b).

To understand conditions of use relative to one another and associated potential exposures under those conditions of use, the life cycle diagram includes the production volume associated with each stage of the life cycle, as reported in the 2016 CDR reporting (U.S. EPA, 2016b). However, the life cycle diagram for HBCD does not include specific production volumes because the information was claimed as confidential business information (CBI).

The 2016 CDR reporting data for HBCD are provided in Table 2-4 from EPA's CDR database (U.S. EPA, 2016b). This information has not changed from that provided in the HBCD Scope Document.

**Table 2-4. Production Volume of HBCD in CDR Reporting Period (2012 to 2015)[a]**

| Reporting Year | | 2012 | 2013 | 2014 | 2015 |
|---|---|---|---|---|---|
| Total Aggregate Production Volume (lbs) | CASRN 25637-99-4 | 1-10 million | 1-10 million | 1-10 million | 1-10 million |
| | CASRN 3194-55-6 | 10-50 million | 10-50 million | 1-10 million | 1-10 million |

[a] The CDR data for the 2016 reporting period is available via ChemView (https://java.epa.gov/chemview) (U.S. EPA, 2016b). Because of an ongoing CBI substantiation process required by amended TSCA, the CDR data available in the HBCD Scope Document is more specific than currently in ChemView.

**HBCD Production Volume (Manufacture and Import)**

Data reported for the CDR period for 2016 for HBCD indicate that between 1 and 10 million lbs of each CASRN were manufactured in or imported into the United States in 2015; the national production volume is CBI (U.S. EPA, 2016b). For both CASRNs, site-specific production volumes for the 2015 reporting year were withheld as TSCA CBI. Six firms comprised of nine sites are identified by the 2016 CDR as manufacturers or importers of HBCD: Chemtura Corporation, Albemarle Corporation, Dow Chemical Company, Campine NV, BASF Corporation, and Styropek USA, Inc (U.S. EPA, 2016b).

Current Status of Domestic Manufacture of HBCD

Industry has indicated complete replacement of HBCD in their product lines (U.S. EPA, 2017g) and that use of stockpiles and exportation was completed in 2017, as discussed in Section 2.2.2.1.

Current Status of Importation of HBCD

The companies that previously reported HBCD import volumes to CDR have stated to EPA that they permanently stopped the activity in 2016 or 2017. The Dow Chemical Company imported 19 metric tons (MT) of HBCD in 2016 and roughly 48 MT in 2017. Dow possessed roughly 41 MT of HBCD in stockpiles as of September 2017, which the company then used to produce XPS foam. By November 2017, Dow had stopped using HBCD at all of its plants and had no intention of importing HBCD in the future. (Dow Chemical Company, 2017).

Similarly, Campine NV indicated in a correspondence with EPA that they had ceased importation of HBCD in 2016 (Campine, 2017). BASF has indicated in a correspondence with EPA (BASF, 2017) that the company ceased importing HBCD in 2016 and currently has no stockpiles. ICL-IP[2] previously manufactured an HBCD-containing flame retardant marketed as FR-1206. However, this product has been discontinued, and ICL-IP has reportedly ceased production of products containing HBCD (Additives for Polymers, 2015). Styropek also indicated in its correspondences with EPA that the company phased out HBCD as a flame retardant in 2016.

Although there are a number of possible source countries for importation of HBCD to the United States, under the Stockholm Convention on Persistent Organic Pollutants (POPs), 171 of the 188 Parties (countries) have agreed to ban the production, use, import, and export of HBCD, consistent with the obligations of that Convention (SCCH, 2018a, b) . The Convention does include a process by which a party can apply for a time limited exemption to continue production and/or use of a listed chemical, however, that exemption is limited to the specific use(s) identified in the Convention. In accordance with Article 4, specific exemptions expire five years after the date of entry into force of the Convention with respect to that particular chemical, unless an additional five-year extension in granted by the Conference of the Parties (SCCH, 2018b). For HBCD, the specific uses for which a Party can register a production or use exemption is limited to use "in EPS and XPS in buildings." According to the *Register of Specific Exemptions* for the Convention, there are currently three Parties registered for production for those uses and six Parties registered for use. The United States is not a Party to the Convention (SCCH, 2018c).

Descriptions of the industrial, commercial and consumer use categories identified from the 2016 CDR (U.S. EPA, 2016b) and included in the life cycle diagram are summarized in Section 2.2.2.2. The descriptions provide a brief overview of the use category; Appendix B contains more detailed descriptions (e.g., process descriptions, worker activities, process flow diagrams, equipment illustrations) for each manufacture, processing, use and disposal category. The descriptions provided below are primarily based on the corresponding industrial function category and/or commercial and consumer product category descriptions from the 2016 CDR and can be found in EPA's Instructions for Reporting 2016 TSCA Chemical Data Reporting (U.S. EPA, 2016a).

Figure 2-1 depicts the life cycle diagram of HBCD from manufacture to the point of disposal. Activities related to distribution (e.g., loading, unloading) will be considered throughout the HBCD life cycle, rather than using a single distribution scenario.

[2] ICL-IP did not report to the 2016 CDR.

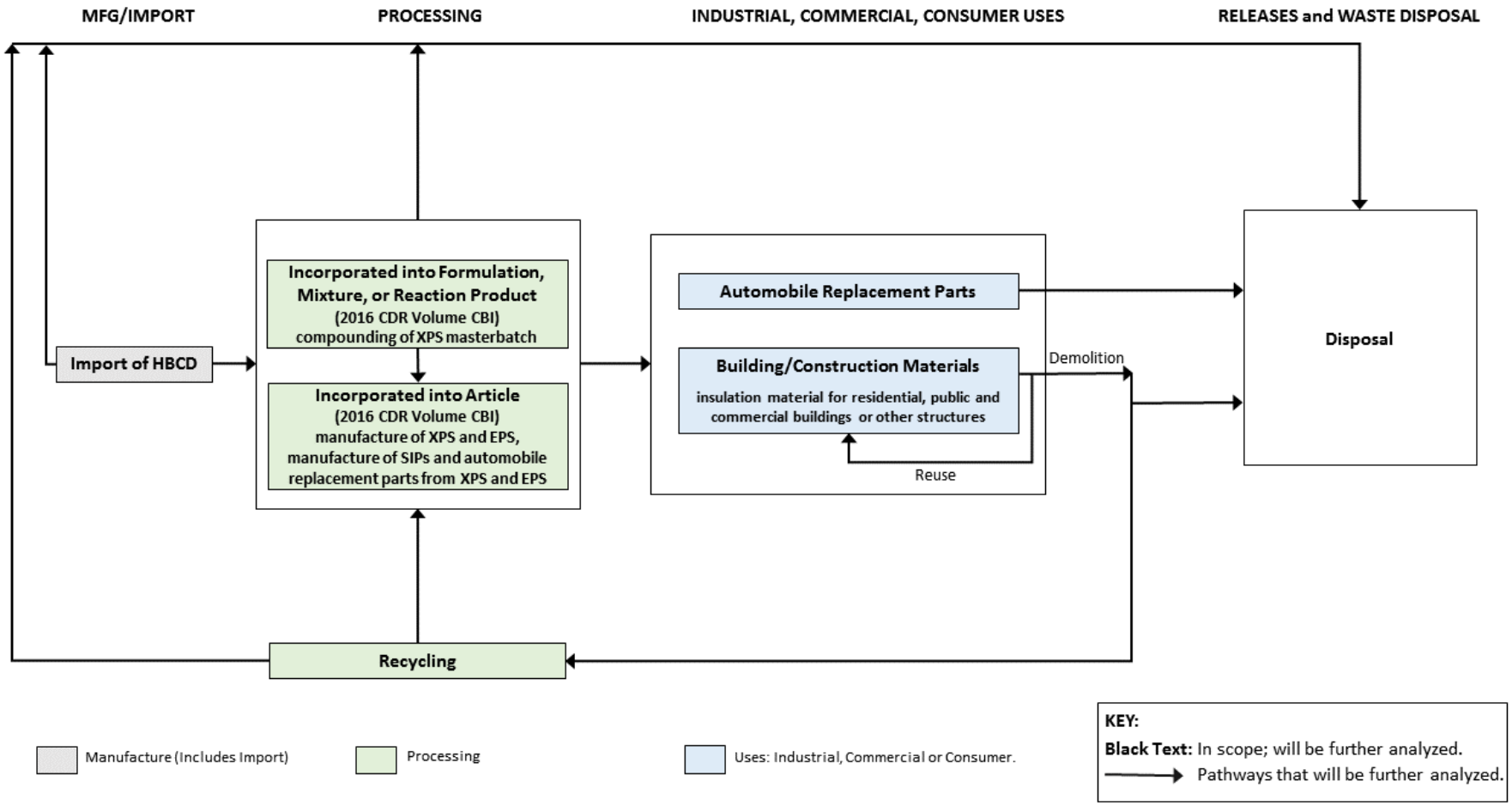


**Figure 2-1. HBCD Life Cycle Diagram**

The life cycle diagram depicts the conditions of use that are within the scope of the risk evaluation during various life cycle stages including manufacturing, processing, use (industrial, commercial, consumer), distribution and disposal. Activities related to distribution (e.g., loading, unloading) will be considered throughout the HBCD life cycle, rather than using a single distribution scenario.

## 2.3 Exposures

For TSCA exposure assessments, EPA expects to analyze exposures and releases to the environment resulting from the conditions of use applicable to HBCD. Post-release pathways and routes will be described to characterize the relationship or connection between the conditions of use of the chemical and the exposure to human receptors, including potentially exposed or susceptible subpopulations and ecological receptors. EPA will take into account, where relevant, the duration, intensity (concentration), frequency and number of exposures in characterizing exposures to HBCD.

### 2.3.1 Fate and Transport

Environmental fate includes both transport and transformation processes. Environmental transport is the movement of the chemical within and between environmental media. Transformation occurs through the degradation or reaction of the chemical with other species in the environment. Hence, knowledge of the environmental fate of the chemical informs the determination of the specific exposure pathways and potential human and environmental receptors EPA expects to analyze in the risk evaluation. Table 2-5 provides environmental fate data that EPA identified and considered in developing the scope for HBCD. This information has not changed from that provided in the HBCD Scope Document.

During problem formulation, EPA/OPPT considered volatilization during wastewater treatment, volatilization from lakes and rivers, biodegradation rates, organic carbon: water partition coefficient (log $K_{OC}$) and bioaccumulation potential when making changes to the conceptual models as described in Section 2.5. Systematic literature review is currently underway, so model results and basic principles were used to support the fate data used in problem formulation.

The environmental fate information on HBCD presented in Table 2-5 is based on information published in a number of publications (U.S. EPA, 2015c, 2014a; NICNAS, 2012b; EC/HC, 2011; EINECS, 2008; U.S. EPA, 2008; OECD, 2007a).

**Table 2-5. Environmental Fate Characteristics of HBCD**

| Property or Endpoint | Value [a] | References |
|---|---|---|
| Direct photodegradation | Does not undergo direct photolysis (estimated) | U.S. EPA (2015c) |
| Indirect photodegradation | 2.1 days (air) | U.S. EPA (2015c) |
| Hydrolysis half-life | Does not undergo hydrolysis | U.S. EPA (2015c) |
| Biodegradation half life | 0% in 28 days (aerobic in wastewater, OECD 301D)<br>$t_{1/2}$ = 63 days (aerobic soil, OECD 307)<br>$t_{1/2}$ = 7 days (anaerobic soil, OECD 308)<br>$t_{1/2}$ = 11-32 days (aerobic sediment, OECD 308)<br>$t_{1/2}$ = 1.1-1.5 days (anaerobic sediment, OECD 308)<br>$t_{1/2}$ = 0.66 days (anaerobic in sludge) | U.S. EPA (2015c) |
| Bioconcentration factor (BCF) | 8,974-18,100 (fish) | U.S. EPA (2015c) |
| Bioaccumulation factor (BAF) | 3,556,000 (estimated) | U.S. EPA (2012b) |

| Property or Endpoint | Value [a] | References |
|---|---|---|
| Organic carbon:water partition coefficient (log $K_{OC}$) | 4.9 | U.S. EPA (2015c) |
| [a] Measured unless otherwise noted. Based on literature review described in (U.S. EPA, 2015c), Problem formulation document https://www.epa.gov/sites/production/files/2015-09/documents/hbcd_problem_formulation.pdf. | | |

HBCD is persistent in environmental media. HBCD is expected to be stable to hydrolysis and direct photolysis. Measured aerobic biodegradation half-lives are on the order of months. Anaerobic biodegradation may be more rapid but in anaerobic conditions, degradation is also slow with half-lives on the order of days. HBCD is expected to sorb to particulates and sediments and has limited mobility in soil. Low water solubility (66 µg/l), organic carbon:water partitioning (log $K_{OC}$ = 4.9) and limited potential for aerobic and anaerobic biodegradation ($t_{½}$ of up to months) suggest that HBCD in wastewater treatment plants (WWTPs) will associate with biosolids which may subsequently be land applied.

HBCD has a low vapor pressure and Henry's law constant so is expected to have limited volatilization from soils and water surfaces. However, in air, HBCD is expected to occur primarily associated with particulates and exposure from dust and atmospheric particulates is likely. HBCD may undergo long-range transport and particulate bound HBCD will be removed from the atmosphere by wet or dry deposition, resulting in widespread occurrence in soil and water.

HBCD is highly bioaccumulative with BCF values of 8,974-18,100 indicating that consumption of animal products from aquatic and terrestrial species (fish, meat, and dairy) may result in exposure from bioaccumulation and trophic magnification. HBCD's estimated upper trophic level bioaccumulation factor (BAF) is 3,556,000 indicating very high bioaccumulation potential. The model prediction was obtained using the default settings of the EPI Suite™ (U.S. EPA, 2012c) BCFBAF module.

### 2.3.2 Releases to the Environment

Releases to the environment from conditions of use (e.g., industrial and commercial processes, commercial or consumer uses resulting in down-the-drain releases) are one component of potential exposure and may be derived from reported data that are obtained through direct measurement, calculations based on empirical data and/or assumptions and models.

A source of information that EPA expects to consider in the risk evaluation in evaluating exposure are data reported under the Toxics Release Inventory (TRI) program, however, TRI data are not yet available for HBCD. Under the Emergency Planning and Community Right-to-Know Act (EPCRA) Section 313 rule, HBCD is a TRI-reportable substance effective November 30, 2016. HBCD is reportable beginning with the 2017 calendar year and has been assigned a 100-pound reporting threshold. The first reporting forms from facilities are due by July 1, 2018.

There may be releases of HBCD from industrial sites to wastewater treatment plants (WWTP), surface water, air and landfill (U.S. EPA, 2015c). Sawing of EPS or XPS foam during commercial and consumer use results in release of HBCD to the environment and emissions of HBCD from EPS and XPS foam and wear of these products result in release of HBCD during their service life (U.S. EPA, 2015c). Disposal of EPS and XPS foam may result in releases to the environment as a result of demolition of buildings or material that is left on or in the soil (U.S. EPA, 2015c).

Articles that contain HBCD may release HBCD to the environment during use or through recycling and disposal. Examples of HBCD releases that are more recently being explored in the literature include release of HBCD from building materials through demolition (Duan et al., 2016) and sorption of suspended particles to clothing and transport down the drain during washing of textiles (Saini et al., 2016).

EPA expects to review these data in conducting the exposure assessment component of the risk evaluation for HBCD.

### 2.3.3 Presence in the Environment and Biota

Monitoring studies or a collection of relevant and reliable monitoring studies provide(s) information that can be used in an exposure assessment. Monitoring studies that measure environmental concentrations or concentrations of chemical substances in biota provide evidence of exposure.

Monitoring and biomonitoring data were identified in EPA's data search for HBCD.

***Environment***

HBCD has been widely detected in both the environment and biota. When considering monitoring studies reported in risk assessments completed to date and monitoring studies reported to open literature, there are hundreds of studies that have reported HBCD in various media ([*HBCD (CASRN 25637-99-4, 3194-55-6, 3194-57-8) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0735]; (NICNAS, 2012b; EC/HC, 2011; EINECS, 2008).

HBCD has been detected in a wide variety of environmental media. Based on review of previously completed assessments and EPA's problem formulation (U.S. EPA, 2015c), HBCD is expected to be present at relatively higher levels in sediment, soil and indoor dust. HBCD is also expected to be present in ambient air, indoor air and surface water at relatively lower levels. Physical-chemical properties influence the fate and transport of HBCD between media. For example, EPA expects to consider partitioning of HBCD to sediment within the water column and to suspended particles and dust in indoor environments (Law et al., 2014). HBCD has also been detected in remote areas as a result of long range transport and in very close proximity to industrial sources and many sampling locations in between (Law et al., 2014).

EPA plans to evaluate and review available environmental monitoring data in the risk evaluation.

***Biota***

HBCD has the potential to both persist ($T_{½}$ of months or longer in some media) and bioaccumulate (BCF = 9000 - 18,000) in the environment (UNEP, 2010). Once HBCD is present in the environment, it is available for uptake by a variety of species, including humans. HBCD has been detected in human milk, adipose tissue, blood and hair. HBCD has been detected in invertebrates, fish, birds, mammals and plants. HBCD is also present in edible fish, plants, milk and other food sources, and there are existing studies that quantify potential dietary exposures (NICNAS, 2012b; EC/HC, 2011; EINECS, 2008).

EPA plans to review available biomonitoring data in the risk evaluation.

### 2.3.4 Environmental Exposures

The manufacturing, processing, distribution, use and disposal of HBCD can result in releases to the environment.

Environmental exposures are informed by releases into the environment, overall persistence, degradation, and bioaccumulation within the environment, and partitioning across different media. EPA will evaluate exposures to aquatic and terrestrial organisms in aquatic and terrestrial environments. EPA will evaluate food-chain relationships where appropriate.

### 2.3.5 Human Exposures

EPA plans to analyze occupational, consumer and general population exposures. Subpopulations, including potentially exposed and susceptible subpopulations, within these exposed groups will also be considered.

#### 2.3.5.1 Occupational Exposures

EPA plans to analyze worker activities where there is a potential for exposure under the various conditions of use described in Section 2.2.2. In addition, EPA may analyze exposure to occupational non-users (i.e. workers, who do not directly handle the chemical but perform work in an area where the chemical is present) depending on available information. When data and information are available to support the analysis, EPA also expects to consider the effect(s) that engineering controls and/or personal protective equipment have on occupational exposure levels.

EPA anticipates inhalation of dust and other respirable particles (for example, particulate generated by hot wire cutting of EPS or XPS foam) as the most important HBCD exposure pathway for workers and occupational non-users (U.S. EPA, 2015c; NICNAS, 2012b; ECHA, 2009c; EINECS, 2008) however, dermal exposure, may also occur when performing certain work activities.

Workers and occupational non-users may be exposed to HBCD when performing activities associated with the conditions of use described in Section 2.2.2, including, but not limited to:

- Repackaging or unloading containers of HBCD powder or pellets.
- Handling, transporting and disposing waste containing HBCD.
- Cutting EPS or XPS foam (e.g., at constructions sites).

Based on these activities, EPA expects to analyze inhalation exposure to particulates and dermal exposure, including skin contact with particulates for workers and may also do so in the case of occupational non-users depending on available information. EPA also expects to consider potential worker exposure via the oral route such as from incidental ingestion of HBCD particulates that deposit in the upper respiratory tract from inhalation exposure.

Occupational exposure limits for HBCD have not been established by the Occupational Safety and Health Administration (OSHA), the American Conference of Government Industrial Hygienists (ACGIH), or the National Institute of Occupational Safety and Health (NIOSH). https://www.ncbi.nlm.nih.gov/books/NBK225635/

#### 2.3.5.2 Consumer Exposures

Exposure routes for consumers using HBCD-containing products and bystanders (non-product users that are incidentally exposed to the product or article, (U.S. EPA, 2017a)) may include inhalation of suspended particulates, dermal exposure due to contact with articles, and ingestion of settled dust and mouthing of articles.

Consumer exposure to articles containing HBCD is somewhat different from consumer exposure to a product where the chemical is consumed during its use and then discarded (for example, a can of spray paint). HBCD is incorporated into articles that may be present during the entire useful life of the article in microenvironments where consumers may be continually exposed until the article is disposed. HBCD-containing articles (e.g., insulation, electronics products, plastic based products and textiles) have relatively long service lives in comparison to other consumer products that are quickly used and discarded. Indoor environments with elevated levels of HBCD in indoor air and dust may contain some combination of articles containing HBCD.

The primary on-going consumer use of HBCD is within EPS and XPS insulation. In the 2015 Problem Formulation and Initial Assessment of HBCD (U.S. EPA, 2015c), EPA did not anticipate evaluating EPS and XPS insulation as a stand-alone scenario and instead planned to analyze indoor exposures from all sources of reported indoor air and dust concentrations. EPA will further analyze the source contribution of EPS and XPS insulation to levels of HBCD in indoor air and dust. EPA will also assess on-going uses of HBCD within automobile replacement parts. EPA plans to analyze uses of recycled articles back into EPS and XPS insulation. EPA does not expect to consider recycled articles, where those articles do not have intended flame retardant applications.

***Inhalation and Oral***

Consumer exposure to HBCD may include inhalation and ingestion exposure related to emissions of HBCD from articles. Indoor air and indoor dust concentrations may vary based on the source strength of emissions associated with the presence of articles. Emission from articles will vary based on the surface area of the article present in the building, the weight fraction of HBCD within the article and building characteristics such as air exchange and inter-zonal air flow. Based on the relatively high octanol: air partition coefficient ($K_{oa}$) and relatively low vapor pressure, HBCD emitted to indoor air is likely to partition to suspended particles and settle to indoor dust rather than be emitted in its vapor phase. EPA expects to further analyze ingestion of dust and inhalation of dust associated with conditions of use of HBCD.

***Dermal***

Consumer exposure to HBCD may include dermal exposure related to direct skin contact with articles containing HBCD. However, there are several factors to be considered and this is likely a relatively minor pathway compared to dermal contact with dust. The contact duration, solubility and diffusivity of HBCD within different articles, and contact surface area of skin all influence potential exposures (EINECS, 2008). EPA expects to consider dermal exposure associated with use of HBCD in EPS and XPS during installation and removal, contact with dust, and with recycled use applications.

There may be some consumers who may have greater exposure potential to HBCD such as:

- Children or adults who spend time in microenvironments with elevated dust or indoor air concentrations due to presence of multiple article which contain elevated levels of HBCD.
- Children or adults who have elevated dermal contact with EPS/XPS insulation containing HBCD.

EPA expects to analyze inhalation, dermal and oral exposures to consumers and bystanders associated with the conditions of use by consumers.

#### 2.3.5.3 General Population Exposures

Wastewater/liquid wastes, solid wastes or air emissions of HBCD could result in potential pathways for oral, dermal or inhalation exposure to the general population.

***Inhalation***

There is the potential for inhalation exposure to HBCD by breathing ambient air and indoor air. Ambient air concentrations may vary by proximity to an industrial source, while indoor air concentrations are discussed in the consumer exposure section. Based on the relatively high $K_{oa}$ and relatively low vapor pressure, HBCD is expected to be present primarily in suspended particles in the air rather than in the vapor phase.

Based on these potential sources and pathways of exposure, EPA expects to analyze inhalation exposures of the general population to air/particulates containing HBCD that may result from the conditions of use of HBCD.

***Oral***

The general population may ingest HBCD via several exposure pathways.

There is potential for oral exposure to HBCD by ingestion of dust and soil; drinking water and breast milk; and edible aquatic and terrestrial biota (e.g., from fishing, hunting, gathering and farming). There is a wide range of dust and soil monitoring data available. Dust concentrations vary widely across different microenvironments and within microenvironments and are generally reported in the ng/g or µg/g range (U.S. EPA, 2015c). Existing exposure assessments outside of the United States have quantified dietary exposure from a variety of food sources and compared these values to other pathways (Environment Canada, 2011; EINECS, 2008).

EPA does not expect to further analyze exposures from drinking water sources. Exposures from drinking water containing HBCD are possible, but are likely to be relatively lower than other oral exposure pathways (Environment Canada, 2011; EINECS, 2008). Drinking water monitoring data is generally unavailable. There are existing data on HBCD concentrations in surface water which are relatively low, below 1 µg/L. The physical-chemical and fate properties of HBCD, such as high sorption, low water solubility, and high $K_{OC}$ indicate that concentrations of HBCD in drinking water would be expected to be low prior to treatment. When sediment monitoring data is used with assumptions about $K_{OC}$, organic content and density of water and sediment, surface water concentrations can be estimated and are generally below the highest levels reported in surface water (ECHA, 2016). These same physical-chemical properties indicate that drinking water treatment processes would further reduce HBCD concentrations in drinking water. Overall, the contribution to exposure to HBCD via drinking water is expected to be low compared to other exposures.

Based on these potential sources and pathways of exposure, EPA expects to analyze oral exposures to the general population that may result from the conditions of use of HBCD.

***Dermal***

There is potential for dermal exposure to HBCD through contact with dust and soil containing HBCD. Dermal exposure is likely to vary based on the contact time with the material, the concentration of HBCD and properties of HBCD that influence dermal absorption (EINECS, 2008).

Based on these potential sources and pathways of exposure, EPA expects to analyze dermal exposures to the general population that may result from the conditions of use of HBCD.

#### 2.3.5.4 Potentially Exposed or Susceptible Subpopulations

TSCA requires EPA to determine whether a chemical substance presents an unreasonable risk to "a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation." TSCA §3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." General population is "the total of individuals inhabiting an area or making up a whole group" and refers here to the U.S. general population (U.S. EPA, 2011).

As part of the Problem Formulation, EPA identified potentially exposed and susceptible subpopulations for further analysis during the development and refinement of the life cycle, conceptual models, exposure scenarios, and analysis plan. In this section, EPA addresses the potentially exposed or susceptible subpopulations identified as relevant based on greater exposure. EPA will address the subpopulations identified as relevant based on greater susceptibility in the hazard section.

Of the human receptors identified in the previous sections, EPA identifies the following as potentially exposed or susceptible subpopulations due to their *greater exposure* that EPA expects to consider in the risk evaluation:

- Workers and occupational non-users.
- Consumers and bystanders associated with consumer use. HBCD has been identified as being used in products available to consumers; however, only some individuals within the general population may use these products. Therefore, those who do use these products are a potentially exposed or susceptible subpopulation due to greater exposure.
- Other groups of individuals within the general population who may experience greater exposures due to their proximity to conditions of use identified in Section 2.2 that result in releases to the environment and subsequent exposures (e.g., individuals who live or work near manufacturing, processing, distribution, use or disposal sites).

There are some reasonably likely exposure scenarios where greater exposure from multiple sources may occur. There may be some individuals who have greater potential for exposure to HBCD such as:

- Children who spend time in microenvironments with elevated dust concentrations.
- Breast-fed infants where concentrations of breast milk containing HBCD are elevated.
- Children or adults who ingest soil or sediment in environments where HBCD concentrations are elevated.
- Children or adults who consume edible aquatic biota or terrestrial biota containing elevated levels of HBCD.

In developing exposure scenarios, EPA will analyze available data to ascertain whether some human receptor groups may be exposed via exposure pathways that may be distinct to a particular subpopulation or lifestage (e.g., children's crawling, mouthing or hand-to-mouth behaviors) and whether some human receptor groups may have higher exposure via identified pathways of exposure due to unique characteristics (e.g., activities, duration or location of exposure) when compared with the general population (U.S. EPA, 2006a).

In summary, in the risk evaluation for HBCD, EPA plans to analyze the following potentially exposed groups of human receptors: workers, occupational non-users, consumers, bystanders associated with consumer use. As described above, EPA may also identify additional potentially exposed or susceptible subpopulations that will be considered based on greater exposure.

## 2.4 Hazards (Effects)

For scoping, EPA conducted comprehensive searches for data on hazards of HBCD, as described in *Strategy for Conducting Literature Searches for HBCD: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0735) (U.S. EPA, 2017f). Based on initial screening, EPA plans to analyze the hazards of HBCD identified in this problem formulation document. However, when conducting the risk evaluation, the relevance of each hazard within the context of a specific exposure scenario will be judged for appropriateness. For example, hazards that occur only as a result of chronic exposures may not be applicable for acute exposure scenarios. This means that it is unlikely that every identified hazard will be analyzed for every exposure scenario.

### 2.4.1 Environmental Hazards

For scoping purposes, EPA consulted the sources of environmental hazard data for HBCD found in Table 2-6. However, EPA also expects to consider other studies (e.g., more recently published, alternative test data) that have been published since these reviews, as identified in the literature search conducted by the Agency for HBCD [*HBCD (CASRN 25637-99-4, 3194-55-6, 3194-57-8) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0735]. Only the on-topic references listed in the Ecological Hazard Literature Search Results were considered as potentially relevant data/information sources for the risk evaluation. Inclusion criteria were used to screen the results of the ECOTOX literature search (as explained in the *Strategy for Conducting Literature Searches for HBCD: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0735) (U.S. EPA, 2017f). Data from the screened literature are summarized below (Table 2-6)as ranges (min-max). EPA plans to review these data/information sources during risk evaluation using the data quality review evaluation metrics and the rating criteria described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018).

**Table 2-6. Summary of Aquatic and Sediment Environmental Hazard Information for HBCD**

| Test Organism | Duration | Endpoint | Hazard Value | Effect Type | Units | Reference |
|---|---|---|---|---|---|---|
| **Aquatic Organisms** | | | | | | |
| **Fish** | Acute | $LC_{50}$ | 0.0025 - >100 | mortality | mg/L | (WILDLIFE INTERNATIONAL LTD, 1997), (Calmbacher, 1978) |
| | Chronic | NOEC | 0.0037 - <500 | growth and reproduction | mg/L | (Zhang et al., 2008; Drottar and Krueger, 2000) |
| | | LOEC | 0.1 | DNA damage | mg/L | (Zhang et al., 2008) |
| | | MATC | >0.032 | Larvae malformations | mg/L | (Hong et al., 2014) |
| **Invertebrates** | Acute | $EC_{50}$ | >0.0032 - 146 | immobility | mg/L | (Wildlife Intl LTD, 1997; BASF, 1990) |
| | Chronic | NOEC | 0.0031 | growth and reproduction | mg/L | (Drottar and Krueger, 1998) |
| | | LOEC | 0.0056 – 0.1 | Growth; gill degeneration | mg/L | (Smolarz and Berger, 2009; Drottar and Krueger, 1998) |
| | | MATC | 0.0042 | growth | mg/L | (Drottar and Krueger, 1998) |
| **Plants** | Chronic | $EC_{50}$ | 0.009 - >500 | Growth; | mg/L | (Walsh et al., 1987); |
| | | MATC | 0.01 | | mg/L | (BASF CORP, 1990) |
| **Amphipod** | | NOEC | 100 – 1,000 | No effect mentioned in Thomas paper | mg/kg dwt | (Thomas et al., 2003a, b) for both ends of range |
| | | LOEC | 500 | Survival | mg/kg dwt | (Thomas et al., 2003a, b) |
| **Oligochaetes** | | NOEC | 3.1 | population | mg/kg dwt | (Oetken et al., 2001) |
| | | LOEC | 28.7 | population | mg/kg dwt | (Oetken et al., 2001) |
| | | MATC | 15.4 (normalized) | population | mg/kg dwt | (Oetken et al., 2001) |
| **Terrestrial Organisms** | | | | | | |
| **Avian** | Chronic | LOEC | 125 | reduction in hatchability | µg/L | (MOEJ, 2009) |
| | | | 15 | reduced chick survival | mg/L | |
| | | | 2.1 | | mg/kg/day | |
| | | | 5 | | mg/L | |
| | | LOEC | 164.3 | reduced corticosterone response in male nestling kestrels, reduced flying activities in juvenile males, delayed response time to predator avoidance in juvenile females | ng/g wet weight of egg | (Kobiliris, 2010) |
| **Earthworm** | Chronic | $EC_{10}$ | 21 | reproduction | mg/kg/dwt. | (Aufderheide et al., 2003) |
| | | NOEC | 128 | | | |
| **Plants** | Chronic | NOEC | >5,000 | Not reported | mg/kg/dwt | (Porch et al., 2002) |

EPA expects to analyze the hazards of HBCD to aquatic organisms including fish, aquatic invertebrates, aquatic plants and sediment invertebrates exposed to relevant media under acute and chronic exposure conditions. Based on the assessments mentioned above, there was acute toxicity to aquatic invertebrates from HBCD, based on mortality and immobilization. Chronic toxicity to aquatic invertebrates (growth and reproduction) was observed when exposed to HBCD. Chronic toxicity was observed in sediment dwelling organisms based on reduced survivability when exposed to HBCD.

EPA expects to analyze the hazards of HBCD to terrestrial organisms including soil invertebrates and avian species exposed to relevant media under acute and chronic exposure conditions. Based on previous assessments, chronic toxicity to terrestrial invertebrates (reproduction) was observed when exposed to HBCD. Also, toxicity to avian species was observed, based on reduced hatchability and survival, when exposed to HBCD.

### 2.4.2 Human Health Hazards

The human health hazard of HBCD has been examined in several publications (U.S. EPA, 2016c, 2014a, d; NICNAS, 2012b; Environment Canada, 2011; EINECS, 2008; U.S. EPA, 2008; OECD, 2007b). EPA expects to consider potential human health hazards associated with HBCD. Based on reasonably available information, the following sections describe the hazards EPA expects to further analyze.

HBCD does not have an existing EPA IRIS Assessment; however, as part of a coordinated agency effort, in the TRI Technical Review of HBCD (U.S. EPA, 2016c), the TSCA Work Plan Problem Formulation and Initial Assessment, (U.S. EPA, 2015c), and *Preliminary Materials for the IRIS Toxicological Review of HBCD* (U.S. EPA, 2014d), non-cancer health hazards of HBCD were compiled and reviewed, including: acute toxicity, liver toxicity, thyroid toxicity, reproductive/developmental toxicity, neurotoxicity, immunotoxicity, sensitization and irritation. EPA relied heavily on this comprehensive review in preparing this Problem Formulation. EPA also expects to evaluate other studies (e.g., more recently published, alternative test data) that have been published since these reviews during the analysis phase of the risk evaluation, as identified in the literature search conducted by the Agency for HBCD [*HBCD (CASRN 25637-99-4, 3194-55-6, 3194-57-8) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0735]. EPA expects to use these previous analyses as a starting point for identifying key and supporting studies to inform the human health hazard assessment, including dose-response analysis. The relevant studies will be evaluated using the data quality criteria in the *Application of Systematic Review in TSCA Risk Evaluations* document (U.S. EPA, 2018).

#### 2.4.2.1 Non-Cancer Hazards

***Acute Toxicity***

Animal studies have observed potential neurological effects and clinical signs of toxicity including death following high-dose acute administration of HBCD (U.S. EPA, 2015c).

***Liver Toxicity***

Increased liver weight has been observed in multiple laboratory animal studies, in both sexes, across species and following both adult and developmental exposures. In mice, HBCD exposure induced evidence of inflammatory changes in the liver and hepatic fatty changes (steatosis) in animals with a high-fat diet (U.S. EPA, 2014d).

***Thyroid Toxicity***
Human epidemiological studies have reported potential effects of HBCD on thyroid hormones. Animal toxicity studies provide stronger evidence of thyroid perturbation associated with HBCD exposure, including altered levels of thyroid hormones, histological changes and increased thyroid weight, with effects observed across multiple lifestages, sexes, species and exposure durations (U.S. EPA, 2014d).

***Reproductive/Developmental Toxicity***
For female reproductive effects, there is some rodent evidence that HBCD may alter fertility and pregnancy outcomes as well as reduce the number of mature and developing follicles in the ovary; however, effects on reproductive organ weight are inconsistent. The potential for HBCD to affect the female reproductive system has not been investigated in humans. For male reproductive effects, there is some epidemiological support of an association between HBCD exposure and altered serum testosterone and sex hormone binding globulin (SHGB) levels; however, animal studies did not report any effects on male reproductive organ weights, reproductive development, hormone concentrations or spermatogenic measures. There is mixed epidemiological data on developmental toxicity of HBCD, while animal toxicity studies suggest that early life exposure to HBCD at high doses can affect various developmental outcomes, including reduced offspring viability, decrements in pup weight and alterations in eye opening (U.S. EPA, 2014d).

***Neurotoxicity***
There is an absence of a strong association between HBCD exposure and developmental neurotoxicity in various neuropsychological domains observed in the limited epidemiological studies that are available; however, there is evidence of potential developmental neurotoxicity in rodents. Perinatal HBCD exposure was shown to alter neurodevelopmental milestones while eliciting changes in locomotor activity and executive function that persisted into adulthood. HBCD exposure also appears to affect other neurological endpoints related to changes in auditory sensitivity, dopamine system function and brain weight in multiple studies. Effects on neurodevelopmental endpoints were observed in both sexes and across a wide range of doses and exposure durations. However, there is currently not any substantial evidence to support concern for neurotoxicity when exposure is limited to adulthood (U.S. EPA, 2014d).

***Immunotoxicity***
The effects of HBCD on both functional and structural immune endpoints have been evaluated in animal models. Overall, immunological effects from HBCD exposure are variable and inconsistent across studies for endpoints such as immune organ weights, hematology or histopathology (U.S. EPA, 2014d), and its relevance to the risk evaluation will require further evaluation.

***Sensitization/Irritation***
There is limited information available suggesting potential mild irritation and sensitizing potential of HBCD (U.S. EPA, 2015c).

#### 2.4.2.2 Genotoxicity and Cancer Hazards

Available data suggest that HBCD is not genotoxic. Existing assessments have also concluded, based on genotoxicity information and a limited lifetime study, that HBCD is not carcinogenic (NICNAS, 2012b; EINECS, 2008; TemaNord, 2008; OECD, 2007b). Although the current data does not appear to provide sufficient evidence that HBCD is carcinogenic, EPA will further evaluate genotoxicity and other cancer hazards in the risk evaluation as part of a systematic review.

#### 2.4.2.3 Potentially Exposed or Susceptible Subpopulations

TSCA requires that the determination of whether a chemical substance presents an unreasonable risk include consideration of unreasonable risk to "a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation" by EPA. TSCA § 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." In developing the hazard assessment, EPA will evaluate available data to ascertain whether some human receptor groups may have greater susceptibility than the general population to the chemical's hazard(s).

## 2.5 Conceptual Models

EPA risk assessment guidance (U.S. EPA, 2014c, 1998), defines Problem Formulation as the part of the risk assessment framework that systematically identifies the factors to be considered in the assessment. It draws from the regulatory, decision-making and policy context of the assessment and informs the assessment's technical approach.

A conceptual model describes the actual or predicted relationships between the chemical substance and receptors, either human or environmental. These conceptual models are integrated depictions of the conditions of use, exposures (pathways and routes), hazards and receptors. The initial conceptual models describing the scope of the assessment for HBCD, have been refined during problem formulation. The changes to the conceptual models in this problem formulation are described along with the rationales.

In this section EPA outlines those pathways that will be included and further analyzed in the risk evaluation; will be included but will not be further analyzed in the risk evaluation; and will not be included in the TSCA risk evaluation and the underlying rationale for these decisions.

EPA determined as part of problem formulation that it is not necessary to conduct further analysis on certain exposure pathways that were identified in the HBCD Scope Document and that remain in the risk evaluation. Each risk evaluation will be "fit-for-purpose," meaning not all conditions of use will warrant the same level of evaluation and the Agency may be able to reach some conclusions without extensive or quantitative risk evaluations. 82 FR 33726, 33734, 33739 (July 20, 2017).

As part of this problem formulation, EPA also identified exposure pathways under regulatory programs of other environmental statutes, administered by EPA, which adequately assess and effectively manage exposures and for which long-standing regulatory and analytical processes already exist, i.e., the Safe Drinking Water Act (SDWA), the Clean Water Act (CWA) and the Resource Conservation and Recovery Act (RCRA). OPPT worked closely with the offices within EPA that administer and implement the regulatory programs under these statutes. In some cases, EPA has determined that the chemicals present in various media pathways (i.e., air, water, land) fall under the jurisdiction of existing regulatory programs and associated analytical processes carried out under other EPA-administered statutes and have been assessed and effectively managed under those programs. EPA believes that the TSCA risk evaluation should generally focus on those exposure pathways associated with TSCA conditions of use that are not adequately assessed and effectively managed under the regulatory regimes discussed above because these pathways are likely to represent the greatest areas of risk concern. As a result, EPA does not expect to include in the risk evaluation certain exposure pathways identified in the HBCD Scope Document.

### 2.5.1 Conceptual Model for Industrial and Commercial Activities and Uses: Potential Exposures and Hazards

The revised conceptual model (Figure 2-2) illustrates the pathways of exposure from industrial and commercial activities and uses of HBCD that EPA plans to evaluate. There are exposures to workers and occupational non-users via the inhalation and oral routes and to workers via the dermal route during processing and use for the conditions of use identified in this problem formulation.

The industrial and commercial activities/uses that EPA expects to consider are those that are conditions of use. As discussed in Section 2.2.2.2, these activities include importation of HBCD; compounding of XPS master batch; manufacture of XPS; manufacture of EPS; manufacture of SIPs; manufacture of automobile replacement parts; and use of XPS, EPS, and SIPs in construction.

EPA expects to further analyze pathways and routes of exposure that may occur during repackaging, processing steps (i.e., plastics compounding; plastics converting and SIP assembly; recycle of EPS), use (i.e., installation/reuse/demolition of EPS/XPS foam) and disposal (i.e., handling of wastes) including:

- Inhalation of dust containing HBCD by workers and occupational non-users. EPA expects this to be an important exposure route for workers and occupational non-users (U.S. EPA, 2015c).
- Dermal exposure to HBCD solids by workers that may occur as a result of handling particulate solids (OECD, 2015; EINECS, 2008).
- Ingestion of HBCD by workers and occupational non-users from ingestion of dust that deposits in the upper respiratory tract and is swallowed.

EPA does not plan to further analyze exposure to liquid. Based on information from the 2016 CDR, all importers reported solid physical forms of HBCD and therefore, worker and non-occupational user exposure to liquid HBCD is not expected.

For each condition of use identified in Table 2-3 a determination was made as to whether or not each unique combination of exposure pathway, route, and receptor will be further analyzed in the risk evaluation. The results of that analysis along with the supporting rationale are presented in Appendix C.

**Waste Handling, Treatment and Disposal**

Figure 2-2 shows that waste handling, treatment and disposal is expected to lead to the same pathways as other industrial and commercial activities and uses. The path leading from the "Waste Handling, Treatment and Disposal" box to the "Hazards Potentially Associated with Acute and/or Chronic Exposures" box was re-routed to accurately reflect the expected exposure pathways, routes, and receptors associated with these conditions of use of HBCD.

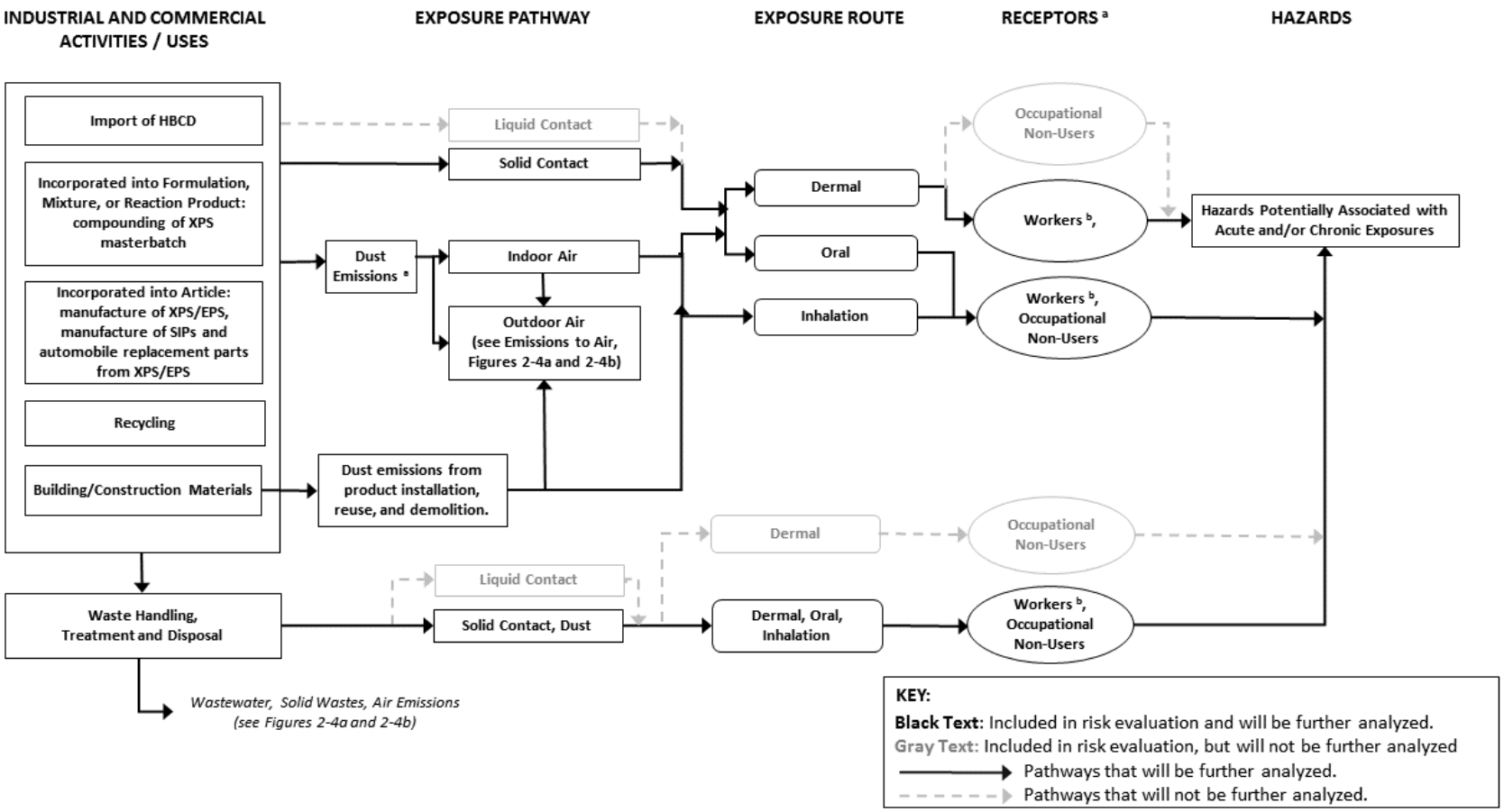


**Figure 2-2. HBCD Conceptual Model for Industrial and Commercial Activities and Uses: Worker and Occupational Non-User Exposures and Hazards**

The conceptual model presents the exposure pathways, exposure routes and hazards to human receptors from industrial and commercial activities and uses of HBCD.

[a] Receptors include potentially exposed or susceptible subpopulations (see Section 2.3.5.4).

[b] When data and information are available to support the analysis, EPA also considers the effect that engineering controls and/or personal protective equipment have on occupational exposure levels.

### 2.5.2 Conceptual Model for Consumer Activities and Uses: Potential Exposures and Hazards

Figure 2-3 presents the conceptual model for human receptors from consumer uses of HBCD. This conceptual model has been modified to indicate the exposure pathways that will and will not be further analyzed. More detailed information can be found in Appendix D.

EPA expects to consider certain conditions of use related to consumer uses. As described in Section 2.2.2.2, these uses include building and construction materials.

HBCD is present in consumer articles, many of which are found in indoor environments such as the home. The service-life of articles will vary based on the type of article (e.g., textile, electronics, structural insulation panel) but are expected to range from months to years. Service-life is defined as the length of time an article or consumer good is used before it is disposed of or recycled. Over this period of time, there is potential for long-term continuous low-level releases which may contribute to levels of HBCD found within indoor dust and air. These articles may be recycled and reintroduced into the indoor environment at the end of their service-life. HBCD within indoor air is expected to be present primarily as a particulate, rather than a vapor. Depending on recycling/reuse patterns and processes for different types of articles, HBCD may continue to be present within articles for another service life of the recycled or reused product.

Figure 2-3 illustrates exposure pathways for consumers from consumer uses of HBCD. EPA expects to analyze pathways and routes of exposure that may occur during use or disposal of building and construction materials or recycled products including:

- Ingestion of suspended or settled dust containing HBCD by consumers and bystanders. Ingestion of suspended dust may occur by inhalation of dust that deposits in the upper respiratory tract and is swallowed. Ingestion of settled dust may occur via hand to mouth behavior.
- Inhalation of suspended dust containing HBCD by consumers and bystanders. EPA expects this to be an important route of exposure.
- Dermal exposure to HBCD solids by consumers that may occur as a result of handling of articles or dermal contact with dust.

The primary route of exposure for consumers to HBCD is via ingestion of suspended or settled dust. This will be evaluated for both EPS/XPS insulation and for replacement automobile parts. Oral exposure related to mouthing of articles is not expected for the primary ongoing use of HBCD in EPS/XPS insulation. Ingestion of dust via hand to mouth behavior may also occur. Younger children (e.g., infants and toddlers) may be susceptible receptors due to higher dust ingestion rates and higher frequency and duration of hand and object to mouth contact, when compared to older children and adults.

Inhalation of suspended dust may also occur from abraded particles or resuspended settled dust and this will be further analyzed.

Dermal exposure to consumers from HBCD containing articles may occur during contact with dust and handling of articles. The potential for HBCD to absorb dermally under different conditions, will be further analyzed during risk evaluation.

The primary routes of exposure resulting from consumer handing of disposal of waste is inhalation and oral ingestion of suspended particulate including dust. Under some conditions such as renovation of a home, it is possible that abraded dust from articles, such as structural insulation panels, could result in elevated levels of dust compared to those typically found in monitoring studies. Renovation and abrasion of dust will be further analyzed during risk evaluation as part of an EPS/XPS exposure scenario rather than as a stand-alone consumer handling and disposal of waste scenario.

EPA does not plan to further analyze liquid contact to HBCD for consumers or bystanders as HBCD is incorporated into articles in the solid form.

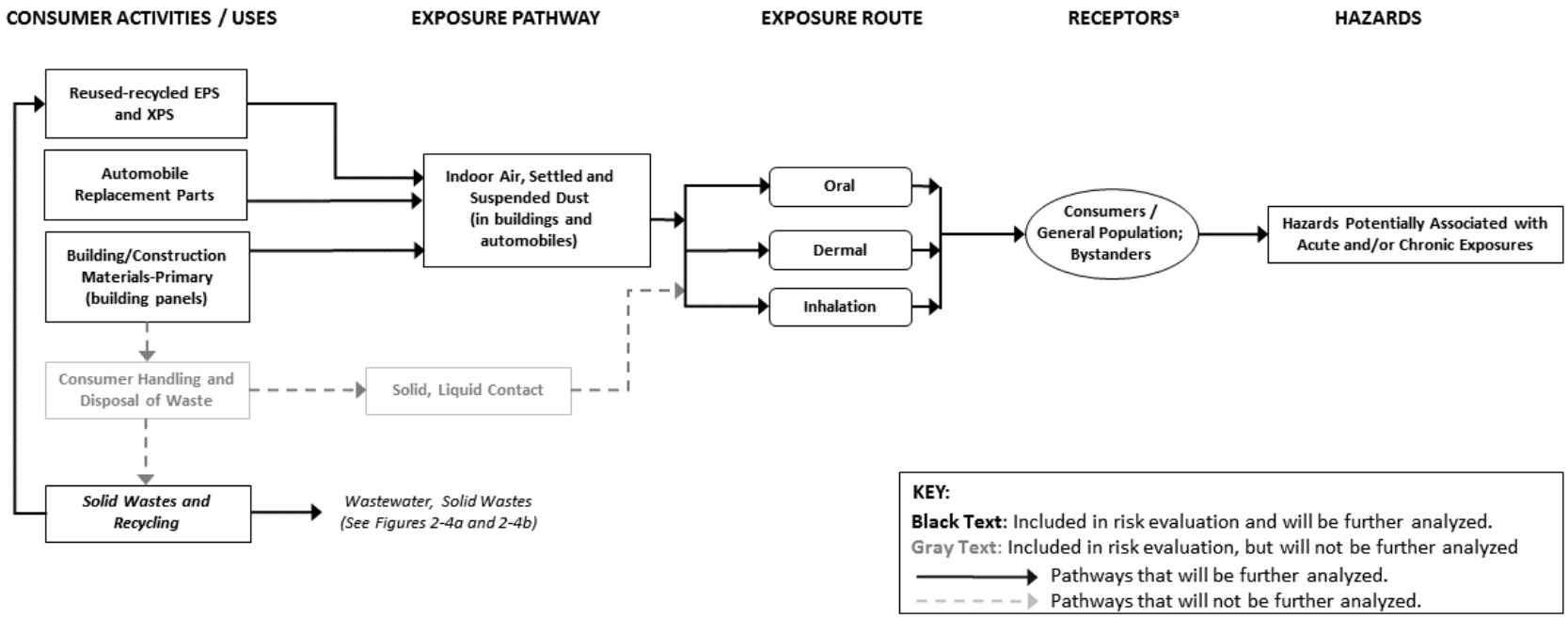


**Figure 2-3. HBCD Conceptual Model for Consumer Activities and Uses: Consumer Exposures and Hazards**

The conceptual model presents the exposure pathways, exposure routes and hazards to human receptors from consumer activities and uses of HBCD.

[a] Receptors include potentially exposed or susceptible subpopulations (see Section 2.3.5.4).

### 2.5.3 Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards

The revised conceptual models (Figure 2-4a and Figure 2-4b) illustrate the expected exposure pathways to human and ecological receptors from environmental releases and waste streams associated with industrial and commercial activities for HBCD that EPA expects to include in the risk evaluation. The pathways that EPA plans to include and analyze further in the risk evaluation are described in Section 2.5.3.1 and are shown in the conceptual models. The pathways that EPA plan to include in the risk evaluation but not further analyze are described in Section 2.5.3.2 and the pathways that EPA does not expect to include in risk evaluation are described in Section 2.5.3.3.

#### 2.5.3.1 Pathways that EPA Plans to Include and Further Analyze in Risk Evaluation

Pathways that EPA expects to further analyze include:

- Emissions to air: The general population including populations and ecological receptors living near industrial and commercial facilities processing, using or disposing of HBCD may be exposed via inhalation of suspended HBCD particulate in the ambient air from fugitive or stack emissions; and ingestion of HBCD from uptake from the environment into food sources (via indirect deposition into water bodies or soil).
- Releases to surface water (and sediment): The general population including populations living near industrial and commercial facilities processing, using or disposing of HBCD may be exposed by incidental ingestion of surface water and suspended particulates and by ingestion of HBCD from uptake (via direct or indirect deposition into water bodies or soil) from the environment into food sources. Aquatic and terrestrial ecological receptors may also be directly exposed due to proximity to surface water and sediment.
- Biosolid application to soil from wastewater: Ecological receptors and the general population including populations living near industrial and commercial facilities processing, using or disposing of HBCD may be exposed by incidental soil ingestion or uptake from the environment into food sources, particularly for backyard fruit and vegetable gardens near facilities.

HBCD has a relatively low water solubility (66 ug/L) and high log $K_{OC}$ (4.9) and tends to sorb to solids in surface water, groundwater and wastewater. It is resistant to aerobic biodegradation ($t_{½}$= months) and hydrolysis; therefore, it is not degraded during wastewater treatment and will tend to associate with sludge. If land applied, treated biosolids will transfer HBCD to soil where it will be taken up by biota and bioaccumulate in the terrestrial and human food chain. From soil, it may be transported to surface water by runoff and particulate erosion and be taken up by and bioaccumulate in aquatic species. Emissions to air are also expected to occur and a long vapor ($t_{½}$ > days) and particulate phase half-life indicates that long range transport can occur. Deposition to soil and water from air may also lead to HBCD concentrations in soil and water far from the source location.

As HBCD is bioaccumulative (estimated BAF of 3,556,000, see Table 2-5), oral exposure via ingestion of food items such as fish, meat, eggs, dairy products and plants are expected. The primary route of exposure for the general population is expected to be via ingestion of terrestrial biota and aquatic biota. There may be additional oral exposure to young children from ingestion of breast milk and from indoor dust exposure.

As shown in Figure 2-4a, EPA anticipates that the general population living near industrial and commercial facilities processing, using or disposing of HBCD may be exposed via several pathways. As

HBCD is persistent and bioaccumulative, releases to the environment from industrial or commercial activities are expected to result in exposures to human receptors via inhalation, ingestion of water, breast milk and edible aquatic and terrestrial biota (e.g., from fishing, hunting, gathering, farming).

Releases of HBCD to the environment from industrial or commercial activities may also result in exposure to aquatic and terrestrial life via contaminated water, sediment or soil as shown in Figure 2-4b. Trophic magnification may result in greater exposure following bioaccumulation. Based on the potential for bioaccumulation, it is expected that terrestrial species will also be exposed to HBCD via the food chain.

***Air Pathways***
Particulate-associated HBCD may result in transport and subsequent inhalation exposure. This is not expected to be a primary route of exposure although those living near a facility which release HBCD may experience higher levels of exposure than the general population. Atmospheric transport and off-site deposition may also contribute to low levels of contamination away from the release location which may contribute to environmental bioaccumulation from water and soil.

***Water Pathways***
Currently, no states or tribes include criteria for HBCD in water quality standards and values are not available for use in NPDES permits. Thus, EPA cannot conclude that risk to human health and aquatic life from exposure to HBCD in ambient waters has been effectively managed. As a result, this pathway will undergo risk evaluation under TSCA. EPA may publish CWA section 304(a) human health or aquatic life criteria for HBCD in the future if it is identified as a priority under the CWA.

***Biosolids Pathways***
This pathway will undergo risk evaluation under TSCA.

***Disposal Pathways***
HBCD or HBCD containing articles may be disposed of in construction and demolition waste landfills by commercial and consumer users. Land disposal of HBCD in EPS/XPS building materials (e.g. insulation) is expected to be the primary disposal pathway for these materials and is likely to occur at construction and demolition landfills.

#### 2.5.3.2 Pathways that EPA Plans to Include in the Risk Evaluation but Not Further Analyze

***Drinking Water Pathways***
Exposures from drinking water containing HBCD are possible, but are likely to be relatively lower than other oral exposure pathways (Environment Canada, 2011; EINECS, 2008). Drinking water monitoring data is generally unavailable. There are existing data on HBCD concentrations in surface water which are relatively low, below 1 µg/L. The physical-chemical and fate properties of HBCD, such as high sorption, low water solubility, and high $K_{OC}$ indicate that concentrations of HBCD in drinking water would be expected to be low prior to treatment. When sediment monitoring data is used with assumptions about $K_{OC}$, organic content and density of water and sediment, surface water concentrations can be estimated and are generally below the highest levels reported in surface water (ECHA, 2016). These same chemical and fate properties would indicate that drinking water treatment processes would

further reduce HBCD concentrations in finished drinking water. Overall, the contribution to exposure to HBCD via drinking water is expected to be low compared to other exposures.

Direct or indirect discharge of wastewater to surface water may occur and runoff from land application fields may transport HBCD into surface water. Leaching to groundwater is expected to be limited by low water solubility and high sorption potential. HBCD has a relatively low water solubility and will tend to sorb to solids in surface and groundwater. It is expected to be removed by water treatment and exposure to the general population via drinking water is expected to be low. HBCD will tend to sorb to subsurface soils. Reductive de-bromination may result in subsurface degradation with $t_{1/2}$ of months or longer. HBCD may migrate to groundwater but exposure via this pathway may be limited.

#### 2.5.3.3 Pathways that EPA Does Not Expect to Include in the Risk Evaluation

Exposures to receptors (i.e. general population, terrestrial species) may occur from industrial and/or commercial uses, industrial releases to air, water or land, and other conditions of use. As described in Section 2.5, EPA does not expect to include in the risk evaluation pathways under programs of other environmental statutes, administered by EPA, which adequately assess and effectively manage exposures and for which long-standing regulatory and analytical processes already exist. These pathways are described below.

***Disposal Pathways***

Because HBCD is not classified as a RCRA hazardous waste, wastes are not expected to be sent to Subtitle C incinerators, due to the higher cost of such incineration as compared with MSW or other incinerators; therefore emissions from hazardous waste incinerators will not be included in the risk evaluation. 40 CFR 264.345 specifies performance standards for hazardous waste incinerators. An incinerator burning hazardous waste must achieve a destruction and removal efficiency (DRE) of 99.99% for each principal organic hazardous constituent. Furthermore, RCRA provisions for site-specific risk assessments and the Hazardous Waste Combustor maximum achievable control technology (MACT) rule provisions for a Residual Risk and Technology Review together cover risks for RCRA hazardous wastes.

EPA does not expect to include on-site releases to land that go to underground injection in its risk evaluation. Environmental disposal of HBCD injected into Class I well types are presumed to be managed and prevented from further environmental release by RCRA and SDWA regulations. Therefore, disposal of HBCD via underground injection is not likely to result in environmental and general population exposures.

EPA does not expect to include on-site releases to land that go to RCRA Subtitle C hazardous waste landfills. Design standards for Subtitle C landfills require double liner, double leachate collection and removal systems, leak detection system, run on, runoff, and wind dispersal controls, and a construction quality assurance program. They are also subject to closure and post-closure care requirements including installing and maintaining a final cover, continuing operation of the leachate collection and removal system until leachate is no longer detected, maintaining and monitoring the leak detection and groundwater monitoring system. Subtitle C landfill operators are required to implement an analysis and testing program to ensure adequate knowledge of waste being managed, and to train personnel on routine and emergency operations at the facility. Hazardous waste being disposed in Subtitle C landfills must also meet RCRA waste treatment standards before disposal. Given these controls, general

population exposure to HBCD in groundwater from Subtitle C landfill leachate is not expected to be a significant pathway.

EPA does not expect to include on-site releases to land from RCRA Subtitle D municipal solid waste landfills (MWSLFs), other than for construction and demolition wastes as described in Section 2.3.5.1. While permitted and managed by the individual states, municipal solid waste landfills (MSWLFs) are required by federal regulations to implement many of the same requirements as Subtitle C landfills. MSWLFs must have a liner system with leachate collection and conduct groundwater monitoring and corrective action when releases are detected. MSWLFs are also subject to closure and post-closure care requirements, as well as providing financial assurance for funding of any needed corrective actions. MSWLFs have also been designed to allow for the small amounts of hazardous waste generated by households and very small quantity waste generators (less than 100 kg per month).

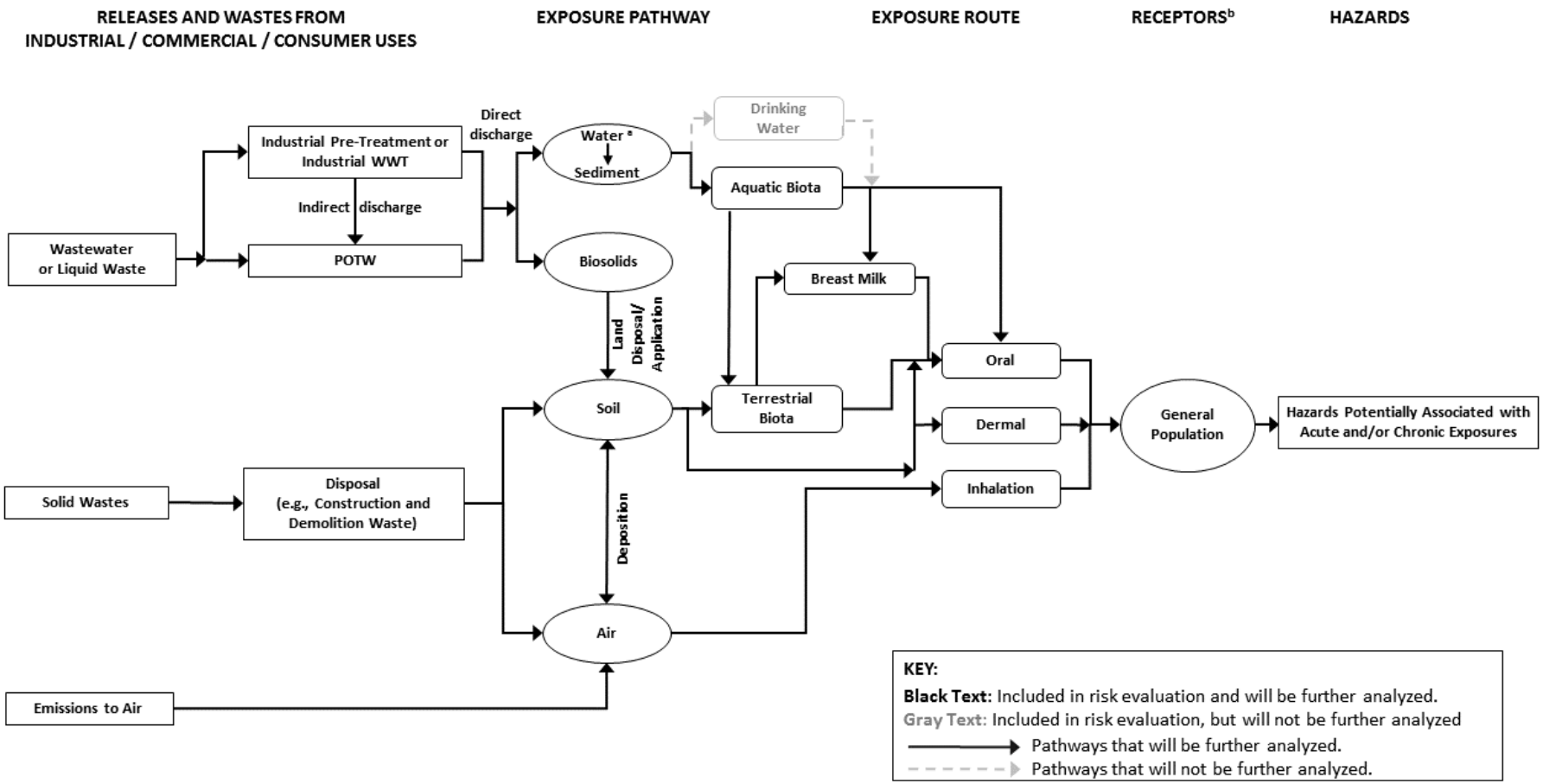


**Figure 2-4a. HBCD Conceptual Model for Environmental Releases and Wastes: General Population Exposures and Hazards**
The conceptual model presents the exposure pathways, exposure routes and hazards to human receptors from releases and wastes from industrial and commercial uses of HBCD.

[a] Industrial wastewater or liquid wastes may be treated on-site and then released to surface water (direct discharge), or pre-treated and released to POTW (indirect discharge). For consumer uses, such wastes may be released directly to POTW (i.e., down the drain). Drinking water will undergo further treatment in drinking water treatment plant. Ground water may also be a source of drinking water.

[b] Receptors include potentially exposed or susceptible subpopulations (see Section 2.3.5.4).

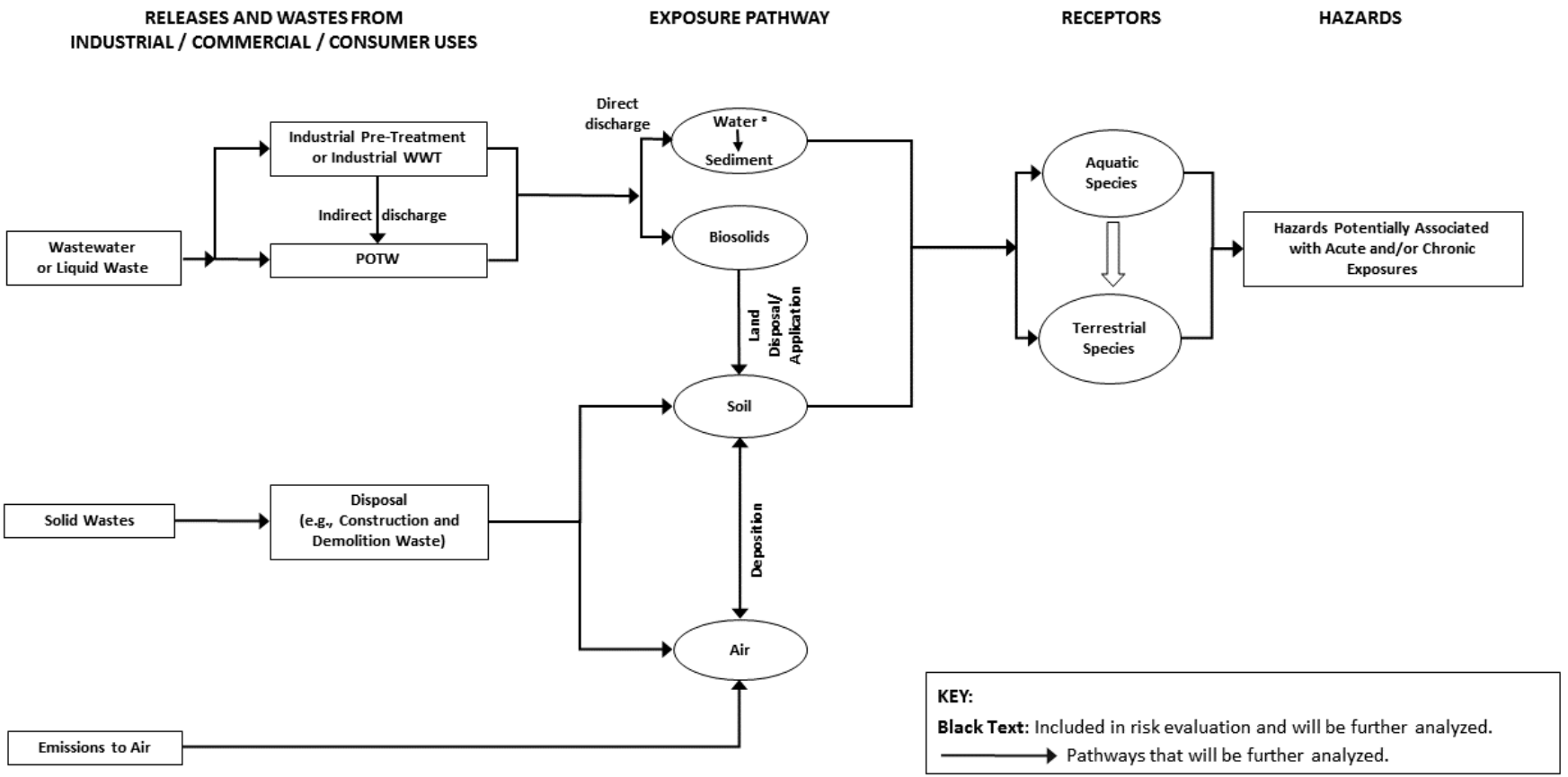


**Figure 2-4b. HBCD Conceptual Model for Environmental Releases and Wastes: Ecological Exposures and Hazards**

The conceptual model presents the exposure pathways and hazards for environmental receptors from industrial and commercial uses of HBCD.

[a] Industrial wastewater or liquid wastes may be treated on-site and then released to surface water (direct discharge), or pre-treated and released to POTW (indirect discharge). For consumer uses, such wastes may be released directly to POTW (i.e., down the drain).

## 2.6 Analysis Plan

The analysis plan presented here is a refinement of the initial analysis plan that was published in the Scope of the Risk Evaluation for HBCD (U.S. EPA, 2017e).

The analysis plan is based on the conditions of use of HBCD, as described in Section 2.2 of this problem formulation. EPA is implementing systematic review approach and/or methods to identify, select, assess, integrate and summarize the findings of studies supporting the TSCA risk evaluation. The analytical approaches and considerations in the analysis plan are used to frame the scope of the systematic review activities for this assessment. The supplemental documents, *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018), provides additional information about the criteria, approaches and/or methods that have been and will be applied to the first 10 chemical risk evaluations.

While EPA has conducted a comprehensive search for reasonably available data as described in the Scope of the Risk Evaluation for HBCD (U.S. EPA, 2017e), EPA encourages submission of additional existing data, such as full study reports or workplace monitoring from industry sources, that may be relevant for further evaluating conditions of use, exposures, hazards and potentially exposed or susceptible subpopulations during risk evaluation. EPA will continue to consider new information submitted by the public.

During the risk evaluation, EPA will rely on the search results *HBCD (CASRN 25637-99-4, 3194-55-6, 3194-57-8) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0735) or perform supplemental searches to address specific questions. Further, EPA may consider any relevant CBI information in the risk evaluation in a manner that protects the confidentiality of the information from public disclosure. The analysis plan is based on EPA's knowledge of HBCD to date which includes a partial, but not complete review of identified information. Should additional data or approaches become available, EPA may refine its analysis plan based on this information.

### 2.6.1 Exposure

Based on their physical-chemical properties, expected sources, and transport and transformation within the outdoor and indoor environment chemical substances are more likely to be present in some media and less likely to be present in others. Media-specific levels will vary based on the chemical substance of interest. For some high-priority chemical substances, non-zero background level(s) can be characterized through a combination of available monitoring data and modeling approaches.

Background levels can be used to:

- Better characterize the overall magnitude and distribution of exposures when considered alongside scenario-specific exposures.
- Serve as a comparison or point of reference for scenario-specific exposure estimates.
    - Scenario-specific exposures that are lower than background exposure levels may not need to be further analyzed.
    - Scenario-specific exposures that are approximately the same or higher than background exposure levels warrant further consideration.

For HBCD, EPA plans to analyze background levels for indoor dust, indoor air, ambient air, surface water, sediment, soil, dietary food sources, aquatic biota, and terrestrial biota. EPA has not yet determined the background levels in these media or how they may be used in the risk evaluation.

Exposure scenarios are unique combinations of sources (uses), exposure pathways, and exposed receptors. Draft release/exposure scenarios corresponding to various conditions of use for HBCD are presented in Appendix D. EPA plans to analyze background exposures and scenario-specific exposures.

#### 2.6.1.1 Environmental Releases

EPA expects to analyze releases to environmental media as follows:

1) **Review reasonably available published literature and other reasonably available information on processes and activities associated with the conditions of use to analyze the types of releases and wastes generated.**

   EPA has reviewed some key data sources containing information on processes and activities resulting in releases, and the information found is described in Appendix B. EPA will continue to review data sources identified in Appendix B during risk evaluation using the evaluation strategy for environmental releases and occupational exposure data sources discussed in the *Application of Systematic Review in TSCA Risk Evaluations and Strategy for Assessing Data Quality in TSCA Risk Evaluations* (U.S. EPA, 2018).

   The specific industrial activities that EPA expects to analyze are summarized in Table 2-7 below:

**Table 2-7. Summary of Industrial Activities EPA Will Analyze**

| Life Cycle Stage | Category | Subcategory | Specific Scenarios that EPA will Assess |
|---|---|---|---|
| Manufacture | Import | Repackaging | Import of HBCD as powder or pellets and/or as part of XPS masterbatch, and/or as part of EPS resin beads to a single site and subsequent repackaging of the imported material and its transfer to other sites for the following purposes:<br>1. The production of XPS master batch at a generic compounding site using the imported HBCD;<br>2. The production of XPS at a generic site for the manufacture of XPS using the imported HBCD or the imported XPS masterbatch.<br>3. The production of EPS at a generic site for the manufacture of EPS using the imported EPS resin beads. |
| Processing | Incorporation into formulation, mixture, or reaction product | Compounding of XPS master batch | The compounding of XPS master batch at a generic site by the processing of imported HBCD |

| Life Cycle Stage | Category | Subcategory | Specific Scenarios that EPA will Assess |
|---|---|---|---|
| | Incorporation into an article | Manufacture of XPS | The manufacture of XPS at a generic site from the XPS master batch produced at a generic compounding site or the imported HBCD or the imported XPS masterbatch. |
| | | Manufacture of EPS | The manufacture of EPS at a generic site from imported EPS resin beads. |
| | | Manufacture of SIPs and automobile replacement parts from XPS or EPS | The manufacture of SIPs at a generic site. |
| | | | The manufacture of replacement automobile parts at a generic site. |

EPA will consider using an import volume of up to 100,000 lbs (i.e. the highest CDR reporting threshold) to estimate releases resulting from repackaging of imported product and subsequent processing (i.e., production of XPS master batch, XPS and EPS). EPA will conduct additional data collection to estimate the quantity of the imported HBCD that is used for the manufacture of XPS and EPS, SIPs, and replacement automobile parts.

Furthermore, EPA will further consider whether EPS and XPS, are recycled to produce products that contain HBCD as a flame retardant. If EPA proceeds with the evaluation of any of the recycling processes, then EPA may perform targeted data searches as needed.

2) **Review reasonably available chemical-specific release data, including measured or estimated release data (e.g., data from risk assessments by other environmental agencies).**

There are currently no reported Toxics Release Inventory (TRI) data for HBCD. EPA will review the TRI data for the first reporting year of 2017 when they become available in approximately July 2018. EPA will continue to review relevant data sources as identified in Appendix B during the risk evaluation. EPA will match identified data to applicable conditions of use and identify data gaps where no data are found for particular conditions of use. EPA will assess releases from the specific industrial activities identified above and will compare the results of this assessment with any release data that will reported in the TRI.

Additionally, for conditions of use where no measured data on releases are available, EPA may use a variety of methods including release estimation approaches and assumptions in the Chemical Screening Tool for Occupational Exposures and Releases ChemSTEER (U.S. EPA, 2013).

3) **Review reasonably available measured or estimated release data for surrogate chemicals that have similar uses and physical properties.**

EPA has not identified surrogate chemicals and data that can be used to estimate releases from uses of HBCD. EPA may conduct targeted searches for surrogate data. For example, EPA may search for data on release of chemicals as a result of building demolition and will then evaluate the utility of any such data as surrogate data for release of HBCD due to building demolition.

4) **Review reasonably available data that may be used in developing, adapting or applying exposure models to the particular risk evaluation.**

This item will be performed after completion of #2 and #3 above. EPA will evaluate relevant data to determine whether the data can be used to develop, adapt or apply models for specific conditions of use (and corresponding release scenarios).

5) **Review and determine applicability of OECD Emission Scenario Documents (ESDs) and EPA Generic Scenarios to estimation of environmental releases.**

EPA has identified potentially relevant OECD Emission Scenario Documents (ESDs) and EPA Generic Scenarios (GS) that correspond to some conditions of use; for example, the 2009 ESD on Plastics Additives and the 2011 ESD on Chemical Industry may be useful. EPA will need to critically review these generic scenarios and ESDs to determine their applicability to the conditions of use assessed.

EPA Generic Scenarios are available at the following: https://www.epa.gov/tsca-screening-tools/using-predictive-methods-assess-exposure-and-fate-under-tsca#fate.

OECD Emission Scenario Documents are available at the following: http://www.oecd.org/chemicalsafety/risk-assessment/emissionscenariodocuments.htm

EPA was not able to identify release scenarios corresponding to several conditions of use (e.g. recycling, construction and demolition) of products containing HBCD. EPA may conduct industry outreach efforts, or perform supplemental, targeted literature searches to better understand the process steps involved in that condition of use before a release assessment can be made.

6) **Map or group each condition of use to a release assessment scenario(s).**

EPA has identified release scenarios and mapped (i.e. grouped) them to relevant conditions of use as shown in B.2. EPA was not able to identify release scenarios corresponding to some conditions of use (e.g. recycling, construction and demolition). EPA will perform targeted research to understand those uses, which may inform identification of release scenarios. EPA may further refine the mapping/grouping of release scenarios based on factors (e.g., process equipment and handling, magnitude of production volume used, and exposure/release sources) corresponding to conditions of use as additional information is identified during risk evaluation.

7) **Evaluate the weight of evidence of environmental release data.**

EPA will rely on the weight of the scientific evidence when evaluating and integrating environmental release data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

#### 2.6.1.2 Environmental Fate

EPA expects analyze fate and transport in environmental media as follows:

1) **Review reasonably available measured or estimated environmental fate endpoint data collected through the literature search.**

A general overview of persistence and bioaccumulation was presented in the TSCA Work Plan Chemical Problem Formulation and Initial Assessment for HBCD (U.S. EPA, 2015c). Key environmental fate characteristics were included in the Scope of the Risk Evaluation for HBCD (U.S. EPA, 2017e) and in previous assessments of HBCD, including those conducted by the US EPA (U.S. EPA, 2014b, 2008), Australian National Industrial Chemicals Notification and Assessment Scheme (NICNAS, 2012b), Environment Canada (Environment Canada, 2011), European Inventory of Existing Commercial Chemical Substances (EINECS, 2008), and the Organization for Economic Cooperation and Development Screening Information Datasets (OECD, 2007b). These information sources will be used as a starting point for the environmental fate assessment. Other sources that will be consulted include those that are identified through the systematic review process. Studies will be evaluated using the evaluation strategies laid out in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018).

If measured values resulting from sufficiently high-quality studies are not available (to be determined through the systematic review process), chemical properties will be estimated using EPI Suite, SPARC, and other chemical parameter estimation models. Estimated fate properties will be reviewed for applicability and quality.

2) **Using measured data and/or modeling, determine the influence of environmental fate endpoints (e.g., persistence, bioaccumulation, partitioning, transport) on exposure pathways and routes of exposure to human and environmental receptors.**

Measured fate data including volatility from water, sorption to organic matter in soil and sediments, aqueous and atmospheric photolysis rates, and aerobic and anaerobic biodegradation rates, along with physical-chemical properties and models such as the EPI Suite™ STP model (which estimates removal in wastewater treatment due to adsorption to sludge and volatilization to air), will be used to characterize the movement of HBCD within and among environmental media and the persistence of HBCD in media.

3) **Evaluate the weight of the evidence of environmental fate data, which include qualitative and quantitative sources of information.**

   EPA will rely on the weight of the scientific evidence when evaluating and integrating environmental fate data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

#### 2.6.1.3 Environmental Exposures

EPA expects to analyze the following in developing its environmental exposure assessment of HBCD:

1) **Review available environmental and biological monitoring data for all media relevant to environmental exposure.**

   For HBCD, environmental media which will be analyzed are sediment, soil, and surface water. In addition, air deposition of HBCD, effluent, landfill leachate, and biosolids may contribute to HBCD levels in sediment, soil, and surface water. Biological media which will be analyzed are targeted species of predatory birds, fish, and invertebrates. Full-text screening is underway, but not yet complete and over 100 monitoring studies have been identified across all media types.

2) **Review reasonably available information on releases to determine how modeled estimates of concentrations near industrial point sources compare with available monitoring data.**

   Available environmental exposure models that meet the TSCA Science Standards and that estimate surface water, sediment, and soil concentrations will be analyzed and considered alongside available surface water, sediment, and soil monitoring data to characterize environmental exposures. Modeling approaches to estimate surface water concentrations, sediment concentrations and soil concentrations generally consider the following inputs: direct release into surface water, sediment, or soil, indirect release into surface water, sediment, or soil (i.e., air deposition), fate and transport (partitioning within media) and characteristics of the environment (e.g., river flow, volume of lake, meteorological data).

3) **Review reasonably available biomonitoring data for predatory bird species. Consider whether these data could be used to compare with comparable species or taxa-specific toxicological benchmarks.**

   Predatory bird species that consume fish with elevated levels of HBCD will be analyzed. If species-specific biomonitoring data matches toxicity studies, direct comparisons can be made. EPA will also consider refining data for other species by using body weight of the birds, fish ingestion rate of birds, and typical fish species consumed.

4) **Determine applicability of existing additional contextualizing information for any monitored data or modeled estimates during risk evaluation.**

There have been changes to use patterns of HBCD over the last few years. Monitoring data or modeled estimates will be reviewed to determine how representative they are of ongoing use patterns.

Any studies which relate levels of HBCD in the environment or biota with specific sources or groups of sources will be evaluated.

HBCD has been widely studied with several monitoring studies reporting detected levels in biota and the indoor and outdoor environment. However, many of these monitoring studies do not attempt to describe potential sources or groups of sources that could have resulted in the presence of HBCD in a given media. EPA will evaluate all monitoring studies, and note any monitoring studies that include some description of source attribution.

5) **Group each condition(s) of use to environmental assessment scenario(s).**

Refine and finalize exposure scenarios for environmental receptors by considering unique combinations of sources (use descriptors), exposure pathways including routes, and populations exposed. For HBCD, the following are noteworthy considerations in constructing exposure scenarios for environmental receptors:

- temporal trends in uses and resulting sources of HBCD to the environment over time
- overall persistence in the environment and bioaccumulation into a wide variety of aquatic and terrestrial species
- characterization of background levels in the environment that are not generally attributable to any one use or source
- possible interactions within food-chains and relative contribution of dietary vs. non-dietary sources for predatory animals

6) **Evaluate the weight of evidence of environmental occurrence data and modeled estimates.**

Both environmental occurrence data and modeled estimates will be evaluated by EPA. EPA will rely on the weight of the scientific evidence when evaluating and integrating environmental occurrence data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

#### 2.6.1.4 Occupational Exposures

EPA expects to analyze both worker and occupational non-user exposures as follows:

1) **Review reasonably available exposure monitoring data for specific condition(s) of use.**

No occupational exposure limits have been established or recommended by OSHA or NIOSH. EPA expects to review monitoring data found in published literature including both personal exposure monitoring data (direct exposure) and area monitoring data (indirect exposures). EPA

has identified data sources that contain measured monitoring data and or/estimated data for the various conditions of use (including import and processing of HBCD), for example, HBCD risk assessments published by the European Chemicals Agency, Environment Canada, and Australia's Department of Health. EPA will review these sources and other data sources (as identified in Appendix B) to extract relevant data for consideration and analysis during risk evaluation.

2) **Review reasonably available exposure data for surrogate chemicals that have uses, volatility and chemical and physical properties similar to HBCD.**

   EPA has not identified surrogate chemicals and data that can be used for estimating occupational exposures to HBCD at this time. Based on cursory review of some data sources, EPA does not anticipate a need to identify surrogate data. However, if surrogate data are needed to augment HBCD-specific data, EPA will review literature sources identified and if surrogate data are found, these data will be matched to applicable conditions of use for potentially filling data gaps.

3) **For conditions of use where data are limited or not available, review existing exposure models that may be applicable in estimating exposure levels.**

   EPA has identified potentially relevant OECD ESDs and EPA GS's corresponding to some conditions of use, for example, the 2009 ESD on Plastics Additives and the 2011 ESD on Chemical Industry. EPA will need to critically review these generic scenarios and ESDs to determine their applicability to the conditions of use assessed. EPA was not able to identify release scenarios corresponding to several conditions of use (e.g. recycling, construction and demolition) of products containing HBCD. EPA may conduct industry outreach efforts or perform supplemental, targeted literature searches to better understand the process steps involved in those conditions of use. EPA will consider the applicability of exposure models in the Chemical Screening Tool for Occupational Exposure and Releases [ChemSTEER (U.S. EPA, 2013)] tool that are routinely used for assessing new chemicals to assess inhalation exposures during various conditions of use. EPA may also need to perform targeted research to identify other models that EPA could use to estimate exposures for certain conditions of use.

4) **Review reasonably available data that may be used in developing, adapting or applying exposure models to a particular risk evaluation scenario.**

   This step will be performed after Steps #2 and #3 are completed. Based on information developed from Steps #2 and #3, EPA will evaluate relevant data to determine whether the data can be used to develop, adapt, or apply models for specific conditions of use (and corresponding exposure scenarios).

5) **Consider and incorporate applicable engineering controls and/or personal protective equipment into exposure scenarios.**

   EPA will review potentially relevant data sources on engineering controls and personal protective equipment as identified in Appendix B to determine their applicability and incorporation into exposure scenarios during risk evaluation.

6) **Map or group each condition of use to occupational exposure assessment scenario(s).**

EPA has identified occupational exposure scenarios and mapped them to relevant conditions of use (see B.2). As presented in the fourth column in Table_Apx C-1. Worker and Occupational Non-User Exposure Conceptual Model Supporting Table, EPA has grouped the scenarios into 8 representative release/exposure scenarios of which 7 will be further analyzed. EPA was not able to identify occupational scenarios corresponding to some conditions of use (e.g. recycling, construction and demolition). EPA may further refine the mapping/grouping of occupational exposure scenarios based on factors (e.g., process equipment and handling, magnitude of production volume used, and exposure/release sources) corresponding to conditions of use as additional information is identified during risk evaluation.

7) **Evaluate the weight of the evidence of occupational exposure data, which may include qualitative and quantitative sources of information.**

EPA will rely on the weight of the scientific evidence when evaluating and integrating occupational data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

#### 2.6.1.5 Consumer Exposures

EPA expects to analyze both consumers using a consumer product and bystanders associated with the consumer using the product as follows:

1) **Group each condition of use to consumer exposure assessment scenario(s).**

Refine and finalize exposure scenarios for consumers by considering unique combinations of sources (ongoing consumer uses), exposure pathways including routes, and exposed populations.

For HBCD, the following are noteworthy considerations in constructing consumer exposure scenarios:

- reasonably available information on sources including the concentration of HBCD in newly made or recycled consumer products and articles including temporal trends associated with such information;
- information characterizing the release potential of HBCD from products and articles into the indoor environment through diffusion from materials to air, physical abrasion, direct transfer to dust, or leaching into sweat, and skin oil;
- populations who may be more greatly exposed to products, including potentially exposed and susceptible subpopulations such as infants, children, pregnant women; and,
- the associated exposure setting and route for exposed populations.

2) **Evaluate the relative potential of indoor exposure pathways based on available data.**

Indoor exposure pathways expected to be relatively higher include dust ingestion and mouthing of products. Indoor exposure pathways expected to be relatively lower include inhalation of indoor air, dermal contact with dust and articles. The data sources associated with these respective pathways have not been comprehensively evaluated, so quantitative comparisons across exposure pathways or in relation to toxicity thresholds are not yet available.

3) **Review existing indoor exposure models that may be applicable in estimating indoor air, indoor dust concentrations, or indoor dust surface loadings.**

Indoor exposure models that estimate emission and migration of SVOCs into the indoor environment are available. These models generally consider mass transfer as informed by the gas-phase mass transfer coefficient, the solid-phase diffusion coefficient, and the material-air partition coefficient. In addition, direct transfer to surface dust or physical abrasion may influence emissions over time. These properties vary based on physical-chemical properties and properties of the material. OPPT's Indoor Environmental Concentrations in Buildings with Conditioned and Unconditioned Zones (IECCU) model and other similar models can be used to estimate indoor air and dust exposures from indoor sources.

4) **Review reasonably available empirical data that may be used in developing, adapting or applying exposure models to a particular risk evaluation scenario. For example, existing models developed for a chemical assessment may be applicable to another chemical assessment if model parameter data are available.**

To the extent other organizations have already modeled an HBCD consumer exposure scenario that is relevant to OPPT's assessment, EPA will evaluate those modeled estimates. In addition, if other chemicals similar to HBCD have been modeled for similar uses, those modeled estimates will also be evaluated. The underlying parameters and assumptions of the models will also be evaluated.

5) **Review reasonably available consumer product-specific sources to determine how those exposure estimates compare with each other and with indoor monitoring data reporting HBCD in specific media (e.g., dust or indoor air).**

The availability of HBCD concentration for various ongoing uses will be evaluated. This data provides the source term for any subsequent indoor modeling. Source attribution between overall indoor air and dust levels and various indoor sources will be analyzed.

6) **Review reasonably available population- or subpopulation-specific exposure factors and activity patterns to determine if potentially exposed or susceptible subpopulations need to be further refined.**

For HBCD, exposure scenarios that involve potentially exposed and susceptible subpopulations will consider age-specific behaviors, activity patterns, and exposure factors unique to those subpopulations. For example, children spend different amounts of time in microenvironments throughout the day.

7) **Evaluate the weight of the evidence of consumer exposure estimates based on different approaches.**

EPA will rely on the weight of the scientific evidence when evaluating and integrating data related to consumer exposure. The weight of the evidence may include qualitative and quantitative sources of information. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

#### 2.6.1.6 General Population

EPA expects to analyze general population exposures as follows:

1) **Refine and finalize exposure scenarios for general population by considering unique combinations of sources and uses, exposure pathways including routes, and exposed populations.**

For HBCD, the following are noteworthy considerations in constructing exposure scenarios for the general population:

- temporal trends in uses and resulting sources/releases of HBCD to the environment over time;
- overall persistence in the environment and bioaccumulation into a wide variety of aquatic and terrestrial species relevant to human consumption;
- characterization of background levels in the environment that are not generally attributable to any one condition of use or source; and,
- consideration of spatial differences between populations located near industrial point sources and those exposed at lower background levels.
- releases to the environment. For HBCD, TRI releases are expected to be reported for 2017. These releases are not yet linked to a specific lifecycle stage and use. Approaches for estimating exposures from the conditions of use as they relate to the reported TRI emissions will be further explored.

EPA plans to evaluate a variety of data types to determine which types are most appropriate when quantifying exposure scenarios. Environmental monitoring data, biomonitoring data, modeled estimates, experimental data, epidemiological data, and survey-based data can all be used to quantify exposure scenarios. In an effort to associate exposure estimates with sources of exposure and/or conditions of use, EPA will consider source apportionment across exposure scenarios during risk evaluation. EPA anticipates that there will be a wide range in the relative exposure potential of the exposure scenarios identified in Appendix C. Source apportionment characterizes the relative contribution of any of the following: a use/source toward a total media concentration, a media concentration toward a total exposure route, or an exposure route toward a total external or internal dose. This consideration may be qualitative, semi-quantitative, or quantitative, and is dependent upon available data and approaches. For example, EPA may consider the co-location of TSCA industrial facilities with available monitoring data or modeled estimates. EPA may compare modeled estimates for discrete outdoor and indoor sources/uses that apply to unique receptor groups. If available, EPA will compare multiple scenario-specific

and background exposure doses estimated from media-specific concentrations and exposure factors with available biomonitoring data. The forward-calculated and back-calculated exposures could be compared to characterize the relative contribution from defined exposure scenarios.

After refining and finalizing exposure scenarios, EPA will quantify concentrations and/or doses for these scenarios. The number of scenarios will depend on how unique combinations of uses, exposure pathways, and receptors are characterized. The number of scenarios is also dependent upon the available data and approaches to quantify scenarios. When quantifying exposure scenarios, EPA plans to use a tiered approach. First-tier analysis is based on data that is readily available without a significant number of additional inputs or assumptions, and may be qualitative, semi-quantitative, or quantitative. First-tier analyses were conducted during problem formulation and are expected to continue during risk evaluation. The results of first tier analyses inform whether scenarios require more refined analysis. Refined analyses will be iterative, and require careful consideration of variability and uncertainty. Should data become available that summarily alters the overall conclusion of a scenario through iterative tiering, EPA can refine its analysis during risk evaluation.

2) **Review available environmental and biological monitoring data for exposure pathways and media to which general population exposures are expected.**

   General population exposure pathways expected to be relatively higher include: dietary ingestion for lipid rich food sources, soil ingestion, sediment ingestion, and inhalation of suspended particles. General population exposure pathways expected to be relatively lower include: drinking water, dietary ingestion for non-lipid rich food sources, incidental ingestion of surface water and suspended particulates during recreation, and dermal contact with particles. In addition, dust ingestion is an important pathway that will be considered for consumer exposure as well for general population exposure. The data sources associated with these respective pathways have not been comprehensively evaluated, so quantitative comparisons across exposure pathways or in relation to toxicity thresholds are not yet available.

3) **For exposure pathways where empirical data is not available, review existing exposure models that may be applicable in estimating exposure levels.**

   For HBCD, media where exposure models will be considered for general population exposure include models that estimate ambient air concentrations, surface water concentrations, sediment concentrations, soil concentrations, and uptake from aquatic and terrestrial environments into edible aquatic and terrestrial organisms.

4) **Consider and incorporate applicable media-specific regulations into exposure scenarios or modeling approaches.**

5) **Review available exposure modeled estimates. For example, existing models developed for a previous HBCD chemical assessment may be applicable to EPA's assessment. In addition, another chemical's assessment may also be applicable if model parameter data are available.**

To the extent other organizations have already modeled an HBCD general population exposure scenario that is relevant to OPPT's assessment, EPA will evaluate those modeled estimates. In addition, if modeled estimates for other chemicals with similar physical chemical properties and similar uses are available, those modeled estimates will also be evaluated. The underlying parameters and assumptions of the models will also be evaluated.

6) **Review available information on releases to determine how modeled estimates of concentrations near industrial point sources compare with available monitoring data.**

The expected releases from industrial facilities are changing over time. Any modeled concentrations based on recent release estimates will be carefully compared with available monitoring data to determine representativeness.

7) **Review available information about population- or subpopulation-specific exposure factors and activity patterns to determine if potentially exposed or susceptible subpopulations need to be further defined (e.g., early life and/or puberty as a potential critical window of exposure).**

For HBCD, exposure scenarios that involve potentially exposed and susceptible subpopulations will consider age-specific behaviors, activity patterns, and exposure factors unique to those subpopulations. For example, children will have different intake rates for dust, soil, and diet than adults.

8) **Evaluate the weight of the evidence of general population exposure estimates based on different approaches.**

EPA will rely on the weight of the scientific evidence when evaluating and integrating data related to general population exposures. The weight of the evidence may include qualitative and quantitative sources of information. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

### 2.6.2 Hazards (Effects)

#### 2.6.2.1 Environmental Hazards

EPA will conduct an environmental hazard assessment of HBCD as follows:

1) **Review reasonably available environmental hazard data, including data from alternative test methods (e.g., computational toxicology and bioinformatics; high-throughput screening methods; data on categories and read-across; in vitro studies).**

- Environmental hazard data will be evaluated using the ecological toxicity data quality criteria outlined in the *Application of Systematic Review in TSCA Risk Evaluations* document. The study evaluation results will be documented in the risk evaluation phase and data from suitable studies will be extracted and integrated in the risk evaluation process.

- Conduct hazard identification (the qualitative process of identifying acute and chronic endpoints) and concentration-response assessment (the quantitative relationship between hazard and exposure) for all identified environmental hazard endpoints. Suitable environmental hazard data will be reviewed for acute and chronic endpoints for mortality and other effects (e.g. growth, immobility, reproduction, etc.). EPA will evaluate the character of the concentration-response relationship (*i.e.* positive, negative or no response) as part of the review.

**2) Derive aquatic and terrestrial concentrations of concern (COC) for acute and, where possible, chronic endpoints.**

The aquatic environmental hazard studies may be used to derive acute and chronic concentrations of concern (COC) for mortality, behavioral, developmental and reproductive or other endpoints determined to be detrimental to environmental populations. Depending on the robustness of the evaluated data for a particular organism (*e.g.* aquatic invertebrates), environmental hazard values (e.g. $EC_x$/$LC_x$/NOEC/LOEC, etc.) may be derived and used to further understand the hazard characteristics of HBCD to aquatic species.

**3) Evaluate the weight of the evidence of environmental hazard data.**

EPA will rely on the weight of the scientific evidence when evaluating and integrating environmental hazard data. The data integration strategy will be designed to be fit-for-purpose. EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

**4) Consider the route(s) of exposure, available biomonitoring data and available approaches to integrate exposure and hazard assessments.**

- Based on the physical-chemical and fate properties (low water solubility and high absorption), EPA plans to consider the aquatic, sediment and terrestrial pathways in the HBCD conceptual model. These organisms are likely to be exposed to HBCD in liquid waste from industrial wastewater treatment facility, municipal and hazardous waste landfills and incineration of municipal hazardous waste pathways. These pathways can result in groundwater and eventually surface water exposure to terrestrial, aquatic and sediment organisms.
- EPA plans to consider benthic and pelagic species in the HBCD conceptual model. HBCD exposure from POTWs can affect these organisms and trophic magnification could result from over exposure following bioaccumulation of HBCD.
- EPA plans to consider soil organisms in the HBCD conceptual model. Land application of biosolids containing HBCD could transfer to soil thus exposing terrestrial organisms.

**5) Conduct an ecological risk characterization of HBCD.**

EPA plans to conduct a risk characterization of HBCD to determine whether there are risks to the aquatic and/or terrestrial environments from the measured levels of HBCD found in wastewater,

surface water, sediment or soil. The data for environmental monitoring and toxicity will be used in this risk assessment to determine if:

- The acute exposure to levels of HBCD measured in wastewater in the US pose risks for adverse effects in aquatic invertebrates, fish, or plants.
- The chronic exposure to levels of HBCD measured in surface water in the US pose risks for adverse effects in aquatic invertebrates, fish, or plants or terrestrial species.
- The chronic exposure to levels of HBCD measured in sediment in the US pose risks for adverse effects in sediment-dwelling invertebrates.

Environmental risk will be characterized by calculating risk quotients (RQs) (U.S. EPA, 1998; Barnthouse et al., 1982). The COCs derived from aquatic and terrestrial organisms hazard data will be used to calculate RQs. The environmental concentration for each compartment (i.e., wastewater, surface water, sediment, soil) will be based on measured and modeled concentrations of HBCD.

**6) Conduct a Persistent, Bioaccumulative, and Toxic (PBT) Assessment of HBCD.**

EPA will assess the persistence, bioaccumulation, and toxic (PBT) potential of HBCD in accordance with U.S. EPA Final Water Quality Guidance for Great Lakes System (U.S. EPA, 1995). EPA will assess the available studies collected from the systematic review process relating to bioaccumulation and bioconcentration (BAF/BCF) of HBCD. In addition, EPA will integrate traditional environmental hazard endpoint values (e.g., $LC_{50}$, LOEC) and exposure concentrations (e.g., surface water concentrations, tissue concentrations) for HBCD with the fate parameters (BAF/BCF/BMF/TMF).

#### 2.6.2.2 Human Health Hazards

EPA expects to analyze human health hazards as follows:

**1) Review reasonably available human health hazard data, including data from alternative test methods (e.g., computational toxicology and bioinformatics; high-throughput screening methods; data on categories and read-across; *in vitro* studies; systems biology).**

Human health studies will be evaluated using the evaluation strategies laid out in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018). For the HBCD risk evaluation, EPA will evaluate information in the *Preliminary Materials for the IRIS Toxicological Review of HBCD* (U.S. EPA, 2014d), *Strategy for Conducting Literature Searches for Cyclic Aliphatic Bromine Cluster (HBCD): Supplemental Document to the TSCA Scope Document*,(U.S. EPA, 2017f, 2002), and studies published after 2015 that were captured in the comprehensive literature search conducted by the agency for HBCD (*Cyclic Aliphatic Bromides Cluster (HBCD) (CASRN: 25637-99-4; 3194-55-6; 3194-57-8) Bibliography: Supplemental File for the TSCA Scope Document* (U.S. EPA, 2017b) using OPPT's structured process described in the document, *Application of Systematic Review in TSCA Risk Evaluations*.

Mechanistic data may include analyses of alternative test data such as novel *in vitro* test methods and high throughput screening. The association between acute and chronic exposure scenarios to

the agent and each health outcome will also be integrated. Study results will be extracted and presented in evidence tables or another appropriate format by organ/system.

2) **In evaluating reasonably available data, determine whether particular human receptor groups may have greater susceptibility to the chemical's hazard(s) than the general population.**

Reasonably available human health hazard data will be evaluated to ascertain whether some human receptor groups may have greater susceptibility than the general population to HBCD hazard(s). Susceptibility of particular human receptor groups to HBCD will be determined by evaluating information on factors that influence susceptibility.

EPA has reviewed some sources containing hazard information associated with susceptible populations and lifestages such as pregnant women and infants. Pregnancy (i.e., gestation) and childhood are potential susceptible lifestages for HBCD exposure. The document *Cyclic Aliphatic Bromides Cluster (HBCD) (CASRN: 25637-99-4; 3194-55-6; 3194-57-8) Bibliography: Supplemental File for the TSCA Scope Document* (U.S. EPA, 2017b) contains a list of studies that will be evaluated to ascertain whether some human receptor groups may have greater susceptibility than the general population to HBCD's hazard(s). Also, EPA/OPPT will further examine the availability of any new chemical-specific information on susceptible populations or the distribution of susceptibility in the general population since the TSCA Work Plan Problem Formulation and Initial Assessment (U.S. EPA, 2015c) and their impact in decreasing or increasing the default uncertainty factors for variability. EPA will review the current state of the literature since the TSCA Work Plan Problem Formulation and Initial Assessment (U.S. EPA, 2015c) in order to potentially quantify these differences for risk evaluation purposes.

3) **Conduct hazard identification (the qualitative process of identifying non-cancer and cancer endpoints) and dose-response assessment (the quantitative relationship between hazard and exposure) for identified human health hazard endpoints.**

Human health hazards from acute and chronic exposures will be identified by evaluating the human and animal data that meet the systematic review data quality criteria described in the *Application of Systematic Review in TSCA Risk Evaluations* document (U.S. EPA, 2018). Data quality evaluation will be performed on key studies identified from the TSCA Work Plan Problem Formulation and Initial Assessment (U.S. EPA, 2015c), *Preliminary Materials for the IRIS Toxicological Review of HBCD* (U.S. EPA, 2014d), *Strategy for Conducting Literature Searches for Cyclic Aliphatic Bromine Cluster (HBCD): Supplemental Document to the TSCA Scope Document*,(U.S. EPA, 2017f, 2002), and studies published after 2015 that were captured in the comprehensive literature search conducted by the agency for HBCD (*Cyclic Aliphatic Bromides Cluster (HBCD) (CASRN: 25637-99-4; 3194-55-6; 3194-57-8) Bibliography: Supplemental File for the TSCA Scope Document;* (U.S. EPA, 2017b). Hazards identified by studies meeting data quality criteria will be grouped by routes of exposure relevant to humans (oral, dermal, inhalation) and by cancer and noncancer endpoints.

Dose-response assessment will be performed in accordance with EPA guidance (U.S. EPA, 2012a, 2011, 1994). Dose-response analyses may be used if the data meet data quality criteria

and if additional information on the identified hazard endpoints are not available or would not alter the analysis.

The cancer mode of action (MOA) determines how cancer risks can be quantitatively evaluated. If cancer hazard is determined to be applicable to HBCD, EPA will evaluate information on genotoxicity and the mode of action for all cancer endpoints to determine the appropriate approach for quantitative cancer assessment in accordance with the U.S. EPA Guidelines for Carcinogen Risk Assessment (U.S. EPA, 2005).

4) **Derive points of departure (PODs) where appropriate; conduct benchmark dose modeling depending on the available data. Adjust the PODs as appropriate to conform (e.g., adjust for duration of exposure) to the specific exposure scenarios evaluated.**

Hazard data will be evaluated to determine the type of dose-response modeling that is applicable. Where modeling is feasible, a set of dose-response models that are consistent with a variety of potentially underlying biological processes will be applied to empirically model the dose-response relationships in the range of the observed data consistent with the EPA *Benchmark Dose Technical Guidance Document*. Where dose-response modeling is not feasible, NOAELs or LOAELs will be identified. Non-quantitative data will also be evaluated for contribution to weight of evidence or for evaluation of qualitative endpoints that are not appropriate for dose-response assessment.

EPA will evaluate whether the available PBPK and empirical kinetic models are adequate for route-to-route and interspecies extrapolation of the POD, or for extrapolation of the POD to standard exposure durations (e.g., lifetime continuous exposure). If application of the PBPK model is not possible, oral PODs may be adjusted by $BW^{3/4}$ scaling in accordance with U.S. EPA (2011), and inhalation PODs may be adjusted by exposure duration and chemical properties in accordance with U.S. EPA (1994).

5) **Evaluate the weight of the evidence of human health hazard data.**

EPA will rely on the weight of the scientific evidence when evaluating and integrating human health hazard data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

6) **Consider the route(s) of exposure (oral, inhalation, dermal), available route-to-route extrapolation approaches, available biomonitoring data and available approaches to correlate internal and external exposures to integrate exposure and hazard assessment.**

At this stage of review, EPA believes there will be sufficient data to conduct dose-response analysis and/or benchmark dose modeling for the oral route of exposure. EPA will also evaluate any potential human health hazards following dermal and inhalation exposure to HBCD, which could be important for worker, consumer, and general population risk analysis. Available data will be assessed to determine whether or not a point of departure can be identified for the dermal

and inhalation routes. This may include using route-to-route extrapolation methods where appropriate, and depending on the nature of available data.

If sufficient toxicity studies are not identified in the literature search to assess risks from dermal and inhalation exposures, then a route-to-route extrapolation from oral toxicity studies would be needed to assess systemic risks from dermal or inhalation exposures. Without an adequate PBPK model, the approaches described in the EPA guidance document *Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part E, Supplemental Guidance for Dermal Risk Assessment)* (U.S. EPA, 2004) could be applied to extrapolate from oral to dermal exposure. These approaches may be able to further inform the relative importance of dermal exposures compared with other routes of exposure. Similar methodology may also be used for assessing inhalation exposures.

### 2.6.3 Risk Characterization

Risk characterization is an integral component of the risk assessment process for both ecological and human health risks. EPA will derive the risk characterization in accordance with EPA's *Risk Characterization Handbook* (U.S. EPA, 2000). As defined EPA's Risk Characterization Policy, "the risk characterization integrates information from the preceding components of the risk evaluation and synthesizes an overall conclusion about risk that is complete, informative and useful for decision makers." Risk characterization is considered to be a conscious and deliberate process to bring all important considerations about risk, not only the likelihood of the risk but also the strengths and limitations of the assessment, and a description of how others have assessed the risk into an integrated picture.

Risk characterization at EPA assumes different levels of complexity depending on the nature of the risk assessment being characterized. The level of information contained in each risk characterization varies according to the type of assessment for which the characterization is written. Regardless of the level of complexity or information, the risk characterization for TSCA risk evaluations will be prepared in a manner that is transparent, clear, consistent, and reasonable (TCCR) (U.S. EPA, 2000). EPA will also present information in this section consistent with approaches described in the Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act (82 FR 33726). For instance, in the risk characterization summary, EPA will further carry out the obligations under TSCA section 26; for example, by identifying and assessing uncertainty and variability in each step of the risk evaluation, discussing considerations of data quality such as the reliability, relevance and whether the methods utilized were reasonable and consistent, explaining any assumptions used, and discussing information generated from independent peer review. EPA will also be guided by EPA's Information Quality Guidelines (U.S, 2002) as it provides guidance for presenting risk information. Consistent with those guidelines, in the risk characterization, EPA will also identify: (1) Each population addressed by an estimate of applicable risk effects; (2) the expected risk or central estimate of risk for the potentially exposed or susceptible subpopulations affected; (3) each appropriate upper-bound or lower bound estimate of risk; (4) each significant uncertainty identified in the process of the assessment of risk effects and the studies that would assist in resolving the uncertainty; and (5) peer reviewed studies known to the Agency that support, are directly relevant to, or fail to support any estimate of risk effects and the methodology used to reconcile inconsistencies in the scientific information.

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# APPENDICES

# Appendix A REGULATORY HISTORY

The chemical substance, HBCD, is subject to federal and state laws and regulations in the United States. The federal laws and regulations applicable to HBCD are listed along with the regulating agencies below in Table_Apx A-1. States also regulate HBCD through state laws and regulations, which are also listed within this section in Table_Apx A-2.

## A.1 Federal Laws and Regulations

**Table_Apx A-1. Federal Laws and Regulations**

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| Toxic Substances Control Act (TSCA) – Section 5(a) | Once EPA determines that a use of a chemical substance is a significant new use under TSCA section 5(a), persons are required to submit a significant new use notice (SNUN) to EPA at least 90 days before they manufacture (including import) or process the chemical substance for that use. | In September 2015, EPA promulgated a SNUR to designate manufacture or processing of HBCD for use as a flame retardant in consumer textiles (apart from use in motor vehicles) as a significant new use. Manufacturers (which includes importers) and processors are required to notify EPA 90 days before commencing the activity (80 FR 57293, September 23, 2015). |
| TSCA – Section 6(b) | EPA is directed to identify and begin risk evaluations on 10 chemical substances drawn from the 2014 update of the TSCA Work Plan for Chemical Assessments. | Cyclic Aliphatic Bromide Cluster (HBCD) is on the initial list of chemicals to be evaluated for unreasonable risk under TSCA (81 FR 91927, December 19, 2016). |
| TSCA – Section 8(a) | The TSCA section 8(a) CDR Rule requires manufacturers (including importers) to give EPA basic exposure-related information on the types, quantities and uses of chemical substances produced domestically and imported into the United States. | HBCD manufacturing (including importing), processing, and use information is reported under the CDR rule (76 FR 50816, August 16, 2011) |
| TSCA – Section 8(b) | EPA must compile, keep current and publish a list (the TSCA Inventory) of each chemical | HBCD (CASRN 25637-99-4 and CASRN 3194-55- |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | substance manufactured, processed or imported into the United States. | 6) was on the initial TSCA Inventory and therefore was not subject to EPA's new chemicals review process (60 FR 16309, March 29, 1995). |
| Emergency Planning and Community Right-to-Know Act (EPCRA) – Section 313 | Requires annual reporting from facilities in specific industry sectors that employ 10 or more full-time equivalent employees and that manufacture, process or otherwise use a TRI-listed chemical in quantities above threshold levels. | EPA listed HBCD on the TRI under 81 FR 85440 effective November 28, 2016. The first TRI reporting deadline for HBCD is July 1, 2018. |

## A.2 State Laws and Regulations

**Table_Apx A-2. State Laws and Regulations**

| State Actions | Description of Action |
|---|---|
| Classification of HBCD as Chemical of Concern to Children; law requiring reporting by manufacturers | Maine classifies HBCD as a chemical of high concern (Maine 38 M.R.S.A. § 1693-A(1))<br>Maine requires manufacturers or distributers to report the use of deca BDE and/or hexabromocylododecane, when intentionally added to certain children's products which are sold in the State of Maine. The first reporting deadline was August 31, 2017. (Rule Chapter 889)<br>http://www.maine.gov/dep/safechem/ |
| | Minnesota classifies HBCD as a chemical of high concern (Toxic Free Kids Act Minn. Stat. 2010 116.9401-116.9407) |
| | Oregon's Toxic-Free Kids Act requires manufacturers of children's products sold in Oregon to report products containing HBCD or other high priority chemicals of concern for children's health if found at or above specific levels in those products. Ultimately, manufacturers are to remove these chemicals from certain products or seek a waiver. Products that fall under this law are those that are marketed to or intended for children. The first deadline for providing notice was January 2018. |
| | Washington requires manufacturers of children's products sold in Washington to report if their product contains certain chemicals of high concern to children, including HBCD. The law also bans from manufacture or sale, in the state, children's products or residential upholstered furniture containing >1,000 ppm of five flame retardants, including HBCD (Wash. Admin. Code § 173-334-130) |

| State Actions | Description of Action |
|---|---|
| Other | In California, HBCD is listed as an initial informational candidate under California's Safer Consumer Products regulations, on the state's Proposition 65 list (Cal. Code Regs, tit. 22, § 69502.3, subd. (a)) |
| | California lists HBCD as a designated priority chemical for biomonitoring. However, California has not yet started biomonitoring HBCD. (California SB 1379) |
| | The Oregon Department of Environmental Quality lists HBCD as a priority persistent pollutant and publishes use, exposure pathways and release data for HBCD (Oregon SB 737) |
| | In Massachusetts, HBCD will be reportable under the Toxics Use Reduction Act beginning in reporting year 2018. (300 CMR 41.00) |

## A.3 International Laws and Regulations

**Table_Apx A-3. Regulatory Actions by other Governments and Tribes**

| Country/Organization | Requirements and Restrictions |
|---|---|
| Canada | In October 2016, the Regulations Amending the Prohibition of Certain Toxic Substances Regulations, 2012 (the Amendments) were published in the Canada Gazette, Part II: Vol. 150, No. 20 - October 5, 2016 and will come into force in December 2016. The Amendments include controls on HBCD that prohibit HBCD and certain products containing the substance. Time-limited exemptions for certain uses are included to allow industry to phase-out their use of HBCD. (Government of Canada) |
| European Union | HBCD is listed as a substance of very high concern (SVHC) and it is also listed under Annex XIV (Authorisation list) of European Union's Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). After August 21, 2015, only persons with approved authorization applications may continue to use the chemical (European Chemicals Agency) |
| | The Waste Electrical and Electronic Equipment (WEEE) directive in the European Union requires the separation of plastics containing brominated flame retardants prior to recycling (European Commission WEEE). |
| Japan | HBCD is subject to mandatory reporting requirements in Japan under the Chemical Substances Control Law (CSCL); specifically, Japan requires type III monitoring for all substances that may interfere with the survival and/or growth of flora and fauna (Ministry of Economy, Trade and Industry Japan). |

| Country/Organization | Requirements and Restrictions |
|---|---|
| Stockholm Convention on POPs | In May 2013, HBCD was added to the United Nation's Stockholm Convention list of POPs with specific exemptions for production and use in EPS or XPS in buildings. As required by the convention, Parties that use these exemptions must register with the secretariat and the exemptions, unless extended in accordance with the obligations of the Convention, expire five years from after the date of entry into force of the Convention with respect to the particular chemical (SCCH, 2018b). |

# Appendix B PROCESS, RELEASE AND OCCUPATIONAL EXPOSURE INFORMATION

This appendix provides information and data found in preliminary data gathering for HBCD.

## B.1 Process Information

Process-related information potentially relevant to the risk evaluation may include process diagrams, descriptions and equipment. Such information may inform potential release sources and worker exposure activities.

### B.1.1 Manufacture (Including Import)

#### B.1.1.1 Import

EPA has not identified specific activities related to the import of HBCD at this time. EPA anticipates that imported chemicals are often stored in warehouses prior to distribution for further processing and use. In some cases, the chemicals may be repackaged into differently sized containers, depending on customer demand, and quality control (QC) samples may be taken for analyses.

### B.1.2 Processing and Distribution

#### B.1.2.1 Incorporated into a Formulation, Mixture or Reaction Product

Incorporation into a formulation, mixture or reaction product refers to the process of mixing or blending of several raw materials to obtain a single product or preparation. HBCD may undergo several processing steps and the processing is dependent on its downstream incorporation into articles, which is discussed in the next subsection. EPA identified the following processing activities for HBCD.

***Compounding into XPS Masterbatch***

HBCD is compounded into an XPS masterbatch prior to being sold to XPS plastic converters, who then convert the XPS into a final article. Compounding likely occurs in a partially open process using extruders. In extruders, blends of polymer, additives and/or masterbatch are mixed either in the hopper or in tumblers and then fed into an extruder comprising one or two screws. These both shear the material and transport it through a heating regime. Volatile emissions may be produced and these are vented at various points in the extruder barrel (OECD, 2004). The compounded masterbatch may be converted into a final extrudate; however, EPA expects that the masterbatch is sent to industrial customers for further processing into a final article. HBCD concentration in the masterbatch is expected to be 50-70% (EINECS, 2008).

#### B.1.2.2 Incorporated into an Article

Incorporation into an article typically refers to a process in which a chemical becomes an integral component of an article (as defined at 40 CFR 704.3) for distribution in commerce. Exact process operations involved in the incorporation of HBCD-containing formulations or reaction products are dependent on the article. EPA identified the following processing activities that incorporate HBCD and HBCD formulations or reaction products into articles.

EPS resin beads are converted into EPS products by expansion and then molding into rigid closed-cell foam. Once expanded, the beads are fused in a steam heated mold to form a specific shape or can be formed in a billet or block that can be hot-wire cut to its desired shape and size by users (Priddy, 2006).

HBCD powder or granules are incorporated into XPS products by extrusion. The HBCD powder or granules are unloaded into a hopper and fed into an extruder along with polystyrene resin, a blowing agent and other ingredients. A viscous plastic fluid is formed in the extruder and is discharged under pressure through a die onto a moving belt at ambient conditions. The blowing agent vaporizes, causing the polymer to expand into a desired shape or form, most likely continuous sheets (boards) of closed cell insulation. Alternatively, a vacuum is used in addition to the blowing agent to cause polymer expansion. XPS masterbatch is similarly converted into XPS products (NICNAS, 2012b; EINECS, 2008; Suh, 2000).

#### B.1.2.3 Recycling

As stated in Section 2.2.2, construction insulation materials are rarely recycled for numerous reasons, including that insulation waste is typically not separated from mixed waste stream. However, reuse and recycle does occur in the United States. At the end-of-life, polystyrene insulation boards (i.e., EPS and XPS foam insulation containing HBCD) may still have beneficial value for insulation. The insulation can be removed in whole and reused in the same capacity. Polystyrene insulation may also be demolished, melted and reformed into new insulation materials boards or other applications. Typically, polystyrene insulation containing HBCD can only be recycled into building insulation or other building applications (U.S. EPA, 2014a).

Electronic products (which may or may not contain HBCD) can also be recycled. HIPS materials constitute more than half the plastic materials recovered from household electronics (Borchardt, 2006). No information was identified that further described the processes used in recovering the plastics from electronics and how those plastics are reprocessed into other products.

### B.1.3 Uses

#### B.1.3.1 Building/Construction Materials

A major use of HBCD is in XPS and EPS foam for continuous insulation applications such as in walls and roofs on the exterior of buildings, ceilings and subfloor systems. The materials may be incorporated into building products such as structural insulated panels or insulating concrete forms or used in other below grade or geotechnical applications for foundations or highways or for dimensional stability or strength applications (e.g., insulated cold storage applications) (U.S. EPA, 2017g, 2014a; NICNAS, 2012b).

### B.1.4 Disposal

Releases from industrial sites to surface water (via direct discharge or indirect discharge through POTWs), air and landfill are expected during manufacture, processing, use, product usage and disposal of HBCD or products containing HBCD (U.S. EPA, 2014a; NICNAS, 2012b; Environment Canada, 2011; EINECS, 2008).

Demolished building materials are classified as Construction and Demolition (C&D) waste, which may be disposed in municipal solid waste landfills (MSWLFs) or C&D landfills (U.S. EPA, 2014a). XPS foam may also be disposed of via waste energy plants.

## B.2 Sources Containing Potentially Relevant Data or Information

Some sources of information and data related to releases and worker exposure were found during the systematic review literature search. Sources of data or information identified in the Analysis Plan Sections 2.6.1.1 and Section 2.6.1.4 are shown in the four tables below. The data sources identified are based on preliminary results to date of the full-text screening step of the systematic review process. Further screening and quality evaluation are on-going. These sources will be reviewed to determine the utility of the data and information in the Risk Evaluation.

**Table_Apx B-1. Potentially Relevant Data Sources for Information Related to Process Description**

| Bibliography | url |
|---|---|
| NICNAS (2001). Polybrominated flame retardants (PBFRs): Priority existing chemical assessment report no. 20. | NICNAS (2001) |
| NICNAS (2012). Hexabromocyclododecane: Priority existing chemical assessment report no. 34. Australia. | NICNAS (2012b) |
| Zhang, H., et al. (2012). "Co-release of hexabromocyclododecane (HBCD) and Nano- and microparticles from thermal cutting of polystyrene foams." Environmental Science and Technology **46**(20): 10990-10996. | Zhang et al. (2012) |
| Morf, L. S., et al. (2005). "Brominated flame retardants in waste electrical and electronic equipment: substance flows in a recycling plant." Environmental Science and Technology **39**(22): 8691-8699. | Morf et al. (2005) |
| Li, L., et al. (2016). "Long-term emissions of hexabromocyclododecane as a chemical of concern in products in China." Environment International **91**: 291-300. | Li et al. (2016) |
| OECD (2009). Emission scenario documents on coating industry (paints, lacquers and varnishes). Paris, France. | OECD (2009) |
| OECD (2015). Emission scenario document on use of adhesives. Paris, France. | OECD (2015) |
| ToxNet Hazardous Substances Data Bank (2017). HSDB: 1,2,5,6,9,10-Hexabromocyclododecane. Bethesda, MD, National Institute of Health, U.S. National Library of Medicine. | ToxNet Hazardous Substances Data Bank (2017) |
| ECHA (2008). Risk assessment: hexabromocyclododecane. Helsinki, Finland. | ECHA (2008) |
| ECHA (2014). Template for third party submission of information on alternatives for applications for authorisation HBCD use in EPS for building applications. Helsinki, Finland. | ECHA (2014) |
| INEOS Styrenics (2017). Analysis of alternatives: HBCDD use in EPS for building applications. Helsinki, Finland, European Chemicals Agency. | INEOS Styrenics (2017) |
| ECHA (2017). Hexabromocyclododecane, Part 2. Helsinki, Finland. | ECHA (2017d) |
| European Flame Retardants Association (2016). Fireaway! the EFRA newsletter. | European Flame Retardants Association (2016) |

**Table_Apx B-2. Potentially Relevant Data Sources for Measured or Estimated Release Data**

| Bibliography | url |
|---|---|
| Kemmlein, S., et al. (2003). "Emissions of organophosphate and brominated flame retardants from selected consumer products and building materials." Atmospheric Environment **37**(39-40): 5485-5493. | Kemmlein et al. (2003) |
| Gorga, M., et al. (2013). "Determination of PBDEs, HBB, PBEB, DBDPE, HBCD, TBBPA and related compounds in sewage sludge from Catalonia (Spain)." Science of the Total Environment **444**: 51-59. | Gorga et al. (2013) |
| Tomko, G. and K. M. Mcdonald (2013). "Environmental fate of hexabromocyclododecane from a new Canadian electronic recycling facility." Journal of Environmental Management **114**: 324-327. | Tomko and Mcdonald (2013) |
| Ni, H. G., et al. (2016). "Brominated flame retardant emissions from the open burning of five plastic wastes and implications for environmental exposure in China." Environmental Pollution **214**: 70-76. | Ni et al. (2016) |
| Li, L., et al. (2016). "Long-term emissions of hexabromocyclododecane as a chemical of concern in products in China." Environment International **91**: 291-300. | Li et al. (2016) |
| OECD (2015). Emission scenario document on use of adhesives. Paris, France. | OECD (2015) |
| ECHA (2008). Risk assessment: hexabromocyclododecane. Helsinki, Finland. | ECHA (2008) |
| ECHA (2017). Chemical safety report: Hexabromocyclododecane and all major diastereoisomers identified. Helsinki, Finland. | ECHA (2017a) |
| ECHA (2009). Background document for hexabromocyclododecane and all major diastereoisomers identified. Helsinki, Finland. | ECHA (2009a) |
| ECHA (2017). Chemical safety report: Hexabromocyclododecane and all major diastereoisomers identified, Part 2. Helsinki, Finland. | ECHA (2017b) |
| ECHA (2015). RAC and SEAC Opinion on an application for authorisation for hexabromocyclododecane. Helsinki, Finland. | ECHA (2015) |
| (2008). Summary risk assessment report: Hexabromocyclododecane. Helsinki, Finland, European Chemicals Agency. | 2008) |
| ECHA (2009). Prioritisation and Annex XIV background information: hexbromocyclododecane. Helsinki, Finland. | ECHA (2009d) |
| European Flame Retardants Association (2013). Fireaway! the EFRA newsletter, Part 2. | European Flame Retardants Association (2013) |
| European Flame Retardants Association (EFRA) (2015). Keeping fire in check an introduction to flame retardants used in transport applications. Brussels, Belgium. | European Flame Retardants Association (EFRA) (2015) |
| European Brominated Flame Retardant Industry Panel (2008). EBFRIP statement RE UBA's publication on brominated flame retardant. Brussels, Belgium. | European Brominated Flame Retardant Industry Panel (2008) |

**Table_Apx B-3. Potentially Relevant Data Sources for Personal Exposure Monitoring and Area Monitoring Data**

| Bibliography | url |
|---|---|
| Thomsen, C., et al. (2007). "Occupational exposure to hexabromocyclododecane at an industrial plant." Environmental Science and Technology **41**(15): 5210-5216. | Thomsen et al. (2007) |
| Harrad, S., et al. (2008). "Concentrations of brominated flame retardants in dust from United Kingdom cars, homes, and offices: causes of variability and implications for human exposure." Environment International **34**(8): 1170-1175. | Harrad et al. (2008) |
| NICNAS (2001). Polybrominated flame retardants (PBFRs): Priority existing chemical assessment report no. 20. | NICNAS (2001) |
| Zhang, H., et al. (2012). "Co-release of hexabromocyclododecane (HBCD) and Nano- and microparticles from thermal cutting of polystyrene foams." Environmental Science and Technology **46**(20): 10990-10996. | Zhang et al. (2012) |
| Rosenberg, C., et al. (2011). "Exposure to flame retardants in electronics recycling sites." Annals of Occupational Hygiene **55**(6): 658-665. | Rosenberg et al. (2011) |
| Saito, I., et al. (2007). "Indoor organophosphate and polybrominated flame retardants in Tokyo." Indoor Air **17**(1): 28-36. | Saito et al. (2007) |
| Velsicol Chem Corp (1978). Industrial hygiene survey, Velsicol Chemical Corporation, El Dorado, Ark Plant, Fire Master 680 Unit and semi-works summary with attachments and cover letter dated 071978. Chicago, IL. | Velsicol Chem Corp (1978) |
| Strid, A., et al. (2014). "Brominated flame retardant exposure of aircraft personnel." Chemosphere **116**: 83-90. | Strid et al. (2014) |
| Kuo, Y., uY, et al. (2014). "Chemical Composition of Nanoparticles Released from Thermal Cutting of Polystyrene Foams and the Associated Isomerization of Hexabromocyclododecane (HBCD) Diastereomers." Aerosol and Air Quality Research **14**(4): 1114-1120. | Kuo et al. (2014) |
| Yi, S., et al. (2016). "Assessment of the occupational and environmental risks of hexabromocyclododecane (HBCD) in China." Chemosphere **150**: 431-437. | Yi et al. (2016) |
| ECHA (2008). Risk assessment: hexabromocyclododecane. Helsinki, Finland. | ECHA (2008) |
| (2008). Summary risk assessment report: Hexabromocyclododecane. Helsinki, Finland, European Chemicals Agency. | 2008) |
| ECHA (2009). Prioritisation and Annex XIV background information: hexbromocyclododecane. Helsinki, Finland. | ECHA (2009d) |

**Table_Apx B-4. Potentially Relevant Data Sources for Engineering Controls and Personal Protective Equipment**

| Bibliography | url |
|---|---|
| Thomsen, C., et al. (2007). "Occupational exposure to hexabromocyclododecane at an industrial plant." Environmental Science and Technology **41**(15): 5210-5216. | Thomsen et al. (2007) |
| NICNAS (2012). Hexabromocyclododecane: Priority existing chemical assessment report no. 34. Australia. | NICNAS (2012b) |
| Rosenberg, C., et al. (2011). "Exposure to flame retardants in electronics recycling sites." Annals of Occupational Hygiene **55**(6): 658-665. | Rosenberg et al. (2011) |
| Velsicol Chem Corp (1978). Industrial hygiene survey, Velsicol Chemical Corporation, El Dorado, Ark Plant, Fire Master 680 Unit and semi-works summary with attachments and cover letter dated 071978. Chicago, IL. | Velsicol Chem Corp (1978) |
| OECD (2015). Emission scenario document on use of adhesives. Paris, France. | OECD (2015) |
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| ToxNet Hazardous Substances Data Bank (2017). HSDB: 1,2,5,6,9,10-Hexabromocyclododecane. Bethesda, MD, National Institute of Health, U.S. National Library of Medicine. | ToxNet Hazardous Substances Data Bank (2017) |
| ECHA (2017). Guidance on safe use: hexabromocyclododecane. Helsinki, Finland. | ECHA (2017c) |
| ECHA (2017). Chemical safety report: Hexabromocyclododecane and all major diastereoisomers identified, Part 2. Helsinki, Finland. | ECHA (2017b) |
| NIOSH (2014). International chemical safety cards (ICDC): Hexabromocyclododecane (mixture of isomers). Atlanta, GA. | NIOSH (2014) |

# Appendix C SUPPORTING INFORMATION FOR OCCUPATIONAL EXPOSURE CONCEPTUAL MODEL

**Table_Apx C-1. Worker and Occupational Non-User Exposure Conceptual Model Supporting Table**

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Analysis | Rationale |
|---|---|---|---|---|---|---|---|---|
| Manufacture | Import | Import | Repackaging of import containers | Liquid | Dermal | Workers | No | According to CDR, all importers reported solid physical forms of HBCD and therefore, exposure to liquid HBCD during repackaging is not likely. |
| | | | | Solid | Dermal | Workers | Yes | Exposure will only occur in the event the imported material is repackaged. In that case, EPA expects potential exposure as a result of dust generation during repackaging of solid particulates. |
| | | | | Fugitive Dust | Inhalation | Workers, ONU | Yes | Exposure will only occur in the event the imported material is repackaged. |
| | | | | Fugitive Dust | Oral | Workers, ONU | Yes | Oral exposure of workers to HBCD may occur through ingestion of dust that deposits in the upper respiratory tract and is swallowed during repackaging. |
| | | | | Liquid, Solid | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| Processing | Incorporated into formulation, mixture or reaction product | Flame retardants used in custom compounding of purchased resin (e.g., compounding in XPS masterbatch) | Plastics compounding | Solid | Dermal | Workers | Yes | EPA expects potential exposure during the unloading of HBCD. |
| | | | | Fugitive Dust | Inhalation | Workers, ONU | Yes | EPA anticipates inhalation of dust as a result of generation of dust during the unloading of HBCD as the most important HBCD exposure pathway. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Analysis | Rationale |
|---|---|---|---|---|---|---|---|---|
| | | | | Fugitive Dust | Oral | Workers, ONU | Yes | Oral exposure of workers to HBCD may occur through ingestion of dust that deposits in the upper respiratory tract and is swallowed. |
| | | | | Solid | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| Processing | Incorporated into articles | Flame retardants used in plastics product manufacturing (manufacture of XPS and EPS foam; manufacture of structural insulated panels (SIPS) and automobile replacement parts from XPS and EPS foam) | Plastics converting; SIP assembly | Solid | Dermal | Workers | Yes | As an additive flame retardant, HBCD is not chemically bonded to the base material (resin) and therefore there may be a potential for release and subsequent exposure during handling. |
| | | | | Fugitive Dust | Inhalation | Workers, ONU | Yes | |
| | | | | Fugitive Dust | Oral | Workers, ONU | Yes | Oral exposure of workers to HBCD may occur through ingestion of dust that deposits in the upper respiratory tract and is swallowed. |
| | | | | Solid | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| Processing | Recycling | Recycling | Recycle of EPS. | Solid | Dermal | Workers | Yes | As an additive flame retardant, HBCD is not chemically bonded to the base material (resin) and therefore there may be a potential for release and subsequent exposure during recycling activities. |
| | | | | Fugitive | Inhalation | Workers, ONU | Yes | |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Analysis | Rationale |
|---|---|---|---|---|---|---|---|---|
| | | | | Fugitive | Oral | Workers, ONU | Yes | Oral exposure of workers to HBCD may occur through ingestion of dust that deposits in the upper respiratory tract and is swallowed. |
| | | | | Solid | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| Distribution in Commerce | Distribution | Distribution | Distribution of bulk raw material; Distribution of formulated products | -- | -- | -- | No | Potential for exposure expected only in the event the packaged raw material or formulated products are damaged, resulting in the potential release of HBCD. |
| Commercial Use | Building/construction materials | Plastic articles (hard): construction and building materials covering large surface areas | Installation/Reuse/Demolition of EPS/XPS foam insulation in residential, public and commercial buildings, and other structures | Solid | Dermal | Workers | Yes | Potential for exposure highly expected because the building/construction materials can be roughly handled during construction use, which could result in the release of HBCD in dust emissions from this activity. |
| | | | | Fugitive and Installation/ Reuse/Demolition Dust | Inhalation | Workers, ONU | Yes | EPA anticipates inhalation of dust and other respirable particles as the most important HBCD exposure pathway. |
| | | | | Fugitive and Installation/ Reuse/Demolition Dust | Oral | Workers, ONU | Yes | Oral exposure of workers to HBCD may occur through ingestion of dust that deposits in the upper respiratory tract and is swallowed. |
| | | | | Solid | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | Automobile replacement parts | Automobile replacement parts | Use of automobile replacement parts | Fugitive dust | Dermal, inhalation and oral | Workers | No | Emissions of HBCD from automobile replacement parts are not expected to be significant and the EPS or XPS that comprises these replacement parts is expected to be covered with other material thereby limiting emissions. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Analysis | Rationale |
|---|---|---|---|---|---|---|---|---|
| Disposal | Waste Handling, Treatment and Disposal | Disposal of HBCD wastes | Worker handling of wastes | Liquid | Dermal | Workers | No | Liquid contact is not assessed due to subcategories of uses that have ceased as discussed in Section 2.2. |
| | | | | Solid | Dermal | Workers | Yes | Highest potential for exposure for workers/occupational non-users would be to wastes from handling HBCD in powder form (e.g., disposal of raw material packaging, baghouse dust). |
| | | | | Fugitive Dust | Inhalation | Workers, ONU | Yes | EPA anticipates inhalation of dust as the most important HBCD exposure pathway. |
| | | | | Fugitive and Settled Dust | Oral | Workers, ONU | Yes | Oral exposure of workers to HBCD may occur through ingestion of dust that deposits in the upper respiratory tract and is swallowed. |
| | | | | Solid | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |

# Appendix D SUPPORTING INFORMATION FOR CONSUMER, GENERAL POPULATION AND ENVIRONMENTAL EXPOSURE CONCEPTUAL MODEL

**Table_Apx D-1. Consumer Exposure Conceptual Model Supporting Table**

| Life Cycle Stage | Category | Subcategory | Release from source | Exposure Pathway | Route | Receptor | Proposed for Further Analysis | Rationale |
|---|---|---|---|---|---|---|---|---|
| Consumer Use | Building/ construction materials | EPS/XPS foam insulation in residential buildings covering large surface areas- hard plastic article | Long-term emission/mass-transfer, Abrasion, Direct Transfer to Dust | Mouthing | Oral | Consumers (children) | No | Consumers are not likely to be in direct contact and mouth EPS insulation. |
| Consumer Use; Consumer Reuse and Recyling | Building/ construction materials | EPS/XPS foam insulation in residential buildings covering large surface areas- hard plastic article | Long-term emission/mass-transfer, Abrasion, Direct Transfer to Dust | Suspended particles in Air | Inhalation | Consumers: Adults and Children with EPS insulation in their residence | Yes | Based on HBCD's relatively low vapor pressure and relatively high octanol-air partition coefficient, it is likely to preferentially partition to smaller suspended particles in the air. Note, EPS and XPS will be compared and may be considered together or separately. |
| | | | Long-term emission/mass-transfer, Abrasion, Direct Transfer to Dust | Settled Dust | Oral Dermal | Consumers: Adults and Children with EPS insulation in their residence | Yes | Based on HBCD's relatively low vapor pressure and relatively high octanol-air partition coefficient, it is likely to preferentially partition to settled dust from the air, and directly to surface dust on the material. |
| | | | Direct contact during installation, renovation, and removal | Abrasion through drilling/sawing Direct contact | Dermal, Inhalation, Oral | Consumers: Adults who install or remove EPS insulation | Yes | Drilling is a common mechanism to attach panels to surfaces. The material may be similarly abraded during renovation and removal. It is expected that adults would perform these activities. EPS insulation is typically in unfinished spaces where children would not spend long amounts of time. |

| Life Cycle Stage | Category | Subcategory | Release from source | Exposure Pathway | Route | Receptor | Proposed for Further Analysis | Rationale |
|---|---|---|---|---|---|---|---|---|
| Consumer Use | Automotive products | Automobile Replacement Parts | Long-term emission/mass-transfer, Abrasion, Direct Transfer to Dust | Suspended particles in Air | Inhalation | Consumers: Adults and Children with replace-ment parts within their automobile | Yes | Based on HBCD's relatively low vapor pressure and relatively high octanol-air partition coefficient, it is likely to preferentially partition to smaller suspended particles in the air. Note, EPS and XPS will be compared and may be considered together or separately. |
| | | | Long-term emission/mass-transfer, Abrasion, Direct Transfer to Dust | Settled Dust | Oral Dermal | Consumers: Adults and Children with replace-ment parts in their automobile | Yes | Based on HBCD's relatively low vapor pressure and relatively high octanol-air partition coefficient, it is likely to preferentially partition to settled dust from the air, and directly to surface dust on the material. |
| Background | All | All | Suspended particles | Indoor Air | Inhalation | Bystander/ Resident | Yes | EPA plans to analyze background levels of HBCD in indoor air. |
| Background | All | All | Settled Dust | Indoor Dust | Ingestion | Bystander/ Resident | Yes | EPA plans to analyze background levels of HBCD in indoor dust and associated ingestion. |
| Background | All | All | Settled Dust | Indoor Dust | Dermal | Bystander/ Resident | Yes | EPA plans to analyze background levels of HBCD in indoor dust and associated dermal exposure. |

**Table_Apx D-2. General Population and Environmental Exposure Conceptual Model Supporting Table**

| Life Cycle Stage | Release | Exposure Pathway / Media | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale |
|---|---|---|---|---|---|---|
| All | Emissions to Air | Near facility ambient air concentrations | Inhalation; Ingestion of suspended particles | General Population: Adults and Children living near facilities | Yes | EPA believes that release of HBCD to air is probable based on a preliminary review of the literature. TRI data will be available starting in mid-2018. EPA is currently conducting a systematic review of the scientific literature. Based on the results of this review, EPA will either confirm the rationale or reach a different conclusion. |
| | | Indirect deposition to nearby bodies of water and soil catchments | Surface water and sediment (lakes)- Ingestion<br>Soil (catchments)- Ingestion<br>Uptake from environment into food sources- Ingestion | General Population: Adults and Children living near facilities | Yes | Based on HBCD's physical chemical properties, it is likely to be released as a particulate and be deposited to nearby water bodies and soil catchments. |
| | | | Surface water and sediment (lakes)<br>Soil (catchments) | Aquatic and Terrestrial Receptors | Yes | |
| All | Industrial pre-treatment and wastewater treatment- | Direct release into surface water and indirect partitioning to sediment | Surface water and Sediment (rivers) | Aquatic and Terrestrial Receptors | Yes | EPA believes that release of HBCD in wastewater is probable based on a preliminary review of the literature. Its subsequent release through the exposure pathway may result in potential for exposure. TRI data will be available starting in mid-2018. EPA is currently conducting a systematic review of the scientific literature. Based on the results of this review, EPA will either confirm the rationale or reach a different conclusion. |

| Life Cycle Stage | Release | Exposure Pathway / Media | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale |
|---|---|---|---|---|---|---|
| | | Direct release into surface water and partitioning to sediment and bioaccumulation into edible aquatic species | Surface water and Sediment (rivers)<br>Uptake from environment into food sources-Ingestion | General Population: Adults and Children living near facilities | Yes | HBCD has been reported in surface water and sediment concentrations near industrial facilities. |
| | | Biosolids application to soil | Soil ingestion<br>Uptake from environment into food sources-Ingestion | General Population: Adults and Children living near facilities | Yes | HBCD has been detected in biosolids and soil samples. |
| | | Biosolids application to soil | Soil | Terrestrial receptors | Yes | HBCD has been detected in soil samples. |
| Disposal | Solid and Liquid Wastes sent to Municipal Incinerator | Indirect deposition to nearby bodies of water and soil catchments | Surface water and sediment (lakes)-Ingestion<br>Soil (catchments)-Ingestion<br>Uptake from environment into food sources-Ingestion | General Population: Adults and Children living near facilities | Yes | Municipal incinerators may release HBCD due to incomplete removal during burning. |
| | Solid and Liquid Wastes sent to Municipal Incinerator | Indirect deposition to nearby bodies of water and soil catchments | Surface water and sediment (lakes)<br>Soil (catchments) | Aquatic and Terrestrial Receptors | Yes | Municipal incinerators may release HBCD due to incomplete removal during burning. |

| Life Cycle Stage | Release | Exposure Pathway / Media | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale |
|---|---|---|---|---|---|---|
| | Municipal landfill and other land disposal | Leachate to POTW and surface water | Ingestion | General Population: Adults and Children living near facilities | Yes | HBCD has been detected in leachate and HBCD containing materials are sent to landfill as part of disposal. |
| | Municipal landfill and other land disposal | Leachate to POTW and surface water and partitioning to sediment | Surface water and sediment (rivers) | Aquatic Receptors | Yes | HBCD has been detected in leachate and HBCD containing materials are sent to landfill as part of disposal. |
| Recycling | Recycling of EPS/XPS materials and emissions to air | Near Facility Ambient Air Concentrations | Inhalation Ingestion of suspended particles | General Population: Adults and Children living near facilities | Yes | EPS/XPS is the primary use HBCD and there is continuing exposure potential near these recycling facilities. |
| | | Indirect deposition to nearby bodies of water and soil catchments | Surface water and sediment (lakes)- Ingestion Soil (catchments)- Ingestion Uptake from environment into food sources- Ingestion | General Population: Adults and Children living near facilities | Yes | EPS/XPS is the primary use of HBCD and there is continuing exposure potential near these recycling facilities. |
| | | Indirect deposition to nearby bodies of water and soil catchments | Surface water and sediment (lakes) Soil (catchments) | Aquatic and Terrestrial Receptors | Yes | EPS/XPS is the primary use HBCD and there is continuing exposure potential near these recycling facilities. |

| Life Cycle Stage | Release | Exposure Pathway / Media | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale |
|---|---|---|---|---|---|---|
| All | Background | Surface water | Ingestion | General Population: Adults and Children; Aquatic and Terrestrial Receptors | Yes | HBCD has been detected in surface water sampling at locations away from facilities. EPA plans to analyze background levels of HBCD in these media |
| | | Sediment | Ingestion | Aquatic Receptors | Yes | HBCD has been detected in sediment sampling locations not near facilities. EPA plans to analyze background levels of HBCD in these media |
| | | Soil | Ingestion | General Population: Adults and Children; Terrestrial Receptors | Yes | HBCD has been detected in soil sampling locations not near facilities. EPA plans to analyze background levels of HBCD in these media |
| | | Aquatic Biota | n/a | Aquatic Receptors | Yes | HBCD has been detected in aquatic biota. EPA plans to analyze background levels of HBCD in these organisms. |
| | | Terrestrial Biota | n/a | Terrestrial receptors | Yes | HBCD has been detected in aquatic biota. EPA plans to analyze background levels of HBCD in these organisms. |
| | | Indoor Air | Inhalation Ingestion of suspended particles | General Population | Yes | HBCD has been detected in a wide range of indoor air and dust samples. It is likely that the predominant source of exposure is from indoor sources. However, other sources could also contribute. Background indoor dust concentrations will also be analyzed |
| | | Indoor Dust | Ingestion, Dermal | General Population | Yes | |
| All | Background | Dietary Food Sources | Ingestion | General Population | Yes | HBCD has been detected in a variety of dietary food sources. These background levels will be analyzed. |
| All | Background | Human Biomonitoring - breast milk | n/a | General Population | Yes | HBCD has been detected in breast milk and this is a source of exposure for nursing infants and helps inform adult exposure intakes. |

| Life Cycle Stage | Release | Exposure Pathway / Media | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale |
|---|---|---|---|---|---|---|
| All | Background | Human Biomonitoring-serum-blood | n/a | General Population | Yes | HBCD has been detected in human matrices. These measured levels may be considered with toxicokinetics data to compare estimates of dose. |

# Appendix E INCLUSION AND EXCLUSION CRITERIA FOR FULL TEXT SCREENING

Appendix E contains the eligibility criteria for various data streams informing the TSCA risk evaluation: environmental fate; engineering and occupational exposure; exposure to the general population and consumers; and human health hazard. The criteria are applied to the *on-topic* references that were identified following title and abstract screening of the comprehensive search results published on June 22, 2017.

Systematic reviews typically describe the study eligibility criteria in the form of PECO statements. PECO stands for Population, Exposure, Comparator and Outcome and the approach is used to formulate explicit and detailed criteria about those characteristics in the publication that should be present in order to be eligible for inclusion in the review. EPA/OPPT adopted the PECO approach or variant to guide the inclusion/exclusion decisions during full text screening.

Inclusion and exclusion criteria were also used during the title and abstract screening, and documentation about the criteria can be found in the *Strategy for Conducting Literature Searches* document published in June 2017 along with each of the TSCA scope documents. The list of on-topic references resulting from the title and abstract screening is undergoing full text screening using the criteria in the PECO statements. The overall objective of the screening process is to select the most relevant evidence for the TSCA risk evaluation. As a general rule, EPA is excluding non-English data/information sources and will translate on a case by case basis.

The inclusion and exclusion criteria for ecotoxicological data have been documented in the ECOTOX SOPs. The criteria can be found at https://cfpub.epa.gov/ecotox/help.cfm?helptabs=tab4) and in the *Strategy for Conducting Literature Searches* document published along with each of the TSCA scope documents.

## E.1 Inclusion Criteria for Data Sources Reporting Environmental Fate Data

EPA/OPPT developed a generic PESO statement to guide the full text screening of environmental fate data sources. PESO stands for Pathways and Processes, Exposure, Setting or Scenario, and Outcomes. Subsequent versions of the PESO statement may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the inclusion criteria in the PESO statement are eligible for inclusion, considered for evaluation, and possibly included in the environmental fate assessment. On the other hand, data sources are excluded if they do not meet the criteria in the PESO statement.

Assessors seek information on various chemical-specific fate endpoints and associated fate processes, environmental media and exposure pathways as part of the process of developing the environmental fate assessment (Table_Apx E-2). Those that will be the focus of the environmental fate assessment for HBCD have been indicated in Table_Apx E-2. The PESO statement and information in Table_Apx E-1 will be used when screening the fate data sources to ensure complete coverage of the processes, pathways and data relevant to the fate of the chemical substance of interest.

| Table_Apx E-1. Inclusion Criteria for Data Sources Reporting Environmental Fate Data | |
|---|---|
| **PESO Element** | **Evidence** |
| **P**athways and **P**rocesses | • Environmental fate, transport, partitioning and degradation behavior across environmental media to inform exposure pathways of the chemical substance of interest<br>• Media of interest may include:<br>– Air<br>– Surface water<br>– Ground water<br>– Soil<br>– Sediment<br>– Biosolids<br>– Other media including anthropogenic materials and media in the indoor environment (e.g., dust)<br>Please refer to the conceptual models for more information about the exposure pathways included in each TSCA risk evaluation. |
| **E**xposure | • Environmental exposure of ecological receptors (i.e., aquatic and terrestrial organisms) to the chemical substance of interest and/or its degradation products and metabolites<br>• Environmental exposure of human receptors, including any potentially exposed or susceptible subpopulations, to the substance of interest and/or its degradation products and metabolites<br><br>Please refer to the conceptual models for more information about the ecological and human receptors included in each TSCA risk evaluation. |
| **S**etting or **S**cenario | Any setting or scenario resulting in releases of the chemical substance of interest into the natural or built environment (e.g., buildings including homes or workplaces, or wastewater treatment facilities) that would expose ecological (i.e., aquatic and terrestrial organisms) or human receptors (i.e., general population, and potentially exposed or susceptible subpopulation) |
| **O**utcomes | • Fate properties which allow assessments of exposure pathways:<br>○ Abiotic and biotic degradation rates, mechanisms, pathways, and products<br>○ Bioaccumulation magnitude and metabolism rates<br>○ Partitioning within and between environmental media (see Pathways and Processes) |

| Table_Apx E-2. Fate Endpoints and Associated Processes, Media and Exposure Pathways Considered in the Development of the Environmental Fate Assessment | | | | | | |
|---|---|---|---|---|---|---|
| **Fate Data Endpoint** | **Associated Process(es)** | **Associated Media/Exposure Pathways** | | | | |
| | | **Surface water, Sediment** | **Soil, Biosolids** | **Groundwater** | **Air** | **Indoor environment, anthropogenic materials, other media** |
| **Required Environmental Fate Data** | | | | | | |
| Abiotic reduction rates or half-lives | Abiotic reduction, Abiotic dehalogenation | X | | | | |
| Aerobic biodegradation rates or half-lives | Aerobic biodegradation | X | X | | | |
| Anaerobic biodegradation rates or half-lives | Anaerobic biodegradation | X | X | X | | |
| Aqueous photolysis (direct and indirect) rates or half-lives | Aqueous photolysis (direct and indirect) | X | | | | |
| Atmospheric photolysis (direct and indirect) rates or half-lives | Atmospheric photolysis (direct and indirect) | | | | X | X |
| Bioconcentration factor (BCF), Bioaccumulation factor (BAF) | Bioconcentration, Bioaccumulation | X | | | | |
| Hydrolysis rates or half-lives | Hydrolysis | X | | | | |
| $K_{AW}$, Henry's Law constant, and other volatilization information | Volatilization | X | X | | X | X |
| $K_{OC}$ and other sorption information | Sorption, Mobility | X | X | X | | |
| **Optional Environmental Fate Data** | | | | | | |
| Abiotic transformation products | Hydrolysis, Photolysis | X | | | X | |
| Aerobic biotransformation products | Aerobic biodegradation | X | X | | | |
| Anaerobic biotransformation products | Anaerobic biodegradation | X | X | X | | |
| Atmospheric deposition information | Atmospheric deposition | | | | X | X |
| Biomagnification and related information | Trophic magnification | X | | | | |

| Table_Apx E-2. Fate Endpoints and Associated Processes, Media and Exposure Pathways Considered in the Development of the Environmental Fate Assessment | | | | | | |
|---|---|---|---|---|---|---|
| Coagulation information | Coagulation, Mobility | X | | | | |
| Desorption information | Sorption, Mobility | X | X | X | | |
| Incineration removal information | Incineration | | | | X | |
| Suspension/resuspension information | Suspension/resuspension, Mobility | X | | | | X |
| Wastewater treatment removal information | Wastewater treatment | X | | | | |

## E.2 Inclusion Criteria for Data Sources Reporting Engineering and Occupational Exposure Data

EPA/OPPT developed a generic RESO statement to guide the full text screening of engineering and occupational exposure literature (Table_Apx E-3). RESO stands for Receptors, Exposure, Setting or Scenario, and Outcomes. Subsequent versions of the RESO statement may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the inclusion criteria specified in the RESO statement will be eligible for inclusion, considered for evaluation, and possibly included in the environmental release and occupational exposure assessments, while those that do not meet these criteria will be excluded.

The RESO statement should be used along with the engineering and occupational exposure data needs table (Table_Apx E-4) when screening the literature.

**Table_Apx E-3. Inclusion Criteria for Data Sources Reporting Engineering and Occupational Exposure Data**

| RESO Element | Evidence |
|---|---|
| **R**eceptors | • **Humans:**<br>Workers, including occupational non-users<br><br>• **Environment:**<br>Aquatic and possibly terrestrial ecological receptors (release estimates input to Exposure)<br><br>Please refer to Appendix C and Appendix D for more information about the ecological and human receptors included in each TSCA risk evaluation. |
| **E**xposure | • Worker exposure to and relevant environmental releases of the chemical substance of interest<br>  ○ Any exposure route (list included: dermal, inhalation, oral) as indicated in the conceptual model<br>  ○ Any relevant media/pathway as indicated in the conceptual model<br><br>Please refer to the conceptual models for more information about the routes and media/pathways included in each TSCA risk evaluation. |
| **S**etting or **S**cenario | • Any occupational setting or scenario resulting in worker exposure and environmental releases (includes all manufacturing, processing, use, disposal indicated in Table_Apx E-4 below. |
| **O**utcomes | • Quantitative estimates* of worker exposures and of relevant environmental releases from occupational settings<br>• General information and data related and relevant to the occupational estimates* |
| * Metrics (e.g., mg/kg/day or mg/m$^3$ for worker exposures, kg/site/day for releases) are determined by toxicologists for worker exposures and by exposure assessors for releases; also, the Engineering Data Needs (Table_Apx E-4) provides a list of related and relevant general information. | |

| Table_Apx E-4. Engineering, Environmental Release and Occupational Data Necessary to Develop the Environmental Release and Occupational Exposure Assessments | |
|---|---|
| **Objective Determined during Scoping** | **Type of Data** |
| General Engineering Assessment (may apply for either or both Occupational Exposures and / or Environmental Releases) | 1. Description of the life cycle of the chemical(s) of interest, from manufacture to end-of-life (e.g., each manufacturing, processing, or use step), and material flow between the industrial and commercial life cycle stages. {Tags: Life cycle description, Life cycle diagram}[a]<br>2. The total annual U.S. volume (lb/yr or kg/yr) of the chemical(s) of interest manufactured, imported, processed, and used; and the share of total annual manufacturing and import volume that is processed or used in each life cycle step. {Tags: Production volume, Import volume, Use volume, Percent PV} [a]<br>3. Description of processes, equipment, unit operations, and material flows and frequencies (lb/site-day or kg/site-day and days/yr; lb/site-batch and batches/yr) of the chemical(s) of interest during each industrial/ commercial life cycle step. Note: if available, include weight fractions of the chemicals (s) of interest and material flows of all associated primary chemicals (especially water). {Tags: Process description, Process material flow rate, Annual operating days, Annual batches, Weight fractions (for each of above, manufacture, import, processing, use)} [a]<br>4. Basic chemical properties relevant for assessing exposures and releases, e.g., molecular weight, normal boiling point, melting point, physical forms, and room temperature vapor pressure. {Tags: Molecular weight, Boiling point, Melting point, Physical form, Vapor pressure, Water solubility} [a]<br>5. Number of sites that manufacture, process, or use the chemical(s) of interest for each industrial/ commercial life cycle step and site locations. {Tags: Numbers of sites (manufacture, import, processing, use), Site locations} [a] |
| Occupational Exposures | 6. Description of worker activities with exposure potential during the manufacture, processing, or use of the chemical(s) of interest in each industrial/commercial life cycle stage. {Tags: Worker activities (manufacture, import, processing, use)} [a]<br>7. Potential routes of exposure (e.g., inhalation, dermal). {Tags: Routes of exposure (manufacture, import, processing, use)} [a]<br>8. Physical form of the chemical(s) of interest for each exposure route (e.g., liquid, vapor, mist) and activity. {Tags: Physical form during worker activities (manufacture, import, processing, use)} [a]<br>9. Breathing zone (personal sample) measurements of occupational exposures to the chemical(s) of interest, measured as time-weighted averages (TWAs), short-term exposures, or peak exposures in each occupational life cycle stage (or in a workplace scenario similar to an occupational life cycle stage). {Tags: PBZ measurements (manufacture, import, processing, use)} [a]<br>10. Area or stationary measurements of airborne concentrations of the chemical(s) of interest in each occupational setting and life cycle stage (or in a workplace scenario similar to the life cycle stage of interest). {Tags: Area measurements (manufacture, import, processing, use)} [a]<br>11. For solids, bulk and dust particle size characterization data. {Tags: PSD measurements (manufacture, import, processing, use)} [a]<br>12. Dermal exposure data. {Tags: Dermal measurements (manufacture, import, processing, use)}<br>13. Data needs associated with mathematical modeling (will be determined on a case-by-case basis). {Tags: Worker exposure modeling data needs (manufacture, import, processing, use)} [a]<br>14. Exposure duration (hr/day). {Tags: Worker exposure durations (manufacture, import, processing, use)}[a]<br>15. Exposure frequency (days/yr). {Tags: Worker exposure frequencies (manufacture, import, processing, use)} [a]<br>16. Number of workers who potentially handle or have exposure to the chemical(s) of interest in each occupational life cycle stage. {Tags: Numbers of workers exposed (manufacture, import, processing, use)} [a]<br>17. Personal protective equipment (PPE) types employed by the industries within scope. {Tags: Worker PPE (manufacture, import, processing, use)} [a]<br>18. Engineering controls employed to reduce occupational exposures in each occupational life cycle stage (or in a workplace scenario similar to the life cycle stage of interest), and associated data or estimates |

| Table_Apx E-4. Engineering, Environmental Release and Occupational Data Necessary to Develop the Environmental Release and Occupational Exposure Assessments | |
|---|---|
| **Objective Determined during Scoping** | **Type of Data** |
| | of exposure reductions. {Tags: Engineering controls (manufacture, import, processing, use), Engineering control effectiveness data} [a] |
| Environmental Releases | 19. Description of sources of potential relevant environmental releases, including cleaning of residues from process equipment and transport containers, involved during the manufacture, processing, or use of the chemical(s) of interest in each life cycle stage. {Tags: Release sources (manufacture, import, processing, use)} [a]<br>20. Estimated mass (lb or kg) of the chemical(s) of interest released from industrial and commercial sites to each relevant environmental medium and treatment and relevant disposal methods, including releases per site and aggregated over all sites (annual release rates, daily release rates) {Tags: Release rates (manufacture, import, processing, use)} [a]<br>21. Relevant release or emission factors. {Tags: Emission factors (manufacture, import, processing, use)} [a]<br>22. Number of release days per year. {Tags: Release frequencies (manufacture, import, processing, use)} [a]<br>23. Data needs associated with mathematical modeling (will be determined on a case-by-case basis). {Tags: Release modeling data needs (manufacture, import, processing, use)} [a]<br>24. Relevant waste treatment methods and pollution control devices employed by the industries within scope and associated data on relevant release/emission reductions. {Tags: Treatment/ emission controls (manufacture, import, processing, use), Treatment/ emission controls removal/ effectiveness data} [a] |
| **Notes:**<br>[a] These are the tags included in the full text screening form. The screener makes a selection from these specific tags, which describe more specific types of data or information.<br><br>**Abbreviations:**<br>hr=Hour<br>kg=Kilogram(s)<br>lb=Pound(s)<br>yr=Year<br>PV=Particle volume<br>PBZ= Personal breathing zone<br>POTW=Publicly owned treatment works<br>PPE=Personal projection equipment<br>PSD=Particle size distribution<br>TWA=Time-weighted average | |

## E.3 Inclusion Criteria for Data Sources Reporting Exposure Data on General Population, Consumers and Ecological Receptors

EPA/OPPT developed PECO statements to guide the full text screening of exposure data/information for human (i.e., general population, consumers, potentially exposure or susceptible subpopulations) and ecological receptors. Subsequent versions of the PECO statements may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the inclusion criteria in the PECO statement are eligible for inclusion, considered for evaluation, and possibly included in the exposure assessment. On the other hand, data sources are excluded if they do not meet the criteria in the PECO statement. The HBCD-specific PECO is provided in Table_Apx E-5.

| Table_Apx E-5. Inclusion Criteria for the Data Sources Reporting HBCD Exposure Data on General Population, Consumers and Ecological Receptors | |
|---|---|
| **PECO Element** | **Evidence** |
| **P**opulation | **Human:** Many different human population groups may be exposed to HBCD – including Potentially Exposed or Susceptible Subpopulations (e.g., children, susceptible populations (lifestages, preexisting conditions, genetic factors, pregnant women, women of child bearing age, infants), general population exposures through all relevant media, populations with subsistence diets (fish, plants, mammals, game animals, etc.), near facility populations, consumers and bystanders. EPA will also consider typical and potentially highly exposed groups within these general categories. Examples may include take-home exposures and renovation scenarios. No chemical-specific exclusions are suggested at this time. Human biomonitoring data to be considered. |
| | **Ecological:** Aquatic biota (edible and non-edible fish, daphnia, marine mammals), sediment dwelling worms, birds, earthworms. Consider ways to target the species list-for example, edible wildlife and species that have eco data. Many different aquatic and terrestrial species may be exposed to HBCD. No chemical specific exclusions are suggested at this time. Wildlife biomonitoring data to be considered. |
| **E**xposure | **Expected Primary Exposure Sources, Pathways, Routes:**<br>• Sources: Manufacturing, Processing, Use, and Disposal of building insulation (extruded polystyrene XPS and expanded polystyrene EPS). Indoor sources/materials that cover a large surface area, are abraded during use, or have high potential for direct contact.<br>• Pathways: dust, soil, food (fish, breastmilk, meat, eggs, dairy), biosolids, sediment, indoor air, outdoor air, media specific background and source attribution to be considered.<br>• Routes of Exposure: oral (dietary ingestion of food, dust ingestion, soil ingestion, indoor air ingestion of particles, mouthing of products/materials. Inhalation (indoor air and outdoor air). Dermal (contact with dust).<br>**Expected Lesser Exposure Sources, Pathways, Routes**<br>• Sources: Manufacturing, Processing, Use, and Disposal of products containing recycled HBCD and associated releases to water, or solid wastes. Indoor sources/materials that are less prevalent and/or contain relatively low concentrations of HBCD.<br>• Pathway: surface water, outdoor air deposition, food (fruits and vegetables), media specific background and source attribution to be considered.<br>• Routes of Exposure: Dermal (contact with soil, contact with products/materials) |
| **C**omparator (Scenario) | **Human:** Consider media-specific background exposure scenarios and use/source specific exposure scenarios as well as which receptors are and are not reasonably exposed across the projected exposure scenarios. |
| | **Ecological:** Consider media-specific background exposure scenarios and use/source specific exposure scenarios as well as which receptors are and are not reasonably exposed across the projected exposure scenarios. |
| **O**utcomes for Exposure Concentration or Dose | **Human:** Both external potential dose and internal dose based on biomonitoring and reverse dosimetry mg/kg/day will be considered (to compare with a wide range of health effects following acute through chronic exposures). |
| | **Ecological:** Surface water concentrations, sediment concentrations, and soil concentrations will be used (to compare with metrics used for ecological toxicity values). Targeted use of wildlife biomonitoring data such as in certain bird species will also be explored. |

## E.4 Inclusion Criteria for Data Sources Reporting Human Health Hazards

EPA/OPPT developed an HBCD-specific PECO statement (Table_Apx E-6) to guide the full text screening of the human health hazard literature. Subsequent versions of the PECOs may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the criteria specified in the PECO statement will be eligible for

inclusion, considered for evaluation, and possibly included in the human health hazard assessment, while those that do not meet these criteria will be excluded according to the exclusion criteria.

In general, the PECO statements were based on (1) information accompanying the TSCA scope document, and (2) preliminary review of the health effects literature from sources cited in the TSCA scope documents. When applicable, these sources (e.g., IRIS assessments, EPA/OPPT's Work Plan Problem Formulations or risk assessments) will serve as starting points to identify PECO-relevant studies.

**Table_Apx E-6. Inclusion and Exclusion Criteria for Data Sources Reporting Human Health Hazards Related to Cyclic Aliphatic Bromide Cluster (HBCD Cluster) Exposure [a]**

| PECO Element | Evidence Stream | Papers/Features Included | Papers/Features Excluded [a] |
|---|---|---|---|
| **Population [b]** | *Human* | • Any population<br>• All lifestages<br>• All study designs:<br>  ○ Controlled exposure, cohort, case-control, cross-sectional, case-crossover | |
| | *Animal* | • All standard whole-organism mammalian species, including rat, mouse, hamster, rabbit, guinea pig, monkey, dog<br>• All lifestages | • Wildlife species<br>• Non-mammalian species<br>• Agricultural species/livestock |
| | ***Mechanistic*** | • Human or animal cells (including nonmammalian model systems), tissues, or biochemical reactions (e.g., ligand-binding assays); bioinformatics pathways of disease analysis; or high-throughput screening data. | |
| **Exposure** | *Human and Animal* | • Exposure to an administered dose or concentration of HBCD<br>• Exposure is measured as a concentration in an environmental medium (e.g., air, dust, soil, diet) or biological fluid or tissue (e.g., blood, milk, urine, adipose tissue), or administered as a controlled dose<br>• Exposure is in vivo<br>• Exposure identified as ***or presumed to be*** from oral, dermal, and inhalation routes | • Not a chemical specific (study population is not exposed to HBCD)<br>• Exposure is to a mixture only, i.e., simultaneous exposure to other chemicals in addition to HBCD (applies to animal studies only)<br>• Exposure via injection (e.g., intravenous [i.v.]) |
| | *Mechanistic* | • Exposure based on concentrations of HBCD (individual α-, β-, or y-isomers or the commercial/technical mixtures) | |
| **Comparator** | *Human* | • A comparison population [not exposed, exposed to lower levels, exposed below detection] for all endpoints | • No comparison population for endpoints |
| | *Animal and Mechanistic* | • Negative controls that are vehicle-only treatment and/or no treatment<br>• No minimum number of dose or concentration groups | • Negative controls ***other than*** vehicle-only treatment or no treatment |
| **Outcome** | *Human and Animal* | • Health Endpoints [b]:<br>  • Irritation<br>  • Sensitization<br>  • Liver effects<br>  • Endocrine/thyroid effects<br>  • Developmental effects<br>  • Immune effects | • No health outcome evaluated (e.g., a study of HBCD exposure levels) |

| | | | |
|---|---|---|---|
| | | • Neurological effects<br>• Reproductive effects<br>• Acute toxicity<br>• Other endpoints [d] | |
| | *Mechanistic* | • Mechanistic data that supports the characterization of the identified endpoints of interest | |
| **General Considerations** | | **Papers/Features Included** | **Papers/Features Excluded** |
| | | • Written in English [e]<br>• Reports primary source or meta-analysis. [a]<br>• Full-text available | • Not written in English<br>• Reports a secondary source (e.g., review papers) [a]<br>• No full-text available (e.g., only a study description/abstract, out-of-print text) |

[a] Some of the studies that are excluded based on the PECO statement may be considered later during the systematic review process. For HBCD, EPA will evaluate studies related to susceptibility and may evaluate toxicokinetic and physiologically based pharmacokinetic models after other data (e.g., human and animal data identifying adverse health outcomes) are reviewed.

[b] EPA will review studies identified in the *Preliminary Materials for the IRIS Toxicological Review of HBCD* (U.S. EPA, 2014d). Mechanistic data will be considered to support hazard characterization for these endpoints.

[c] Measurement of HBCD includes individual α-, β-, or y-isomer; commercial or technical mixtures of HBCD isomers; CASRN 3194-55-6 (1,2,5,6,9,10-hexabromocyclododecane technical mixtures); CASRN 25637-99-4 (hexabromocyclododecane, all isomers)

[d] EPA may screen for hazards other than those listed in the scope document if they were identified in the updated literature search that accompanied the scope document.

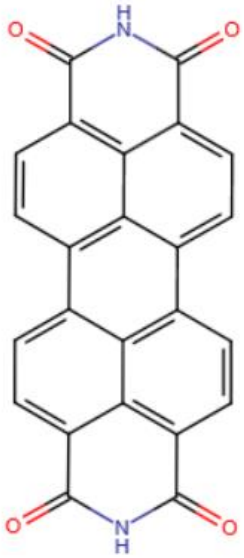
[e] EPA may translate studies as needed.

United States
Environmental Protection Agency

EPA Document# 740-R1-7021
May 2018
Office of Chemical Safety and
Pollution Prevention

# Problem Formulation of the Risk Evaluation for C.I. Pigment Violet 29 (Anthra[2,1,9-def:6,5,10-d'e'f']diisoquinoline-1,3,8,10(2H,9H)-tetrone)

# CASRN: 81-33-4




***May 2018***

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**Docket**
Supporting information can be found in public docket: EPA-HQ-OPPT-2016-0725.

**Disclaimer**
Reference herein to any specific commercial products, process or service by trade name, trademark, manufacturer or otherwise does not constitute or imply its endorsement, recommendation or favoring by the United States Government.

# ABBREVIATIONS

| | |
|---|---|
| °C | Degrees Celsius |
| AICS | Australian Inventory for Chemical Substances |
| atm | atmosphere(s) |
| BAF | Bioaccumulation factor |
| BCF | Bioconcentration factor |
| CASRN | Chemical Abstracts Service Registry Number |
| CBI | Confidential Business Information |
| CDR | Chemical Data Reporting |
| C.I. | Colour Index |
| CCL | Contaminant Candidate List |
| $cm^3$ | Cubic centimeters |
| CPMA | Color Pigments Manufacturing Association |
| CWA | Clean Water Act |
| DSL | Domestic Substances List (Canada) |
| ECHA | European Chemicals Agency |
| EINECS | European Inventory of Existing Commercial Chemical Substances |
| EPA | Environmental Protection Agency |
| ETAD | Ecological and Toxicological Association of Dyes and Organic Pigments Manufacturers |
| EU | European Union |
| FDA | Food and Drug Administration |
| g | Grams |
| g/mole | Grams per Unit-Molar Mass |
| hPa | Hectopascal |
| IECSC | Inventory of Existing Chemical Substances Produced or Imported in China |
| IRIS | Integrated Risk Information System |
| L | Liter(s) |
| K | Thousand |
| lb | Pound |
| Log $K_{oc}$ | Logarithmic Soil Organic Carbon:Water Partition Coefficient |
| Log $K_{ow}$ | Logarithmic Octanol:Water Partition Coefficient |
| $m^3$ | Cubic Meter(s) |
| mg | Milligram(s) |
| NOAEL | No Observed Adverse Effect Level |
| NPDES | National Pollutant Discharge Elimination System |
| NZloC | New Zealand Inventory |
| OECD | Organisation for Economic Co-operation and Development |
| OPPT | Office of Pollution Prevention and Toxics |
| PICCS | Philippines Inventory of Chemicals and Chemical Substances |
| POTW | Publicly owned treatment works |
| PS | Polystyrene |
| PUR | Polyurethane |
| PVC | Polyvinyl chloride |
| RegDet | Regulatory Determination |
| SAN | Styrene Acrylonitrile |
| SAR | Structure-activity relationship |
| SB | Styrene Butadiene |
| SDS | Safety Data Sheet |
| SDWA | Safe Drinking Water Act |
| TSCA | Toxic Substances Control Act |
| U.S. | United States |
| µm | Micrometer |

# EXECUTIVE SUMMARY

TSCA § 6(b)(4) requires the U.S. Environmental Protection Agency (EPA) to establish a risk evaluation process. In performing risk evaluations for existing chemicals, EPA is directed to "determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of costs or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator under the conditions of use." In December of 2016, EPA published a list of 10 chemical substances that are the subject of the Agency's initial chemical risk evaluations (81 FR 91927), as required by TSCA § 6(b)(2)(A). C.I. Pigment Violet 29 was one of these chemicals.

TSCA § 6(b)(4)(D) requires that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use and potentially exposed or susceptible subpopulations that the Administrator expects to consider. In June 2017, EPA published the Scope of the Risk Evaluation for C.I. Pigment Violet 29 (U.S. EPA, 2017c). As explained in the scope document, because there was insufficient time for EPA to provide an opportunity for comment on a draft of the scope, as EPA intends to do for future scope documents, EPA is publishing and taking public comment on a problem formulation document to refine the current scope, as an additional interim step prior to publication of the draft risk evaluation for C.I. Pigment Violet 29. Comments received on this problem formulation document will inform development of the draft risk evaluation.

This problem formulation document refines the conditions of use, exposures and hazards presented in the scope of the risk evaluation for C.I. Pigment Violet 29 and presents refined conceptual models and analysis plans that describe how EPA expects to evaluate the risk for C.I. Pigment Violet 29. EPA also identifies any conditions of use, hazards, or exposure pathways which were included in the scope document but which EPA does not plan to further analyze in the risk evaluation. EPA expects to be able to reach conclusions about particular conditions of use, hazards, or exposure pathways without further analysis and therefore plans to conduct no further analysis on those conditions of use, hazards or exposure pathways in order to focus the Agency's resources on more extensive or quantitative analyses. EPA may, on a case-by case basis, exclude certain activities that EPA has determined to be conditions of use in order to focus its analytical efforts on those exposures that are likely to present the greatest concern, and consequently merit a risk evaluation. EPA's overall objectives in the risk evaluation process are to conduct timely, relevant, high-quality, and scientifically credible risk evaluations within the statutory deadlines, and to evaluate the conditions of use that raise greatest potential for risk. 82 FR 33726, 33728 (July 20, 2017).

C.I. Pigment Violet 29 is an organic pigment found in the following uses: (1) colorant primarily in paints and coatings, plastics and rubber products, merchant ink for commercial printing; (2) intermediate to create or adjust the color of other perylene pigments; (3) formulation, mixture, or reaction product; and (4) consumer watercolor and artistic color. EPA has received public comments specific to the C.I. Pigment Violet 29 Scope Document (U.S. EPA, 2017c; available in the public docket: EPA-HQ-OPPT-2016-0725), which have been reviewed and addressed within the relevant text of this document.

Environmental and human health hazard studies characterizing the physical/chemical properties, environmental fate, human health, and environmental hazards of C.I. Pigment Violet 29 were identified in the European Chemicals Agency (ECHA) Database (ECHA, 2017b) and FDA's Food Additive Petition (FAP) 8B4626 for C.I. Pigment Violet 29 (BASF, 1998a), the results of which were consistent

with the ECHA studies. EPA has reviewed the robust study summaries of physical/chemical properties, environmental fate, human health hazard and environmental hazard studies in these databases, (summarized in Appendix C- Appendix F) and obtained the full study reports from the data owners for in-depth review. In addition, EPA has reviewed the *on-topic* literature from the Pigment Violet 29 (81-33-4) Bibliography: Supplemental File for the TSCA Scope Document (U.S. EPA, 2017a). No *on-topic* references were identified in the literature search for environmental fate, exposure (i.e., general population and consumers), environmental and human health hazards of C.I. Pigment Violet 29 (U.S. EPA, 2017a). A review of the three engineering/occupational exposure citations identified as *on-topic* revealed that these references are not relevant to the risk evaluation of C.I. Pigment Violet 29. Twenty other *on-topic* references previously identified were examined and found to be about pigments other than C.I. Pigment Violet 29 and will be excluded from further consideration. A preliminary review of these study summaries indicates that C.I. Pigment Violet 29 presents a low hazard to human health and environmental receptors.

Analysis of manufacturing conditions, uses and engineering controls of C.I. Pigment Violet 29 indicates that releases from manufacturing, processing, distribution, use and disposal are expected to be limited. Physical-chemical characteristics (i.e., low vapor pressure, low water solubility, high sorption to organic matter, high molecular weight, high Log $K_{ow}$) indicate exposures would be limited if C.I. Pigment Violet 29 is released to the environment.

All potential exposure pathways to workers, consumers, general population and the environmental receptors resulting from the manufacturing and use of C.I. Pigment violet 29 are included in the risk evaluation. However, based on limited releases, low potential for environmental and human exposures, and low toxicity profile for mammals and aquatic species, EPA concludes that further analysis of these exposure pathways to workers, consumers, general population and environmental receptors is not warranted for C.I. Pigment Violet 29.

The analysis plan for C.I. Pigment Violet 29 therefore consists of evaluating the study reports received by the Agency to ensure that the studies are scientifically sound and the results are consistent with EPA's preliminary review of the robust summaries in the ECHA database and the FDA Food Additive Petition (FAP) 8B4626 for C.I. Pigment Violet 29 (BASF, 1998a). If the review of these study reports indicates that the results are not scientifically sound or consistent with the robust summary reports, EPA may conduct additional analysis in developing the Draft Risk Evaluation for C.I. Pigment Violet 29, which may include changes to the pathways analyzed.

EPA is soliciting public comment on this problem formulation document for C.I. Pigment Violet 29, as an additional interim step, prior to publication of the Draft Risk Evaluation. EPA will carefully consider comments and additional data/information received as it develops the Draft Risk Evaluation. As per EPA's final rule, *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act*, EPA will also take comment and peer review the Draft Risk Evaluation for C.I. Pigment Violet 29.

# 1 INTRODUCTION

This document presents for comment the problem formulation of the risk evaluation for C.I. Pigment Violet 29 under the Frank R. Lautenberg Chemical Safety for the 21st Century Act. The Frank R. Lautenberg Chemical Safety for the 21st Century Act amended the Toxic Substances Control Act, the Nation's primary chemicals management law, on June 22, 2016. The new law includes statutory requirements and deadlines for actions related to conducting risk evaluations of existing chemicals.

In December of 2016, EPA published a list of 10 chemical substances that are the subject of the Agency's initial chemical risk evaluations (81 FR 91927), as required by TSCA § 6(b)(2)(A). These 10 chemical substances were drawn from the 2014 update of EPA's TSCA Work Plan for Chemical Assessments, a list of chemicals that EPA identified in 2012 and updated in 2014 (currently totaling 90 chemicals) for further assessment under TSCA. EPA's designation of the first 10 chemical substances constituted the initiation of the risk evaluation process for each of these chemical substances, pursuant to the requirements of TSCA § 6(b)(4). Additional background information and rationale for C.I. Pigment Violet 29's inclusion list of the first 10 chemicals is provided in Appendix A-1.

TSCA § 6(b)(4)(D) requires that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use and potentially exposed or susceptible subpopulations that the Administrator expects to consider, within 6 months after the initiation of a risk evaluation. The Scope Documents for all first 10 chemical substances were issued on June 22, 2017. The first 10 problem formulation documents are a refinement of what was presented in the first 10 scope documents. TSCA § 6(b)(4)(D) does not distinguish between scoping and problem formulation, and requires EPA to issue scope documents that include information about the chemical substance, including hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations that the Administrator expects to consider in the risk evaluation. In the future, EPA expects scoping and problem formulation to be completed prior to the issuance of scope documents and intends to issue scope documents that include problem formulation.

As explained in the scope document, because there was insufficient time for EPA to provide an opportunity for comment on a draft of the scope, as EPA intends to do for future scope documents, EPA is publishing and taking public comment on a problem formulation document to refine the current scope, as an additional interim step prior to publication of the draft risk evaluation for C.I. Pigment Violet 29. Comments received on this problem formulation document will inform development of the draft risk evaluation.

The Agency defines problem formulation as the analytical phase of the risk assessment in which "the purpose for the assessment is articulated, the problem is defined, and a plan for analyzing and characterizing risk is determined" (see Section 2.2 of the Framework for Human Health Risk Assessment to Inform Decision Making) (U.S. EPA, 2014). The outcome of problem formulation is a conceptual model(s) and an analysis plan. The conceptual model describes the linkages between stressors and adverse human health effects, including the stressor(s), exposure pathway(s), exposed life stage(s) and population(s), and endpoint(s) that will be addressed in the risk evaluation (U.S. EPA, 2014). The analysis plan follows the development of the conceptual model(s) and is intended to describe the approach for conducting the risk evaluation, including its design, methods and key inputs and intended outputs as described in the EPA Human Health Risk Assessment Framework (U.S. EPA,

2014). The problem formulation documents refine the initial conceptual models and analysis plans that were provided in the scope documents.

During problem formulation, EPA identified any conditions of use, hazards, or exposure pathways which were included in the scope document and that EPA expects to include in the risk evaluation but which EPA does not expect to further analyze in the risk evaluation. EPA expects to be able to reach conclusions about particular conditions of use, hazards or exposure pathways without further analysis and therefore plans to conduct no further analysis on those conditions of use, hazards or exposure pathways in order to focus the Agency's resources on more extensive or quantitative analyses. Each risk evaluation will be "fit-for-purpose," meaning not all conditions of use will warrant the same level of evaluation and the Agency may be able to reach some conclusions without comprehensive or quantitative risk evaluations. 82 FR 33726, 33734, 33739 (July 20, 2017).

EPA received comments on the published scope document for C.I. Pigment Violet 29 and has considered the comments specific to C.I. Pigment Violet 29 in this problem formulation document. EPA is soliciting public comment on this problem formulation document and when the draft risk evaluation is issued the Agency intends to respond to comments that are submitted. In its draft risk evaluation, EPA may revise the conclusions and approaches contained in this problem formulations, including the conditions of use and pathways covered and the conceptual models and analysis plans, based on comments received.

## 1.1 Regulatory History

EPA conducted a search of existing domestic and international laws, regulations and assessments pertaining to C.I. Pigment Violet 29. EPA compiled this summary from data available from federal, state, international and other government sources, as cited in Appendix A. EPA evaluated and considered the impact of existing laws and regulations (e.g., regulations on landfill disposal, design, and operations) in the problem formulation step to determine what, if any further analysis might be necessary as part of the risk evaluation. Consideration of the nexus between these existing regulations and TSCA uses may additionally be made as detailed/specific conditions of use and exposure scenarios are developed in conducting the analysis phase of the risk evaluation. This is discussed in detail in Section 2.5.2. As part of the problem formulation, background information on the inclusion of C.I. Pigment Violet 29 in 2012 and 2014 TSCA Work Plans was added to Appendix A-1.

***Federal Laws and Regulations***

C.I. Pigment Violet 29 is subject to one federal statute or regulation, other than TSCA, that is implemented by the U.S. Food and Drug Administration. A summary of federal laws, regulations and implementing authorities, including the U.S. Food and Drug Administration, is provided in Appendix A-2. In response to comments from the Color Pigments Manufactures Association (CPMA) (EPA-HQ-OPPT-2016-0725-0039), (CPMA, 2017b), EPA has clarified that C.I. Pigment Violet 29 does not have any regulatory restrictions under Federal Hazardous Substance Act (FHSA) and Consumer Product Safety Commission (CPSC) as had been indicated in the scope. Therefore, these regulations were removed from Appendix A-2.

***State Laws and Regulations***

C.I. Pigment Violet 29 is not subject to state statutes or regulations implemented by state agencies or departments.

***Laws and Regulations in Other Countries and International Treaties or Agreements***
In response to a comment (EPA-HQ-OPPT-2016-0725-0039) indicating that additional countries have C.I. Pigment Violet 29 on their chemical inventory list, EPA has added chemical inventories for China, Korea, New Zealand, the Philippines, Taiwan and Vietnam to Appendix A-3 . C.I. Pigment Violet 29 is listed on the Canadian Inventory of the 23,000 substances on the Domestic Substances List (DSL) but the Ecological Risk Classification for C.I. Pigment Violet 29 did not meet the criteria for categorisation as a prioritized substance for further evaluation. These determinations for C.I. Pigment Violet 29 and seven other similar pigments were made using a combination of QSAR modeling and hazard data for analogous pigments with low solubility (Pigment Red 149; CAS RN 4948-15-6). The conclusion of this screening was consistent with EPA's findings and indicated that because of low toxicity and low solubility, C.I. Pigment Violet 29 did not meet the criteria for further evaluation and the potential hazard is low (Environment Canada, 2006).

## 1.2 Data and Information Collection

EPA/Office of Pollution Prevention and Toxics (OPPT) generally applies a systematic review process and workflow that includes: (1) data collection; (2) data evaluation; and (3) data integration of the scientific data used in risk evaluations developed under TSCA. Scientific analysis is often iterative in nature as new knowledge is obtained. Hence, EPA/OPPT expects that multiple refinements regarding data collection will occur during the process of risk evaluation. Additional information that may be considered and was not part of the initial comprehensive bibliographies will be documented in the Draft Risk Evaluation for C.I. Pigment Violet 29.

***Data Collection: Data Search***
EPA/OPPT conducted chemical-specific searches for data and information on: physical and chemical properties; environmental fate and transport; conditions of use information; environmental exposures, human exposures, including potentially exposed or susceptible subpopulations; environmental hazard, human health hazard, including potentially exposed or susceptible subpopulations.

EPA/OPPT designed its initial data search to be broad enough to capture a comprehensive set of sources containing information potentially relevant to the risk evaluation. For most disciplines, the search was not limited by date and was conducted on a wide range of data sources, including but not limited to: peer-reviewed literature and gray literature (e.g., publicly-available industry reports, trade association resources, government reports). When available, EPA/OPPT relied on the search strategies from recent assessments, such as EPA Integrated Risk Information System (IRIS) assessments and the National Toxicology Program's (NTP) *Report on Carcinogens*, to identify relevant references and supplemented these searches to identify relevant information published after the end date of the previous search to capture more recent literature. EPA/OPPT also searched for relevant information published after the end date of the previous search to capture more recent literature. *Strategy for Conducting Literature Searches for Pigment Violet 29: Supplemental File for the TSCA Scope Document* provides details about the data sources and search terms that were used in the initial search (U.S. EPA, 2017d).

***Data Collection: Data Screening***
Following the data search, references were screened and categorized using selection criteria outlined in *Strategy for Conducting Literature Searches for Pigment Violet 29: Supplemental File for the TSCA Scope Document* (U.S. EPA, 2017d). Titles and abstracts were screened against the criteria as a first step with the goal of identifying a smaller subset of the relevant data to move into the subsequent data extraction and data evaluation steps. Prior to full-text review, EPA/OPPT anticipates refinements to the

search and screening strategies, as informed by an evaluation of the performance of the initial title/abstract screening and categorization process.

The categorization scheme (or tagging structure) used for data screening varies by scientific discipline (i.e., physical and chemical properties; environmental fate and transport; chemical use/conditions of use information; human and environmental exposures, including potentially exposed or susceptible subpopulations identified by virtue of greater exposure; human health hazard, including potentially exposed or susceptible subpopulations identified by virtue of greater susceptibility; and environmental hazard). Within each data set, there are two broad categories or data tags: (1) o*n-topic* references or (2) *off-topic* references. *On-topic* references are those that may contain data and/or information relevant to the risk evaluation. O*ff-topic* references are those that do not appear to contain data or information relevant to the risk evaluation. *Strategy for Conducting Literature Searches for Pigment Violet 29: Supplemental File for the TSCA Scope Document* discusses the inclusion and exclusion criteria that EPA/OPPT used to categorize references as *on-topic* or *off-topic* (U.S. EPA, 2017d).

Additional data screening using sub-categories (or sub-tags) was also performed to facilitate further sorting of data/information - for example, identifying references by source type (e.g., published peer-reviewed journal article, government report); data type (e.g., primary data, review article); human health hazard (e.g., liver toxicity, cancer, reproductive toxicity); or chemical-specific and use-specific data or information. These sub-categories are described in *Strategy for Conducting Literature Searches for Pigment Violet 29: Supplemental File for the TSCA Scope Document* and were used to organize the different streams of data during the stages of data evaluation and data integration steps of systematic review.

Results of the initial search and categorization results can be found in the *Pigment Violet 29 (CASRN: 81-33-4) Bibliography: Supplemental File for the TSCA Scope Document* (U.S. EPA, 2017a). This document provides a comprehensive list (bibliography) of the sources of data identified by the initial search and the initial categorization for *on-topic* and *off-topic* references. Because systematic review is an iterative process, EPA/OPPT expects that some references may move from the *on-topic* to the *off-topic* categories, and vice versa. Moreover, targeted supplemental searches may also be conducted to address specific needs for the analysis phase (e.g., to locate specific data needed for modeling); hence, additional *on-topic* references not initially identified in the initial search may be identified as the systematic review process proceeds.

## 1.3 Data Screening During Problem Formulation

The *Pigment Violet 29 (CASRN: 81-33-4) Bibliography: Supplemental File for the TSCA Scope Document* did not identify any *on-topic* literature search results for environmental fate, exposure (general population and consumers), environmental and human health hazards of C.I. Pigment Violet 29 (U.S. EPA, 2017a) with the exception of the study summaries in the ECHA Database, three engineering/occupational exposure literature search results and the two studies from Food Additive Petition (FAP) 8B4626 (BASF, 1998a): (1) Solubility of C.I. Pigment Violet 29 in ethanol and; (2) Reverse mutation assay AMES test using *Salmonella typhimurium* and *Escherichia coli*. Further review of the three engineering/occupational exposure citations identified as *on-topic* revealed that these references are not relevant to the C.I. Pigment Violet 29 risk evaluation. The full study report for the solubility of C.I. Pigment Violet 29 in ethanol has been reviewed by EPA and summarized in Section 2.1. The full study report for the Reverse mutation assay AMES test using *Salmonella typhimurium* and *Escherichia coli* has been received by the agency and will be reviewed according to the evaluation strategy discussed below.

The *Pigment Violet 29 (CASRN: 81-33-4) Bibliography: Supplemental File for the TSCA Scope Document* also identified twenty other references previously cited in OPPT's documents. Based on a comment received [(EPA-HQ-2016-0725-0039) (CPMA, 2017b)], EPA conducted a second title/abstract screening and determined that some of these references were not relevant to C.I. Pigment Violet 29. As such, these references were excluded from further consideration for C.I. Pigment Violet 29. EPA also identified a number of EPA guidance documents and previous OPPT documents and plans to consider them during the development of the draft risk evaluation for C.I. Pigment Violet 29. Appendix B contains a list of the *on-topic* references that were excluded from further consideration for C.I. Pigment Violet 29.

EPA plans to review the full study reports related to physical/chemical characteristics, environmental fate, human health and environmental hazard of C.I. Pigment Violet 29 using the evaluation strategies as described in *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a). These studies correspond to robust summaries in the ECHA Database as well as a full study report for the Ames assay from the Food Additive Petition (FAP) 8B4626. The study quality evaluation of the study reports is intended to confirm or update the conclusions of the robust summaries available from the ECHA Database that were used to support the preliminary findings discussed in this problem formulation document.

# 2 PROBLEM FORMULATION

As required by TSCA, the scope of the risk evaluation identifies the conditions of use, hazards, exposures and potentially exposed or susceptible subpopulations that the Administrator expects to consider. To communicate and visually convey the relationships between these components, EPA included in the scope document a life cycle diagram and conceptual models that describe the actual or potential relationships between C.I. Pigment Violet 29 and human and environmental receptors. For this problem formulation, EPA conducted a preliminary data review of reasonably available fate, exposure and hazard data and determined its suitability for analysis and to identify exposure pathways, receptors and health endpoints for analysis. EPA summarized the outcome of this evaluation in conceptual models that illustrate the exposure pathways, receptor populations and effects that will be subject to further analysis in the risk evaluation (Section 2.5). EPA also prepared an analysis plan to convey the proposed approach to conducting the risk evaluation (Section 2.6).

## 2.1 Physical and Chemical Properties

Physical-chemical properties influence the environmental behavior and the toxic properties of a chemical, thereby informing the potential conditions of use, exposure pathways and routes and hazards that EPA intends to consider. The C.I. Pigment Violet 29 scope document had physical and chemical properties based on estimated values (U.S. EPA, 2017c). During problem formulation, the physical and chemical properties have been updated, where possible, to reflect measured values from the ECHA Database and are provided in Table 2-1. An estimated value for the octanol/water partition coefficient (Log $K_{OW}$) is presented in Table 2-1. The measured partition coefficient could not be determined due to poor solubility in octanol and water; thus, the estimated Log $K_{OW}$ of 3.76 is applicable for this evaluation. EPA plans to review the full study reports identified in Table_Apx C-1, which the Agency has received from the data owner(s), using the evaluation strategies as described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a).

**Table 2-1. Physical and Chemical Properties of C.I. Pigment Violet 29**

| Property | Value | Reference |
|---|---|---|
| Molecular Formula | $C_{24}H_{10}N_2O_4$ | (ECHA, 2017b) |
| Molecular Weight | 390.35 g/mole | (U.S. EPA, 2012b) |
| Physical Form | Solid | (ECHA, 2017b) |
| Melting Point | No melting point found < 400˚C | (ECHA, 2017b) |
| Boiling Point | Not available | |
| Density | 1.584 g/cm$^3$ at 20 ℃ | (ECHA, 2017b) |
| Vapor Pressure | < 0 hPa at 20˚C | (ECHA, 2017b) |
| Vapor Density | Not available | |
| Water Solubility | 0.01 mg/L at 20˚C | (ECHA, 2017b) |
| Log $K_{OW}$ | 3.76 (estimated) | (U.S. EPA, 2012b) |
| Henry's Law Constant | 1.84E-021 atm-m$^3$/mole (estimated) | (U.S. EPA, 2012b) |
| Flash Point | Not available | |
| Auto Flammability | Not available | |
| Viscosity | Not available | |
| Refractive Index | Not available | |
| Dielectric Constant | Not available | |

C.I. Pigment Violet 29 is a Colour Index name used in sales of products containing anthra[2,1,9-def:6,5,10-d'e'f']diisoquinoline-1,2,8,10(2H,9H)-tetrone, CASRN 81-33-4. The name "C.I. Pigment Violet 29" is assigned, copyrighted and maintained by the Society of Dyers and Colourists and the American Association of Textile Colorists and Chemists (EPA-HQ-OPPT-2016-0725-0039). The Colour Index is an international standard and classification system describing essential colorants which comprise commercial dyes and pigments.

Anthra[2,1,9-def:6,5,10-d'e'f']diisoquinoline-1,2,8,10(2H,9H)-tetrone identified by CASRN 81-33-4, is a violet or red-brown pigment and called by the following Colour Index names: C.I. Pigment Violet 29 and C.I. Pigment Brown 26. The difference in color between C.I. Pigment Brown 26 and C.I. Pigment Violet 29 is related to particle size and not crystal form (Sun Chemical, 2017a).

EPA preliminarily reviewed a full study report of the solubility of C.I. Pigment Violet 29 in ethanol from the Food and Drug Administration's Food Additive Petition (FAP) 8B4626 (BASF, 1998a). According to FAP 8B4626, solubility of various pigments including C.I. Pigment Violet 29 was done in 8% and 95% ethanol. In the study, the solubility in 8% ethanol is reported as 0.0046 mg/L and 0.015 mg/L in 95% ethanol. Based on these results, C.I. Pigment Violet 29 has very low solubility in ethanol. Solubility of C.I. Pigment Violet 29 was also assessed in octanol. The solubility in octanol is reported as 0.07 mg/L. The water solubility of C.I. Pigment Violet 29 is 0.01 mg/L per ECHA Database. Based on all solubility test results, C.I. Pigment Violet 29 has low solubility.

There are no known by-products or degradation products resulting from the manufacture of C.I. Pigment Violet 29. There is a residual amount of naphthalimide, the starting material used in the fusion, at approximately 1% (Sun Chemical, 2017a). Per robust study summary reports from the ECHA Database, the hazard profile of naphthalimide is low for human health and environmental receptors (ECHA, 2017a). Based on the minimal amount of naphthalimide released from manufacturing and low hazard,

EPA will not conduct any further analysis of the naphthalimide residual associated with C.I. Pigment Violet 29 production.

## 2.2 Conditions of Use

TSCA § 3(4) defines the conditions of use as ‘‘the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of.”

Pigments are widely used and found in a wide range of products that are colored. Below is specific use information for C.I. Pigment Violet 29.

### 2.2.1 Data and Information Sources

Since conditions of use has not changed since the issuance of the C.I. Pigment Violet 29 scope document (U.S. EPA, 2017c) on June 22, 2017, the conditions of use remain the same for problem formulation.

### 2.2.2 Identification of Conditions of Use

To determine the current conditions of use of C.I. Pigment Violet 29 and inversely, activities that do not qualify as conditions of use, EPA conducted extensive research and outreach. This included EPA’s review of published literature and online databases including the most recent data available from EPA’s Chemical Data Reporting program (CDR) and Safety Data Sheets (SDSs). EPA also conducted online research by reviewing company websites of potential manufacturers, importers, distributors, retailers, or other users of C.I. Pigment Violet 29 and queried government and commercial trade databases. EPA also received comments on the *Scope of the Risk Evaluation for Pigment Violet 29* (U.S. EPA, 2017c) that were used to determine the current conditions of use. In addition, EPA convened meetings with companies, industry groups, chemical users, states, environmental groups, and other stakeholders to aid in identifying conditions of use and verifying conditions of use identified by EPA. Those meetings included a February 14, 2017 public meeting with such entities and a September 15, 2017 meeting with several representatives from trade associations.

As explained in the final rule for Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act, TSCA section 6(b)(4)(D) requires EPA to identify "the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations the Administrator expects to consider” in a risk evaluation, suggesting that EPA may exclude certain activities that EPA has determined to be conditions of use on a case-by-case basis. (82 FR 33736, 33729; July 20, 2017). For example, EPA may exclude conditions of use that the Agency has sufficient basis to conclude would present only de minimis exposures or otherwise insignificant risks (such as use in a closed system that effectively precludes exposure or use as an intermediate) or that have been adequately assessed by another regulatory agency.

The activities that EPA no longer believes are conditions of use or that were otherwise excluded during problem formulation are described in Section 2.2.2.1. The conditions of use included in the scope of the risk evaluation are summarized in Section 2.2.2.2.

#### 2.2.2.1 Categories and Subcategories Determined Not to be Conditions of Use or Otherwise Excluded During Problem Formulation

No conditions of use were excluded during problem formulation; thus, Table 2-3 from the C.I. Pigment Violet 29 Scope Document (U.S. EPA, 2017c) remains the same and is presented in Table 2-2 below.

#### 2.2.2.2 Categories and Subcategories of Conditions of Use in Scope of the Risk Evaluation

Because no conditions of use were excluded during problem formulation, Table 2-2 below remains the same as presented in the C.I. Pigment Violet 29 Scope Document [Table 2-3 in (U.S. EPA, 2017c)] and in Section 2.2.2.1.

**Table 2-2. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation**

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| Manufacture | Domestic manufacture | Domestic manufacture | U.S. EPA (2016b) |
| | Import | Import | |
| Processing | Processing - Incorporating into formulation, mixture, or reaction product | Paints and Coatings | U.S. EPA (2016b); Public Comment, EPA-HQ-OPPT-2016-0725-0006 |
| | | Plastic and Rubber Products | U.S. EPA (2016b); Public Comment, EPA-HQ-OPPT-2016-0725-0006 |
| | Processing - Use as an Intermediate | Creation or adjustment to other perylene pigments | U.S. EPA (2016b); Public Comment, EPA-HQ-OPPT-2016-0725-0006; Public Comment, EPA-HQ-OPPT-2016-0725-0008 |
| | Recycling | Recycling | U.S. EPA (2016b); Use Document, EPA-HQ-OPPT-2016-0725-0004 |
| Distribution in commerce | Distribution | Distribution | Use Document, EPA-HQ-OPPT-2016-0725-0004; Public Comment, EPA-HQ-OPPT-2016-0725-0006 |
| Industrial/commercial/ consumer use | Plastic and rubber products | Automobile plastics | Use Document, EPA-HQ-OPPT-2016-0725-0004; Public Comment, EPA-HQ-OPPT-2016-0725-0006 |
| | | Industrial carpeting | Public Comment, EPA-HQ-OPPT-2016-0725-0006 |
| | Paints and coatings | Automobile (OEM and refinishing) | Public Comment, EPA-HQ-OPPT-2016-0725-0006; Public Comment, EPA-HQ-OPPT-2016-0725-0013; Public Comment, EPA-HQ-OPPT-2016-0725-0009 |
| | | Coatings and basecoats | Public Comment, EPA-HQ-OPPT-2016-0725-0008; Public Comment, EPA-HQ-OPPT-2016-0725-0007 |
| | Merchant ink for commercial printing | Merchant ink | Use Document, EPA-HQ-OPPT-2016-0725-0004; |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| | | | Public Comment, EPA-HQ-OPPT-2016-0725-0006 |
| | Other uses | Applications in odor agents, cleaning/washing agents, surface treatment, absorbents and adsorbents, laboratory chemicals, light-harvesting materials, transistors, molecular switches, solar cells, optoelectronic devices, paper, architectural uses, polyester fibers, adhesion, motors, generators, vehicle components, sporting goods, appliances, agricultural equipment and oil and gas pipelines | Use Document, EPA-HQ-OPPT-2016-0725-0004 |
| | Consumer watercolor and acrylic paints | Professional quality watercolor and acrylic artist paint | Use Document, EPA-HQ-OPPT-2016-0725-0004 |
| Disposal | Emissions to Air | Air | Standard EPA approach, no sources specific to C.I. Pigment Violet 29 found |
| | Wastewater | Industrial pre-treatment | |
| | | Industrial wastewater treatment | |
| | | Publicly owned treatment works (POTW) | |
| | | Underground injection | |
| | Solid wastes and liquid wastes | Municipal landfill | |
| | | Hazardous landfill | |
| | | Other land disposal | |
| | | Municipal waste incinerator | |
| | | Hazardous waste incinerator | |
| | | Off-site waste transfer | |

[a] These categories appear in the life cycle diagram (Figure 2-1), reflect CDR codes and broadly represent conditions of use of C.I. Pigment Violet 29 in industrial and/or commercial settings.
[b] These subcategories reflect more specific uses of C.I. Pigment Violet 29.

#### 2.2.2.3 Overview of Conditions of Use and Lifecycle Diagram

The life cycle diagram provided in Figure 2-1 depicts the conditions of use that are considered within the scope of the risk evaluation during various life cycle stages including manufacturing, processing, distribution, use (industrial, commercial, consumer; when distinguishable) and disposal. Additions or changes to conditions of use based on additional information gathered or analyzed during problem formulation are described further in Sections 2.2.2.1 and 2.2.2.2. The activities that EPA determined are out of scope during problem formulation are not included in the life cycle diagram. The information is grouped according to Chemical Data Reporting (CDR) processing codes and use categories (including functional use codes for industrial uses and product categories for industrial, commercial and consumer uses), in combination with other data sources (e.g., published, peer reviewed literature and consultation with stakeholders), to provide an overview of conditions of use. EPA notes that some subcategories of

use may be grouped under multiple CDR categories (Appendix D in Instructions for Reporting 2016 TSCA Chemical Data Reporting), (U.S. EPA, 2016a).

Use categories include the following: "industrial use" means use at a site at which one or more chemicals or mixtures are manufactured (including imported) or processed. "Commercial use" means the use of a chemical or a mixture containing a chemical (including as part of an article) in a commercial enterprise providing saleable goods or services. "Consumer use" means the use of a chemical or a mixture containing a chemical (including as part of an article, such as furniture or clothing) when sold to or made available to consumers for their use (U.S. EPA, 2016b).

To understand conditions of use relative to one another and associated potential exposures under those conditions of use, the life cycle diagram includes the volume information associated with each stage of the life cycle, as reported in the 2016 CDR reporting (U.S. EPA, 2016b).

The 2016 CDR reporting data for C.I. Pigment Violet 29 are provided in Table 2-3 (U.S. EPA, 2016b). The 2016 CDR reporting period encompasses production and import volumes for 2012 to 2015. The C.I. Pigment Violet 29 scope document 2012 production volume data was the aggregate production volume for the 2012 CDR reporting cycle and the 2016 CDR data was not presented due to CBI claims. During problem formulation, EPA worked with the CDR reporter to remove CBI claims, such that Table 2-3 now shows 2016 CDR data including the final production volume for 2012; therefore, the production volumes for 2012 differed slightly between the C.I. Pigment Violet 29 scope document and this problem formulation document.

**Table 2-3. Production Volume of C.I. Pigment Violet 29 in Chemical Data Reporting (CDR) Reporting Period (2012 to 2015) [a, b]**

| Reporting Year | 2012 | 2013 | 2014 | 2015 |
|---|---|---|---|---|
| Total Aggregate Production Volume (lbs) | 517,980 [c] | 474,890 | 535,139 | 603,420 |

[a] Sun Chemical has waived all claims of CBI for C.I. Pigment Violet 29 in the 2016 CDR (Sun Chemical, 2017b).
[b] The CDR data for the 2016 reporting period is available via ChemView (https://java.epa.gov/chemview) (U.S. EPA, 2016b). Because of an ongoing CBI substantiation process required by amended TSCA, the CDR data available in the problem formulation document is more specific and up-to-date than currently in ChemView.
[c] Final production volume for 2012 reported in 2016 CDR reporting cycle.

Descriptions of the industrial, commercial and consumer use categories identified from the 2016 CDR and included in the life cycle diagram are summarized below (U.S. EPA, 2016b).

Sun Chemical Corporation is the only U.S. manufacturer of C.I. Pigment Violet 29 that reported to CDR in 2012 and 2016 (U.S. EPA, 2012a). EPA is also aware of C.I. Pigment Violet 29 being imported into the United States below the reporting threshold of 25,000 lbs per year from a confidential source per comments from CPMA [EPA-HQ-OPPT-2016-0725-0006, (CPMA, 2017a).

Figure 2-1 shows the production volume of C.I. Pigment Violet 29 that is associated with each life cycle stage. The imported material is used for merchant ink for commercial printing, other uses, and consumer watercolor and artistic color (Figure 2-1, (CPMA, 2017a)). This information also indicates that import volume is considerably less than the manufacturing volume.

Four primary industrial and commercial uses and one consumer use have been identified for C.I. Pigment Violet 29:

- Use as an intermediate to create or adjust color of other perylene pigments (~90%)
- Incorporation into paints and coatings used primarily in the automobile industry (~5%)
- Incorporation into plastic and rubber products used primarily in automobiles and industrial carpeting (~5%)
- Use in merchant ink for commercial printing (< 1%)
- Consumer watercolors and artistic color (unknown minor volume)

Public comments on the C.I. Pigment Violet 29 Use Document [EPA-HQ-OPPT-2016-0725-0004, (U.S. EPA, 2017b)] and 2016 CDR (U.S. EPA, 2016b), indicate 90% of the 2015 domestic production volume (540,000 lbs) is processed as a site-limited intermediate in the manufacture of other perylene pigments. This use is corroborated by the American Coatings Association statement that C.I. Pigment Violet 29 is used to adjust the color of other perylene pigments [(EPA-HQ-OPPT-2016-0725-0008), (ACA, 2017)].

Approximately 10% of the production volume (~60,000 lbs) is processed and used in either commercial paints and coatings (~30,000 lbs) or commercial plastic and rubber products (~30,000 lbs). The 2012 CDR did not indicate these products were intended for or specifically marketed to children (U.S. EPA, 2012a). Automotive and industrial coatings that include metallic finishes and textile printing are types of commercial paints and coatings [(EPA-HQ-OPPT-2016-0725-0006), (CPMA, 2017a)]. C.I. Pigment Violet 29 can be a component in a variety of plastics applications such as polyolefins, polyvinyl chloride (PVC), polyurethane (PUR), polystyrene (PS), styrene butadiene (SB), styrene acrylonitrile (SAN) and other polymers (BASF, 1998b), (COLORS, 2011). Less than 1% of the production volume (~6,000 lbs) is processed into ink and then used in merchant ink for commercial printing.

An unknown minor volume of C.I. Pigment Violet 29 is used in consumer watercolor and acrylic paints. Furthermore, C.I. Pigment Violet 29 used in professional artistic paint products is less than 1% of total sales [(EPA-HQ-OPPT-2016-0725-0039), (CPMA, 2017b)]. The 2012 CDR did not indicate use of C.I. Pigment Violet 29 in products intended for children (U.S. EPA, 2012a). In the 2017 comments on C.I. Pigment Violet 29 Use Document [(EPA-HQ-OPPT-2016-0725-0006), (CPMA, 2017a)], commenters indicated they are not aware of C.I. Pigment Violet 29 being used for paints that are marketed to children, although there are no explicit age-related restrictions on the purchase of professional artistic paints such as watercolors and acrylics. However, consumer products that are widely available, like watercolor and acrylic paints, could be reasonably foreseen to be used by children.

The changes in life cycle diagram since June 22, 2017 include showing the estimated releases from manufacturing and updated production volume values where applicable, as a result of CBI claims being removed.

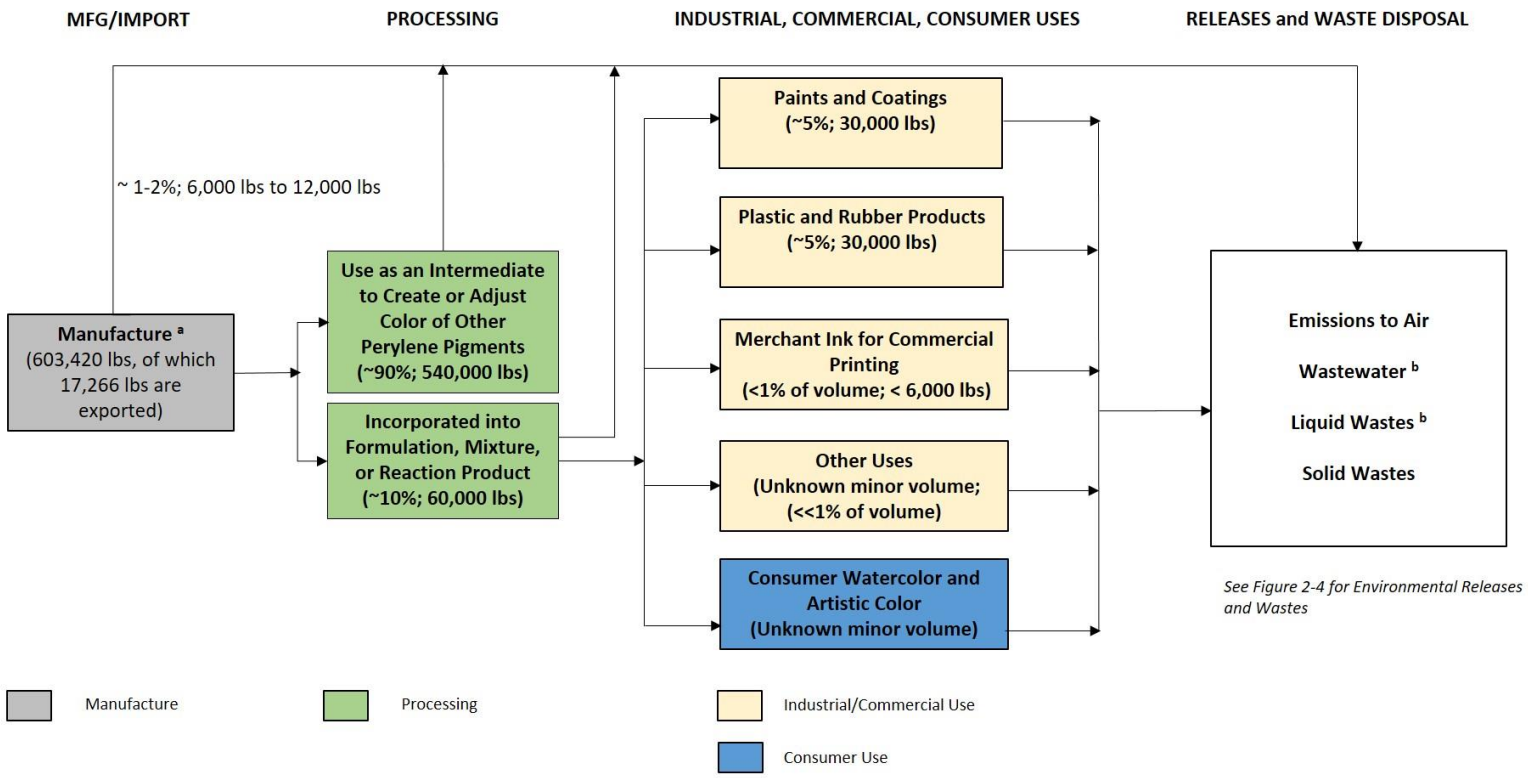


**Figure 2-1. C.I. Pigment Violet 29 Life Cycle Diagram**

The life cycle diagram depicts the conditions of use during various life cycle stages including manufacturing, processing, use (industrial, commercial, consumer), distribution and disposal. The production volumes shown are for reporting year 2015 from the 2016 CDR reporting period. Activities related to distribution (e.g., loading, unloading) will be considered throughout the C.I. Pigment Violet 29 life cycle, rather than using a single distribution scenario.

[a] 603,420 lbs does not include import volumes since it is below the CDR reporting threshold of 25,000 lbs (CPMA, 2017a); however, uses of imported C.I. Pigment Violet 29 are represented in the LCD.

[b] Wastewater: combination of water and organic liquid, where the organic content than < 50%. Liquid Wastes: combination of water and organic liquid, where the organic content is > 50%.

## 2.3 Exposures

For TSCA exposure assessments, EPA expects to evaluate exposures and releases to the environment resulting from the conditions of use applicable to C.I. Pigment Violet 29. Post-release pathways and routes will be described to characterize the relationship or connection between the conditions of use for C.I. Pigment Violet 29 and the exposure to human receptors, including potentially exposed or susceptible subpopulations and environmental receptors. EPA will consider, where relevant, the duration, intensity (concentration), frequency and number of exposures in characterizing exposures to C.I. Pigment Violet 29.

### 2.3.1 Fate and Transport

Environmental fate includes both transport and transformation processes. Environmental transport is the movement of the chemical within and between environmental media. Transformation occurs through the degradation or reaction of the chemical with other species in the environment. Hence, knowledge of the environmental fate of the chemical informs the determination of the specific exposure pathways and potential human and environmental receptors EPA expects to consider in the risk evaluation.

During problem formulation, EPA considered volatilization during wastewater treatment, volatilization from lakes and rivers, biodegradation rates, and organic carbon:water partition coefficient (log $K_{OC}$) and bioaccumulation potential when making changes, as described in Section 2.5, to the conceptual models. Systematic literature review is currently underway, so model results, robust study summaries from ECHA, and basic principles were used to support the fate data used in problem formulation.

The C.I. Pigment Violet 29 (U.S. EPA, 2017c) fate properties described here are based on review of ECHA robust study summaries (ECHA, 2017b) and EPA EPI Suite estimated values (U.S. EPA, 2017c) as summarized in Table 2-4. As indicated previously, EPA's literature search (U.S. EPA, 2017a) did not identify any other *on-topic* references pertinent to fate and transport of C.I. Pigment Violet 29.

C.I. Pigment Violet 29 is expected to be highly persistent and has low bioaccumulation potential. Preliminary review of robust summaries for studies related to biodegradation indicates that it is not readily biodegradable. Due to its physical properties, it is expected to bind strongly to soil organic matter and migration through soil to groundwater is likely to be minimal. If released to water, hydrolysis is expected to be negligible. Based on its estimated Henry's Law Constant, C.I. Pigment Violet 29 is not expected to volatilize from environmental waters. If released to air, it is unlikely to undergo direct photolysis and expected to be in the particulate phase. Based on its estimated indirect photodegradation half-life of 7 hours, it is considered to degrade moderately to slowly by reaction with atmospheric hydroxyl radicals.

**Table 2-4. Environmental Fate Characteristics of C.I. Pigment Violet 29**

| Property or Endpoint | Value [a] | References |
|---|---|---|
| Indirect photodegradation | 7.0 hours (estimated) [b] | U.S. EPA (2012b) |
| Hydrolysis half-life | Stable | |
| Biodegradation | Low biodegradability: 010% degradation in 28 days (OECD 301F) | ECHA (2017b) |
| Bioconcentration factor (BCF) | Low bioconcentration: BCF=140 (estimated) [b] | U.S. EPA (2012b) |
| Bioaccumulation factor (BAF) | BAF = 50 (estimated) [b] | U.S. EPA (2012b) |
| Soil organic carbon:water partition coefficient (Log $K_{OC}$) | 5.0 (estimated) [b] | U.S. EPA (2012b) |

[a] Measured unless otherwise noted.
[b] There are limited pigment data in the EPI Suite training set, therefore values should be used with caution.

Fate test data EPA identified in the ECHA Database for this chemical includes biodegradation and activated sludge respiration inhibition testing (ECHA, 2017b). During problem formulation, EPA requested and received these studies from the data owner(s):

1. OECD Guideline 301 F: Biodegradability: Manometric Respirometry Test
2. OECD Guideline 209: Activated Sludge, Respiration Inhibition Test

EPA plans to review the full study reports for these tests using the evaluation strategies as described in *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a).

However, pigments commonly exist as aggregates in particles sizes of approximately 0.1 µm and exhibit low affinity for water and octanol. The bioaccumulation of such aggregates is likely limited by their molecular weight and size.

### 2.3.2 Releases to the Environment

C.I. Pigment Violet 29 is manufactured and imported as a solid and in solution and has a low vapor pressure (<0 hPa at 20˚C). It is handled and processed as a dry powder and formulation during all conditions of use. Because the chemical is not volatile at process temperatures during any conditions of use, evaporative losses (volatile fugitive air emissions) are not expected.

The sole domestic manufacturer of C.I. Pigment Violet 29 has estimated standard yield loss of 1-2% of the volume during the manufacturing (6,000- 12,000 lbs for 2015) (Mott, 2017b). Most of the lost C.I. Pigment Violet 29 is captured and disposed such that a very minimal amount is released. Potential release sources at this site and sites that process and use C.I. Pigment Violet 29 include, but are not limited to: residual material in storage and transfer containers that are subsequently cleaned or disposed of, pigment that is spilled during the handling of the dry powder during transfer operations, equipment cleaning, and overspray of coatings.

Air and water releases directly to the environment from manufacturing are expected to be limited based on information provided from the domestic manufacturer. Dust handling systems are in place at the manufacturing facility that capture dust in baghouses. The efficiency rate is greater than 99.5% (Mott, 2017b; Sun Chemical, 2017b). Spilled pigment from handling of the dry powder is collected and placed in contaminated industrial waste bins. The bags and waste bins are subsequently sent to a licensed industrial waste handler for disposal (CPMA, 2017a). One to two percent of produced C.I. Pigment

Violet 29 is lost during handling and most are channeled to an on-site aboveground biological wastewater treatment system that captures C.I. Pigment Violet 29 (Mott, 2017b). Of this material that is captured during the wastewater treatment process, greater than 95% of the wastewater treatment residue is disposed of at either the Oak Ridge Landfill in Dorchester County or the Berkeley County Landfill, RCRA Subtitle-D lined landfills permitted under the authority of South Carolina Regulation Number 61-107.19 Solid Waste Management (Mott, 2017a), (RCRAInfo Facility Information). Less than 0.1% of produced C.I. Pigment Violet 29 is released to surface waters (0.6 lb/day, as reported by the manufacturer).

C.I. Pigment Violet 29 is supplied to formulator as dry powders, press cakes, or slurries. Pigments grinding or milling is required when the size of the particles in the dispersion needs to be reduced. After grinding and/or milling, C.I. Pigment Violet 29 is blended with other additives and solvents. Formulated paint and coatings (5% of total production volume) are filtered prior to packaging. For plastics and rubber (5% of total production volume), pigments and other additives are mixed with polymer resins and other raw materials to produce compound resin master batch. It is then transferred into an extruder where it is converted into pellets, sheets, films, or pipes. The extruded plastics are shipped to downstream converting sites where they are formed into the desired shape through a variety of converting methods, including extrusion, injection molding and thermoforming.

No data pertaining to environmental releases from the twenty downstream industrial facilities that process C.I. Pigment Violet 29 into plastics, paints and coatings were identified. These uses account for 10% of the total production volume. However, CPMA indicated that all of these facilities are subject to EPA and state regulations resulting in limiting releases to air, water, and land of materials to the environment.

Exposure and releases are possible when handling concentrated C.I. Pigment Violet 29 but once it is encapsulated in plastics or paint resins, it is not expected to leach out [21 CFR 178.3297, (BASF, 1998a)].

No specific release information for C.I. Pigment Violet 29 was found in the references identified during the full-text screening of the *on-topic* references under the Engineering section of *Pigment Violet 29 (CASRN: 81-33-4) Bibliography: Supplemental File for the TSCA Scope Document* (U.S. EPA, 2017a). However, releases to the environment from the conditions of use are possible (e.g., from manufacturing and use as a site-limited intermediate which is ~1-2%; incorporation into plastics, paints and coatings; application of coatings).

Based on information provided by the domestic manufacturer that is summarized above, releases from the manufacturing site are expected to be limited. Based on the information from industries, use information, and the physical properties of C.I. Pigment Violet 29, most of the waste from manufacturing as well as the various processing and uses are expected to be sent to landfills or incineration for disposal and only limited quantities are expected to be released to surface water.

### 2.3.3 Presence in the Environment and Biota

Monitoring studies or a collection of relevant and reliable biomonitoring studies provide(s) information that can be used in an exposure assessment. Monitoring studies that measure environmental concentrations or concentrations of chemical substances in biota provide evidence of exposure. EPA did not find environmental monitoring data (e.g., presence in air, soil, sediment, surface water, or biota) indicating the presence of C.I. Pigment Violet 29 in the U.S. or internationally (U.S. EPA, 2017a). EPA also did not find biomonitoring data for C.I. Pigment Violet 29 (U.S. EPA, 2017a). Although the

persistence and tendency to sorb to sediment means that there is the potential for entry into the aquatic food web, available data indicate that the BAF is low so uptake and bioaccumulation is likely to be limited.

### 2.3.4 Environmental Exposures

The manufacturing, processing, distribution, use and disposal of C.I. Pigment Violet 29 can result in releases to the environment. In this section, EPA presents exposures to aquatic and terrestrial organisms.

As outlined above, physical-chemical and fate properties as well as engineering controls limiting manufacturing (the largest use) releases are expected to result in limited exposure to water and sediment, groundwater via biosolids, landfill leaching, and air. It is estimated that less than one pound per day of C.I. Pigment Violet 29 is being released as the overall total of the National Pollutant Discharge Elimination System (NPDES)-permitted total suspended solids (TSS) discharges from the sole US manufacturer (Mott, 2017b). Because volumes used by downstream users are markedly less than the manufacturer (less than 5% each), it is expected that there will be minimal releases to water and sediment, groundwater via biosolids, landfill leaching, and air.

Where releases do occur, they are expected to result in limited environmental exposures. Specifically, releases of C.I. Pigment Violet 29 to water and sediment could occur during the wastewater treatment process following manufacturing/processing through possible releases of TSS, but these releases and corresponding aquatic exposures are expected to be limited since the high sorption of this chemical to organic matter (Log $K_{oc}$ = 5.0; see Table 2-4) will result in the vast majority of C.I. Pigment Violet 29 being captured as sludge in wastewater treatment facilities which is subsequently disposed of via incineration or landfill disposal. Similarly, the strong sorption properties would be expected to limit exposure via migration to groundwater from C.I. Pigment Violet 29 disposed of in landfills or applied via biosolids.

Air exposures from both incineration and fugitive releases from manufacturing and/or processing are expected to be low due to described fate properties and waste handling practices. Specifically, due to the low vapor pressure and volatility of C.I. Pigment Violet 29 (Henry's Law Constant $<1x10^{-10}$ atm-$m^3$/mole; Section 2.3.1 (U.S. EPA, 2017c)). Industrial wastes are sent to licensed industrial waste handlers where destruction removal efficiencies for incinerators are expected to be >99% (CPMA, 2017a).

### 2.3.5 Human Exposures

Human exposure to C.I. Pigment Violet 29 through occupational (Figure 2-2), consumer (Figure 2-3) or general population (Figure 2-4) activities and uses is possible, but exposures via all routes (oral, dermal, and inhalation) are expected to be low when physical-chemical properties are considered.

#### 2.3.5.1 Occupational Exposures

Workers may be exposed via inhalation and dermal routes. However, absorption via inhalation pathways is expected to be low due to low water solubility and dermal absorption is estimated to be negligible for the neat material (because it is a solid of high molecular weight), and poor absorption in solution (based on high molecular weight and low solubility). EPA received inhalation exposure monitoring information from the domestic manufacturer of C.I. Pigment Violet 29. The information indicates a workplace air concentration of 0.5 mg/$m^3$ over a 12-hour shift (Mott, 2017a). It is not clear if the monitoring result was for C.I. Pigment Violet 29 or for total dust. If the level was for total dust, the actual air concentration of C.I. Pigment Violet 29 is likely to be lower than 0.5 mg/$m^3$ (i.e., lower exposure).

Oral contact is not a relevant pathway for workers manufacturing C.I. Pigment Violet 29 since eating is not allowed in the production and laboratory work areas and proper personal protective equipment (PPE) are expected to be worn at the sole C.I. Pigment Violet 29 US manufacturing facility (Mott, 2017a). In addition, oral absorption is negligible due to low water solubility.

For downstream processors and users, worker exposure via inhalation through particulates that deposit in the upper respiratory tract or oral routes such as incidental ingestion of C.I. Pigment Violet 29 residue on hands is possible. These exposures are possible during handling solids and spray application of coatings containing C.I. Pigment Violet 29. However, oral and inhalation exposures to downstream processors and users are likely to be limited due to the use of PPEs and negligible oral absorption due to low water solubility [(BASF, 2017), (Sun Chemical, 2017d), (CPMA, 2017a)].

EPA reviewed available Safety Data Sheets (SDSs) for C.I. Pigment Violet 29. The SDSs recommend the use of personal protective equipment to minimize exposure, including the use of chemical-resistant protective gloves and safety glasses with side-shields or a face shield if a splashing hazard exists. It also recommends adequate ventilation when handling C.I. Pigment Violet 29 [(BASF, 2017), (Sun Chemical, 2017d), (Sun Chemical, 2017c)].

The domestic manufacturer of C.I. Pigment Violet 29 also indicates that workers in production and laboratory areas at their facility wear long sleeves and gloves to prevent dermal exposure (Mott, 2017a). Furthermore, while limited exposures are deemed possible, and as mentioned above, absorption via dermal and inhalation routes is expected to be low (see Section 2.4.2.1).

#### 2.3.5.2 Consumer Exposures

Possible exposure pathways/routes for C.I Pigment Violet 29 in consumer products are through liquid contact with paint and subsequent dermal absorption or oral ingestion (Figure 2-3). Inhalation is not identified as a route of exposure for consumers since C.I. Pigment Violet 29 is not expected to be released from consumer watercolor and artistic color as a vapor due to its low vapor pressure. Consumer exposures via oral and dermal routes are expected to be limited based on physical-chemical properties of C.I. Pigment Violet 29. Oral ingestion is expected to be negligible due to the low water solubility (see Table 2-1; 0.01 mg/L) and dermal absorption is estimated to be negligible for the neat material (because it is a solid of high molecular weight) and poor absorption in liquid (based on high molecular weight and low solubility). Further, C.I. Pigment Violet 29 was approved as a colorant for food packaging and is expected to remain within plastics (Appendix A-2). Therefore, consumer exposures associated with identified consumer uses are expected to be limited.

#### 2.3.5.3 General Population Exposures

General population exposures to C.I. Pigment Violet 29 are expected to be limited due to the limited releases of C.I Pigment Violet 29 outlined above (Section 2.3.4). Possible exposure routes for the general population include oral ingestion of water or groundwater and inhalation of air associated with releases of C.I. Pigment Violet 29 (Figure 2-4). Oral ingestion of C.I. Pigment Violet 29 is expected to be negligible due to low concentrations expected in surface and ground water. This low concentration in water is due to high capture efficiency of C.I. Pigment Violet 29 during the waste water treatment process limiting releases to surface water and strong sorption to soil reducing migration to groundwater (Section 2.3.4). Additionally, physical-chemical properties indicate that even if ingested, absorption would be expected to be limited due to low water solubility. Inhalation of C.I. Pigment Violet 29 is expected to be limited due to limited fugitive and incineration air releases (Figure 2-4, Section 2.3.2). Low volatilization rates will limit fugitive air releases as vapor (Section 2.3.1), while engineering

controls during manufacturing capture the majority of any C.I. Pigment Violet 29 that would be released (see Section 2.3.1). Downstream industrial facilities are subject to EPA and state regulations that would be expected to similarly limit air releases (Section 2.3.2). Furthermore, absorption via inhalation is expected to be low due to low water solubility. Dermal exposures, should they occur, are expected to be limited because dermal absorption is estimated to be negligible because it is a solid of high molecular weight and solubility.

#### 2.3.5.4 Potentially Exposed or Susceptible Subpopulations

TSCA requires the determination of whether a chemical substance presents an unreasonable risk to "a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation" by EPA. TSCA § 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." General population is "the total of individuals inhabiting an area or making up a whole group" and refers here to the U.S. general population (U.S. EPA, 2011).

As part of the Problem Formulation, EPA identified potentially exposed and susceptible subpopulations for further analysis during the development and refinement of the life cycle, conceptual models, exposure scenarios, and analysis plan. In this section, EPA addresses the potentially exposed or susceptible subpopulations identified as relevant based on greater exposure. EPA will address the subpopulations identified as relevant based on greater susceptibility in the hazard section.

Exposures of C.I. Pigment Violet 29 would be expected to be higher amongst workers and consumers using C.I. Pigment Violet 29 as compared to the general population. However, these potential exposures are likely to be limited due to physical-chemical and fate properties resulting in limited absorption and engineering controls during the manufacturing, processing and use of C.I. Pigment Violet 29 as outlined above.

## 2.4 Hazards (Effects)

For scoping, EPA conducted comprehensive searches for data on hazards of C.I. Pigment Violet 29, as described *in* *Strategy for Conducting Literature Searches for Pigment Violet 29: Supplemental File for the TSCA Scope Document* (U.S. EPA, 2017d). No specific human health or environmental hazard information for C.I. Pigment Violet 29 was identified during the full-text screening of the *on-topic* references under the human health hazard or environmental hazard sections of *Pigment Violet 29 (CASRN: 81-33-4) Bibliography: Supplemental File for the TSCA Scope Document* (U.S. EPA, 2017a). Based on initial screening of the robust summaries available in the ECHA and FAP databases the hazards to human and environmental receptors are expected to be low. EPA plans to confirm the low hazards of C.I. Pigment Violet 29 by reviewing the study reports that were used to formulate the robust summaries. When conducting the risk evaluation, the relevance of any hazard within the context of a specific exposure scenario will be judged for appropriateness. For C.I. Pigment Violet 29, exposures are expected to be low. This means that it is unlikely that exposure scenarios will be further analyzed in the risk evaluation.

### 2.4.1 Environmental Hazards

As indicated previously, the environmental hazard data identified for C.I. Pigment Violet 29 were the studies described in the robust summaries in ECHA Database (ECHA, 2017b).

Aquatic toxicity data were available, which measured the acute toxicity of C.I. Pigment Violet to a fish, aquatic invertebrate, and aquatic plant species. Appendix E presents the robust summaries available from the ECHA Database that EPA used to preliminarily characterize the environmental hazard of C.I. Pigment Violet 29.

The Agency is currently in possession of full study reports for the following studies:

- OECD Guideline 203: Fish Acute Toxicity Test
- OECD Guideline 202: *Daphnia* sp., Acute Immobilization Test
- OECD Guideline 221: *Lemna* sp., Growth Inhibition test

EPA will review all full study reports during risk evaluation using the data quality review evaluation metrics and the rating criteria described in *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a).

Review of the robust summaries indicates that no adverse effects were observed in fish (acute), aquatic invertebrate (acute), and aquatic plants at the limit of solubility for C.I. Pigment Violet 29. Based on the lack of adverse effects observed, EPA preliminarily concludes that the aquatic hazard is low for C.I. Pigment Violet 29. This is consistent with the Canadian Ecological Risk Classification for C.I. Pigment Violet 29, discussed in Appendix A-1, where it was determined that C.I. Pigment Violet 29 did not meet the criteria for categorisation as a prioritized substance for further evaluation and the potential hazard is low.

As noted in Section 2.3.1, C.I. Pigment Violet 29 is not expected to degrade in the environment, so EPA has no concerns for environmental degradation products for C.I. Pigment Violet 29.

No studies were identified that characterized the effects of chronic exposure of C.I. Pigment Violet 29 to aquatic species, or the effects to terrestrial species. As a result of uncertainties inherent in extrapolating between acute and chronic exposure regimes and dissimilar environmental receptors, multiple lines of evidence were considered to evaluate the potential for hazards under chronic aquatic exposure conditions and to terrestrial organisms. The combination of low hazard of C.I. Pigment Violet 29 to aquatic species, low hazard in mammalian tests (see Section 2.4.2), the low limit of solubility, low vapor pressure, low bioaccumulation potential, low environmental releases and resulting exposures from manufacturing, use, and disposal, as well as low absorption (see Section 2.4.2) indicate that hazard to terrestrial and aquatic receptors from acute and chronic exposures to C.I. Pigment Violet 29 is expected to be low.

### 2.4.2 Human Health Hazards

C.I. Pigment Violet 29 does not have an existing EPA IRIS Assessment; however there is available toxicity data on C.I. Pigment Violet 29 from ECHA (ECHA, 2017b) and the Food Additive Petition (FAP) 8B4626 (BASF, 1998a). EPA plans to review these studies using the approaches and/or methods described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a) to ensure that EPA is considering information that has been made available. Based on the reasonably available information, the following sections describe the hazards EPA expects to further analyze.

#### 2.4.2.1 Non-Cancer Hazards

As indicated previously, the human health hazard data identified for C.I. Pigment Violet 29 were those described in the robust summaries in ECHA Database (ECHA, 2017b). Several of the studies were

referenced in the Food Additive Petition (FAP) 8B4626 (BASF, 1998a). The results of the studies referenced in the FAP were compared against the results of the summaries in the ECHA database and were found to be consistent. No additional information was available in the FAP to define the non-cancer hazards of C.I Pigment Violet 29.

The Agency is currently in possession of the full study reports for the human health studies summarized in Appendix F:

- OECD Guideline 401: Acute Oral Toxicity with Rats
- OECD Guideline 404: Acute Dermal Irritation/Corrosion
- OECD Guideline 405: Acute Eye Irritation/Corrosion
- OECD Guideline 429: Skin Sensitisation: Local Lymph Node Assay
- OECD Guideline 421: Reproduction / Developmental Toxicity Screening Test
- Non-Guideline Acute Toxicity: Acute Intraperitoneal Toxicity with Rats
- Non-Guideline Acute Toxicity: Acute Inhalation Toxicity with Rats

Together, these full study reports represent all the human health data on C.I. Pigment Violet 29 found in the ECHA Database. Additional study summaries were identified in the ECHA database, but these were found to be conducted on analogous chemicals, so these studies were not requested at this time. EPA will review all full study reports and the expanded summary documents during risk evaluation using the data quality review evaluation metrics and the rating criteria described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a).

Preliminary review of the robust summaries indicates lack of effects in any standard toxicity test. These findings are consistent with the expectation that C.I. Pigment Violet 29 is poorly absorbed by all routes (oral, dermal, and inhalation) due to its physical-chemical properties.

In March 2013, CPMA submitted study summaries for Perylene Pigments including C.I. Pigment Violet 29 for the High Production Volume (HPV) Test Program (CPMA, 2017a). The tests specifically for C.I. Pigment Violet 29 were eye irritation and skin irritation (EPA-HQ-OPPT-2016-0725-0006). These summaries indicated no skin or eye irritation.

#### 2.4.2.2 Genotoxicity and Cancer Hazards

Genotoxicity data are available for C.I. Pigment Violet 29, including those summarized in the ECHA Database (ECHA, 2017b) and the Food Additive Petition (FAP) 8B4626 (BASF, 1998a).

The Agency is currently in possession of the following full study reports of genotoxicity tests summarized in Appendix F:

- OECD Guideline 476: *In vitro* Mammalian Cell Gene Mutation Test
- Reverse mutation assay AMES test using *Salmonella typhimurium* and *Escherichia coli* from Food Additive Petition (FAP) 8B4626 (BASF, 1998a).

EPA will review all full study reports during risk evaluation using the data quality review evaluation metrics and the rating criteria described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a).

EPA also considered potential carcinogenicity during problem formulation. Perylene, the 5-ring polycyclic hydrocarbon moiety in the center of C.I. Pigment Violet 29, has been shown to be a negative or marginal carcinogen in limited studies (IARC, 2010). This low carcinogenicity potential is supported by structure-activity relationship (SAR) analysis and EPA's OncoLogic cancer expert system (available at https://www.epa.gov/tsca-screening-tools/oncologictm-computer-system-evaluate-carcinogenic-potential-chemicals) because the arrangement of the five benzene rings in perylene does not favor metabolic activation to epoxides. The addition of the imides groups to perylene to form C.I. Pigment Violet 29 is expected to decrease solubility, increase bulkiness and thereby further reduce the likelihood of carcinogenic potential. Testing for carcinogenicity of C.I. Pigment Violet 29 has not been conducted. However, negative genotoxicity results, SAR considerations and the expected negligible absorption and uptake of C.I. Pigment Violet 29, support EPA's conclusion that C.I. Pigment Violet 29 is unlikely to be a carcinogen.

#### 2.4.2.3 Potentially Exposed or Susceptible Subpopulations

TSCA requires that the determination of whether a chemical substance presents an unreasonable risk include consideration of unreasonable risk to "a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation" by EPA. TSCA § 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." In developing the hazard assessment, EPA will analyze available data to ascertain whether some human receptor groups may have greater susceptibility than the general population to the chemical's hazard(s).

## 2.5 Conceptual Models

EPA risk evaluation guidance (U.S. EPA, 1998; U.S. EPA, 2014), defines Problem Formulation as the part of the risk evaluation framework that identifies the major factors to be considered in the evaluation. It draws from the regulatory, decision-making and policy context of the risk evaluation and informs the evaluation's technical approach.

A conceptual model describes the actual or predicted relationships between the chemical substance and receptors, either human or environmental. These conceptual models are integrated depictions of the conditions of use, exposures (pathways and routes), hazards and receptors. The initial conceptual models describing the scope of the risk evaluation for C.I. Pigment Violet 29, have been refined during problem formulation. The changes to the conceptual models in this problem formulation are described along with the rationales.

In this section EPA outlines whether pathways will be included and further analyzed in the risk evaluation; will be included but will not be further analyzed in risk evaluation; and will not be included in the TSCA risk evaluation and the underlying rationale for these decisions.

EPA determined as part of problem formulation that it is not necessary to conduct further analysis on the exposure pathways that were identified in the C.I. Pigment Violet 29 scope document (U.S. EPA, 2017c) and that remain in the risk evaluation. Each risk evaluation will be "fit-for-purpose," meaning not all conditions of use will warrant the same level of evaluation and the Agency may be able to reach some conclusions without extensive or quantitative risk evaluations. 82 FR 33726, 33734, 33739 (July 20, 2017). EPA expects to be able to reach conclusions about particular hazards or exposure pathways without extensive evaluation and plans to conduct no further analysis on those hazards or exposure pathways in order to allow EPA to focus the Agency's resources on more extensive or quantitative

analyses. As discussed below, EPA preliminarily determined that there are no environmental release and waste pathways for the environment or general populations that EPA plans to further analyze in the risk evaluation.

A conceptual model describes the actual or predicted relationships between the chemical substance and receptors, either human or environmental. These conceptual models are integrated depictions of the conditions of use, exposures (pathways and routes), hazards and receptors. The initial conceptual models describing the scope of the risk evaluation for C.I. Pigment Violet 29, have been refined during problem formulation, where no exposure pathways are expected to be assessed further. The changes to the conceptual models in this problem formulation are described along with the rationales. Figure 2-2 and Figure 2-3 illustrate the flow of C.I. Pigment Violet 29 from chemical manufacture and processing through potential exposure pathways to effects to human receptors (e.g., workers, consumers, general population). Figure 2-4 illustrates the flow of C.I. Pigment Violet 29 from chemical manufacture and processing through potential exposure pathways to effects to environmental receptors (e.g., terrestrial and aquatic wildlife).

### 2.5.1 Conceptual Model for Industrial and Commercial Activities and Uses: Potential Exposures and Hazards

The revised conceptual model for Industrial and Commercial Activities and Uses (Figure 2-2) describes the pathways of exposure from industrial and commercial activities and uses of C.I. Pigment Violet 29 that EPA plans to include in the risk evaluation. The C.I. Pigment Violet 29 Scope Document presented possible exposure pathways and exposure routes to human and environmental receptors associated with environmental releases and waste handling, treatment and disposal of C.I. Pigment Violet 29 for industrial and commercial activities (U.S. EPA, 2017c). During problem formulation, EPA further analyzed the potential exposures and hazards to workers and has refined the conceptual models accordingly with releases, pathways and routes of exposure that EPA has concluded do not warrant further analysis indicated in Figure 2-2.

***Inhalation***

Mist and dust emissions from fugitive and stack emissions are expected to be limited. Air emissions are typically relevant for volatile and/or dusty materials and since C.I. Pigment Violet 29 is not volatile, the vapor pathway is not relevant. Since the vapor pressure of C.I. Pigment Violet 29 is nil, the vapor release during uses of paint is not a concern. Also, dust handling systems are in place at the manufacturing facility where the dried powder is added or discharged from the equipment and 99.5% of dust is captured in baghouses. The resulting dust and bags are handled as contaminated industrial waste and sent to a licensed waste handler for disposal. Absorption of C.I. Pigment Violet 29 via inhalation is also expected to be negligible based on low water solubility. Inhalation monitoring has shown that exposure was about 0.5 $mg/m^3$ over a 12-hr work shift (Mott, 2017a). Due to the low potential for inhalation exposure and low potential absorption and low inhalation toxicity, this pathway will not be further analyzed in the risk evaluation.

***Oral***

Oral contact is not a relevant pathway for workers manufacturing C.I. Pigment Violet 29 since eating is not allowed in the production and laboratory work areas and proper personal protective equipment are expected to be worn at the sole C.I. Pigment Violet 29 US manufacturing facility (Mott, 2017a). In addition, oral absorption is negligible due to low water solubility. EPA plans no further analysis of this pathway for workers or occupational non-users in the risk evaluation.

***Dermal***

Dermal absorption is estimated to be negligible when C.I. Pigment Violet 29 is a solid, and low if it is in solution based on the low water solubility and high molecular weight. Dermal exposure is possible if C.I. Pigment Violet 29 is formulated in solvent. However, based on the review of the robust summaries of human health data in the ECHA Database (ECHA, 2017b), hazards to human health are expected to be low. Dermal absorption of C.I. Pigment Violet 29 is estimated to be negligible for the neat material since it is a solid, and poor dermal absorption if it is in solution based on the low water solubility and high molecular weight. EPA plans no further analysis of this pathway for workers or occupational non-users in the risk evaluation.

***Waste handling, treatment and disposal***

Figure 2-2 shows that waste handling, treatment and disposal is expected to lead to the same low hazard conclusion as other industrial and commercial activities and uses. During problem formulation, EPA further analyzed the potential exposures and hazards to consumers and bystanders and has refined the conceptual models accordingly. Releases of C.I. Pigment Violet 29 from recycling of used papers and plastic articles containing C.I. Pigment Violet 29 is possible. However, due to its low water solubility and high sorption to particulates and biosolids, most C.I. Pigment Violet 29 in aqueous waste streams is expected to be captured in the waste water treatment systems. As a result of the lack of exposure expected to result from this pathway, EPA plans no further analysis of this pathway for workers or occupational non-users in the risk evaluation. Figure 2-3 in the C.I. Pigment Violet 29 Scope Document presented the possible exposure pathways, exposure routes and hazards to human receptors from consumer activities and uses of C.I. Pigment Violet 29 (U.S. EPA, 2017c). Due to these releases, pathways and routes of exposure, EPA has concluded no further analysis of these pathways is warranted, as indicated in Figure 2-3.

***Consumer Handling and Recycling and Disposal of Waste***

Releases of C.I. Pigment Violet 29 from recycling of used papers and plastic articles containing C.I. Pigment Violet 29 is possible. However, due to its low water solubility, any C.I. Pigment Violet 29 in aqueous waste stream is expected to be captured in the waste water treatment systems. As the majority of C.I. Pigment Violet 29-containing consumer waste consists of consumer products that are expected to enter the consumer waste streams for landfill disposal or recycling, consumer exposure to these products is low, as these activities take place in licensed waste management facilities. Similarly, C.I. Pigment Violet 29 in paints and plastics is expected to remain embedded in these materials, thereby limiting exposure. Due to the low potential for exposure resulting from consumer activities and low toxicity to human receptors, EPA plans no further analysis of these pathways for consumer activities in the risk evaluation.

### 2.5.2 Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards

The revised conceptual model (Figure 2-4) in the C.I. Pigment Violet 29 Scope Document presents possible exposure pathways, exposure routes, and hazards to human and environmental receptors from environmental releases and wastes of C.I. Pigment Violet 29 (U.S. EPA, 2017c). During problem formulation, EPA further analyzed the potential exposures and hazards to the general population and environmental receptors and has refined the conceptual models accordingly with releases, pathways and routes of exposure that EPA has concluded do not warrant further analysis indicated in Figure 2-4.

#### 2.5.2.1 Pathways That EPA Plans to Include and Further Analyze in the Risk Evaluation

There are no environmental release and waste pathways for the environment or general populations that EPA plans to further analyze in the risk evaluation.

#### 2.5.2.2 Pathways that EPA Plans to Include in the Risk Evaluation but Not Further Analyze

***Ambient Water and Drinking Water Pathways***

Currently, no states or tribes include criteria for C.I. Pigment Violet 29 in water quality standards and values are not available for use in NPDES permits. Thus, EPA cannot conclude that risk to human health and aquatic life from exposure to C.I. Pigment Violet 29 in ambient waters has been effectively managed. As a result, this pathway is included in the Risk Evaluation. EPA may publish CWA section 304(a) human health or aquatic life criteria for Pigment Violet 29 in the future if it is identified as a priority under the CWA.

As described in Section 2.3.2, releases to water are expected to be limited from the sole U.S. manufacturer and downstream users. Chemicals may enter surface water via either direct release to water or release after treatment at POTWs, in compliance with an NPDES discharge permit. Due to low water solubility and its solid physical state, direct releases of C.I. Pigment Violet 29 to water are expected to partition into particulates and sediment; but the amounts are expected to be limited due to minimal releases to surface water. Likewise, C.I. Pigment Violet 29 releases from downstream users to POTWs would be expected to separate during settling in primary treatment due to low water solubility and to partition largely to the biosolids and particulates during secondary treatment. Sorption to particulates and biosolids are expected to be strong and water solubility is low; therefore, biosolids that contain C.I. Pigment Violet 29 are expected to lead to negligible migration to ground water. Hence, C.I. Pigment Violet 29 concentrations in surface water and groundwater are expected to be low based on limited releases and physical-chemical properties (low water solubility).

Based on the environmental fate described, C.I. Pigment Violet 29 is also not expected to be present in drinking water (surface or ground water) at significant levels and hence, oral ingestion of water is deemed an insignificant exposure pathway for C.I. Pigment Violet 29. Furthermore, as described previously, even if oral ingestion occurs, absorption of C.I. Pigment Violet 29 is expected to be limited due to its very low water solubility. This conclusion is supported by available experimental human health hazard data showing no adverse effects as a result of exposure to C.I. Pigment Violet 29 in both acute and repeated-dose studies. Hence, EPA concludes that further analysis for risk to the general population from oral exposures is not warranted.

Environmental hazard data reported in the ECHA Database indicate no effects were observed at the solubility limit for C.I. Pigment Violet 29 in toxicity tests with an aquatic plant, an aquatic invertebrate and a fish. Taken together with the limited releases expected to water (wastewater (direct/indirect) and groundwater), EPA concludes that further analysis of exposures to aquatic species from exposure to C.I. Pigment Violet 29 is not warranted. Similarly, as a result of the low potential for exposure to terrestrial environmental receptors and low acute toxicity to the surrogate species (aquatic and mammalian), further risk analysis to terrestrial environmental receptors is not warranted. As indicated above, this is consistent with the Canadian Ecological Risk Classification for C.I. Pigment Violet 29, discussed in Appendix A-1.

***Air Pathway***

As indicated in Sections 2.3.1 and 2.3.2, low volatilization rates will limit fugitive air releases as vapor, while engineering controls capture the majority of any C.I. Pigment Violet 29 that would be released during incineration. Dust handling systems are in place at the manufacturing facility that capture C.I. Pigment Violet 29 lost as dust during manufacturing. The efficiency rate is greater than 99.5% (Mott, 2017b; Sun Chemical, 2017b). Furthermore, absorption via inhalation is expected to be low due to low water solubility. Due to the low potential for inhalation exposure and low potential absorption and low inhalation toxicity, this pathway will not be further evaluated in the risk evaluation.

***Disposal Pathways***

The sole domestic manufacturer of C.I. Pigment Violet 29 has estimated standard yield loss of 1-2% of the volume during the manufacturing (6,000- 12,000 pounds for 2015) (Mott, 2017b). Greater than 95% of this loss is estimated to be captured via on-site above ground biological wastewater treatment system that captures C.I. Pigment Violet 29 as well as dust handling systems in place at the manufacturing facility, which capture dust in baghouses (Mott, 2017b).

As indicated above, and in Section 2.3.2, the sole U.S. manufacturer of C.I. Pigment Violet 29 sends its non-hazardous wastewater treatment residuals (sludge) to the Oak Ridge Landfill in Dorchester County or the Berkeley County Landfill. Both landfills are RCRA Subtitle-D lined landfills permitted under the authority of South Carolina Regulation Number 61-107.19.

In addition to design standards for Subtitle-D lined landfills which are intended to limit the potential for leachate, sorption to particulates and biosolids for C.I. Pigment Violet 29 are expected to be strong and water solubility is low, so leaching of C.I. Pigment Violet 29 from landfills is expected to be negligible. C.I. Pigment Violet 29 contained in consumer products is expected to be encapsulated in plastics or paint resins, which further limits the potential for leaching from disposal of these products. Due to the low potential for exposure, low hazards to human health and low hazard to environmental receptors, EPA concludes further evaluation of exposures resulting from disposal to landfills is not warranted.

As indicated in Section 2.3.2, the sole U.S. manufacturer of C.I. Pigment Violet 29 sends its non-hazardous wastewater treatment residuals (sludge) to the Oak Ridge Landfill in Dorchester County or the Berkeley County Landfill. Both of these landfills are RCRA Subtitle-D lined landfills permitted under the authority of South Carolina Regulation Number 61-107.19, so land application of biosolids is not expected to be a release pathway for the manufacturer, so this pathway is outside of scope of this assessment. Similarly, EPA does not plan to include on-site releases to land that go to underground injection. There are no current underground injection sites for C.I. Pigment Violet 29 and none are expected; so this disposal pathway is also outside the scope of this evaluation.

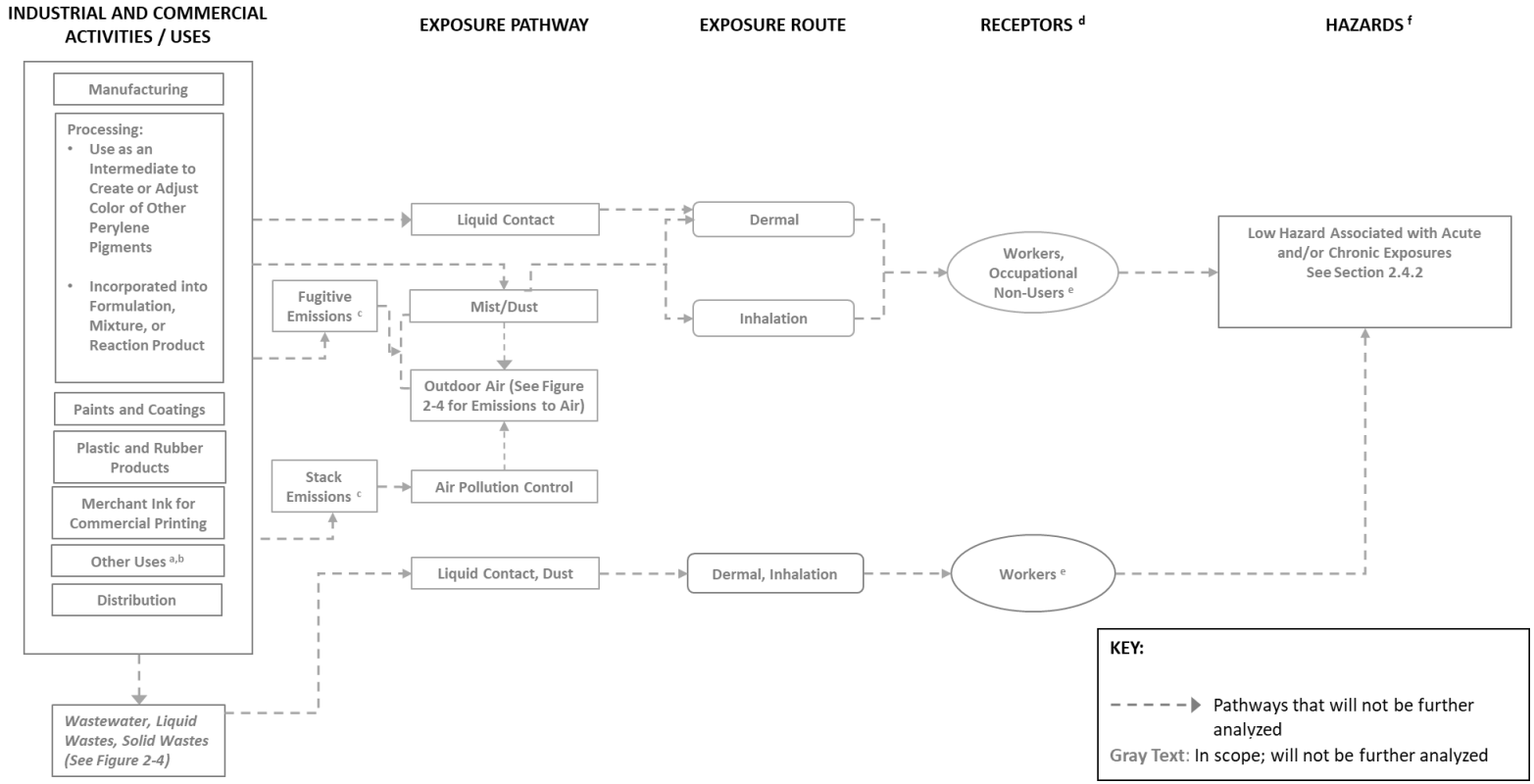


**Figure 2-2. C.I. Pigment Violet 29 Conceptual Model for Industrial and Commercial Activities and Uses: Potential Exposures and Hazards**

The conceptual model presents the exposure pathways, exposure routes and hazards to human receptors from industrial and commercial activities and uses of C.I. Pigment Violet 29.

[a] Other uses of C.I. Pigment Violet 29 may include: applications in odor agents, cleaning/washing agents, surface treatment, absorbents and adsorbents, laboratory chemicals, pharmaceuticals, light-harvesting materials, transistors, molecular switches, solar cells, optoelectronic devices, paper, architectural uses, polyester fibers, adhesion, motors, generators, vehicle components, sporting goods, appliances, agricultural equipment and oil and gas pipelines

[b] Some products are used in both commercial and consumer applications.

[c] Stack air emissions are emissions that occur through stacks, confined vents, ducts, pipes or other confined air streams. Fugitive air emissions are those that are not stack emissions, and include fugitive equipment leaks from valves, pump seals, flanges, compressors, sampling connections, open-ended lines; evaporative losses from surface impoundment and spills; and releases from building ventilation systems.

[d] Receptors include potentially exposed and susceptible subpopulations.

[e] When data and information are available to support the analysis, EPA also considers the effect that engineering controls and/or personal protective equipment (PPE) have on occupational exposure levels.

[f] EPA will review full study reports to confirm preliminary low hazard conclusions.

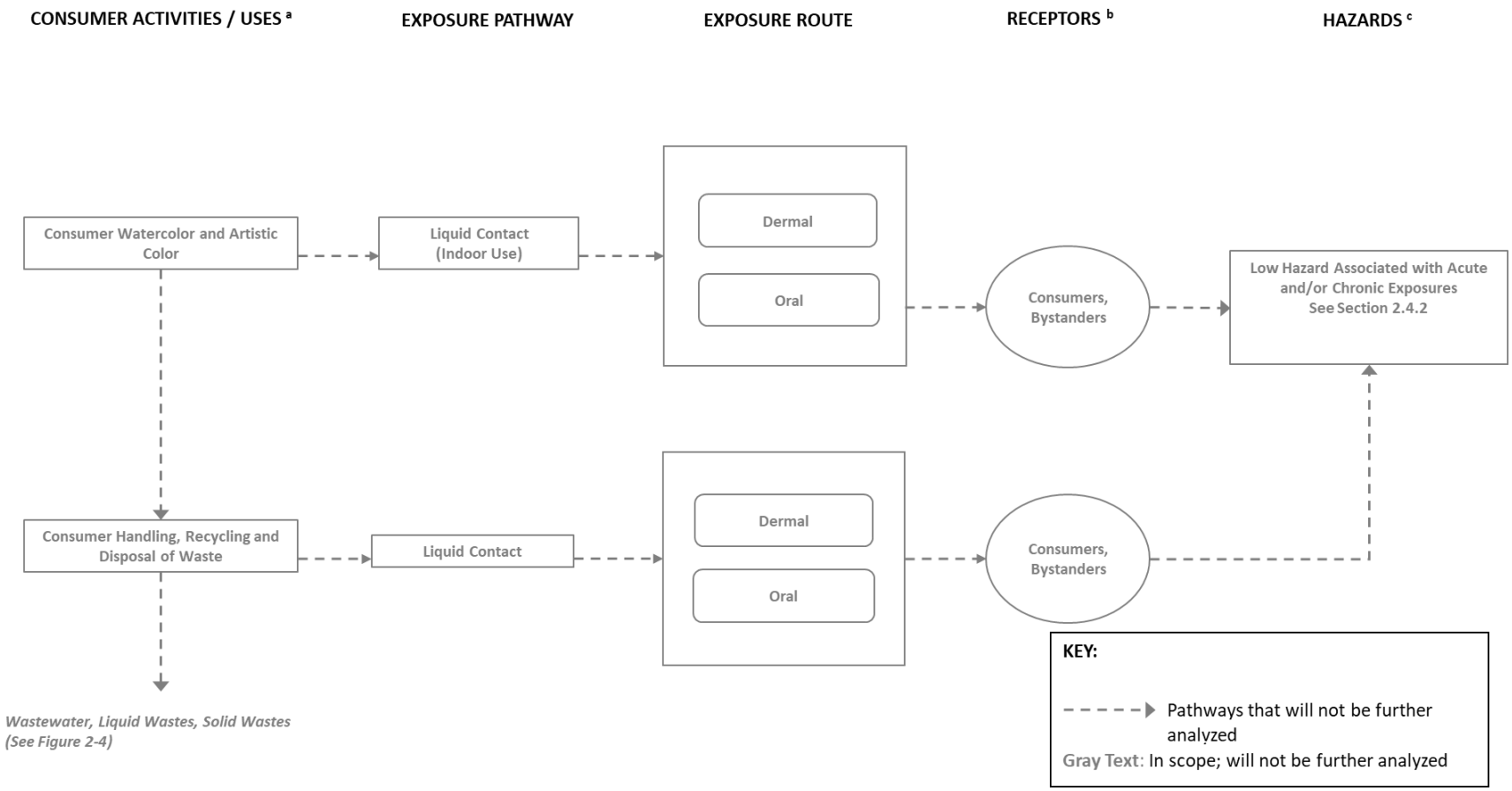


**Figure 2-3. C.I. Pigment Violet 29 Conceptual Model for Consumer Activities and Uses: Potential Exposures and Hazards**
The conceptual model presents the exposure pathways, exposure routes and hazards to human receptors form consumer activities and uses of C.I. Pigment Violet 29.

[a] Some products are used in both commercial and consumer applications.
[b] Receptors include potentially exposed or susceptible populations.
[c] EPA will review full study reports to confirm preliminary low hazard conclusions.

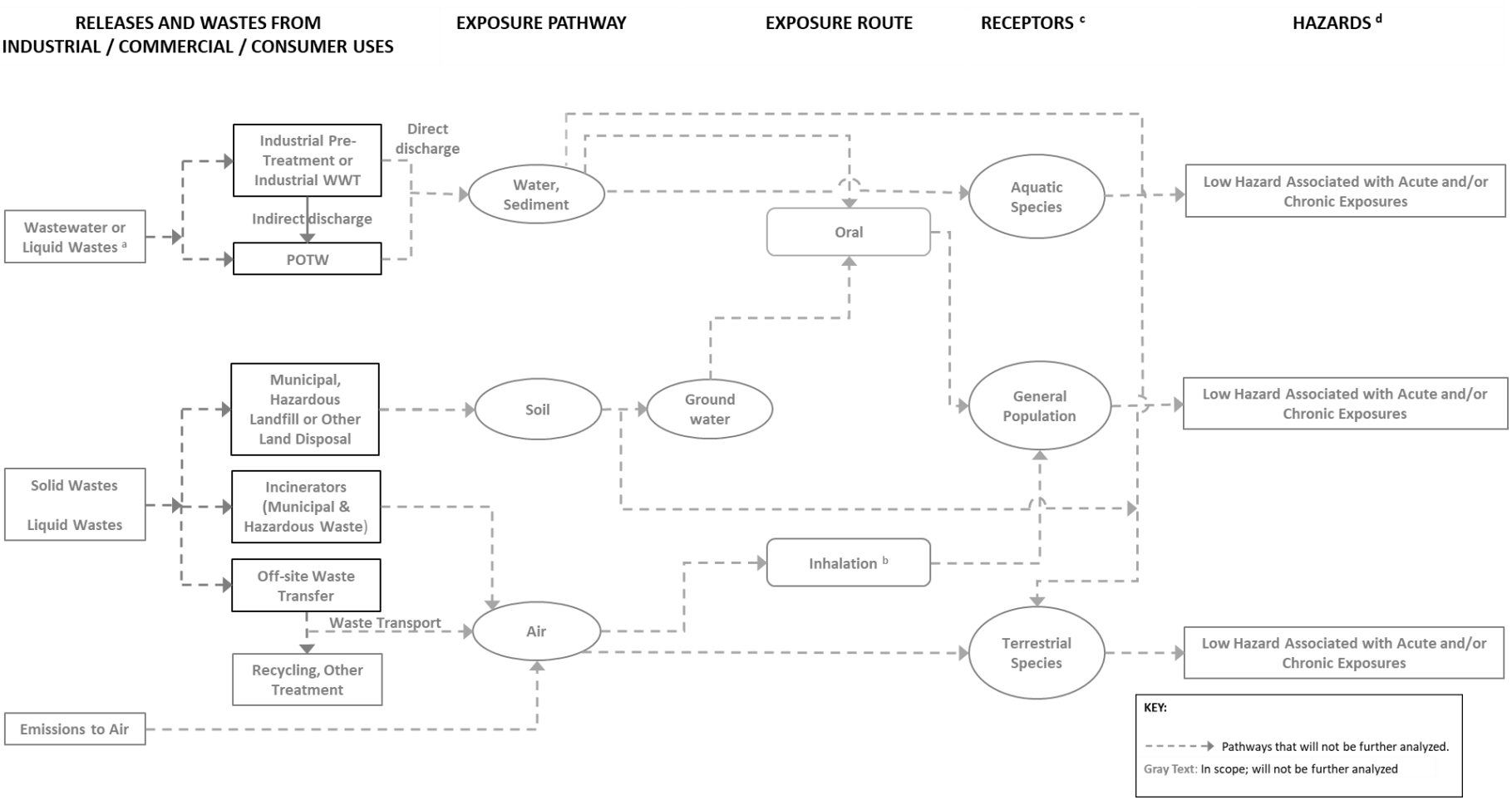


**Figure 2-4. C.I. Pigment Violet 29 Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards**

The conceptual model presents the exposure pathways, exposure routes and hazards to human and environmental receptors from environmental releases and wastes of C.I. Pigment Violet 29.

[a] Industrial wastewater or liquid wastes may be treated on-site and then released to surface water (direct discharge), or pre-treated and released to POTW (indirect discharge). For consumer uses, such wastes may be released directly to POTW (i.e., down the drain). Drinking water will undergo further treatment in drinking water treatment plant. Groundwater may also be a source of drinking water.

[b] Presence of mist to the environment is not expected.

[c] Receptors include potentially exposed or susceptible populations.

[d] EPA will review full study reports to confirm preliminary low hazard conclusions.

## 2.6 Analysis Plan

As described in Section 2.5, due to physical-chemical and fate properties, limited use volumes outside the manufacturing site, limited environmental releases, and low absorption by all routes of exposure, it is concluded further analysis of exposure pathways to workers, consumers and the general population is not warranted. As noted, EPA has obtained full study reports for all physical and chemical properties, environmental fate, environmental hazard and human health hazard data from the ECHA Database (ECHA, 2017b) and the Food Additive Petition (FAP) 8B4626 (BASF, 1998a). The full study reports will be reviewed by EPA as it develops the Draft Risk Evaluation. The low environmental and human health hazards reported in these robust study summaries led the EPA to preliminarily conclude that C.I. Pigment Violet 29 presents a low hazard to human health and environmental receptors. The aquatic study summaries indicated that no effects were observed up to the solubility limit of C.I. Pigment Violet 29, while the acute and repeated-dose study summaries for human health reported no adverse effects. If, upon review of the full study reports, the results are not scientifically sound or consistent with the robust summary reports, EPA may conduct additional analysis to characterize the potential risks of this chemical, which could include changes to the pathways analyzed.

Based on all currently available information, including robust study summaries indicating low hazard, EPA preliminarily proposes no further analysis of environmental releases and exposure pathways. EPA will review any public comments and additional data/information prior to the publication of the Draft Risk Evaluation and incorporate these responses in the Draft Risk Evaluation. As per EPA's final rule, Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act, EPA will also take comment and peer review the Draft Risk Evaluation for C.I. Pigment Violet 29.

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# APPENDICES

# Appendix A. REGULATORY HISTORY

## A-1 Background Information on the Inclusion of C.I. Pigment Violet 29 in TSCA 2012 and 2014 Work Plans

C.I. Pigment Violet 29 was added to the TSCA Work Plan in 2012. As described in detail in the Methodology (U.S. EPA, 2012c), all chemicals on the Work Plan were scored by 3 criteria: hazard, exposure and persistence and bioaccumulation. The criteria were scored from 1-3, where 3 is the highest concern and 1 is the lowest concern. See Table_Apx A-1 for scoring of C.I. Pigment Violet 29. The purpose of the Work Plan was not to evaluate risk, but used as a tool for screening chemicals.

**Table_Apx A-1: 2014 TSCA Work Plan**

| Chemical Name | When was the chemical added? | Hazard Criteria Met | Hazard Score | Exposure Criteria Met | Exposure Score | Persistence & Bioaccumulation Criteria Met | Persistence & Bioaccumulation Score | Use | Risk Assessment Status and Other Actions | CASRN |
|---|---|---|---|---|---|---|---|---|---|---|
| Anthra[2,1,9-def:6,5,10-d'e'f'] diisoquinoline-1,3,8,10(2H,9H)-tetrone (Pigment Violet 29) | Added 2012 | Aquatic toxicity | 3* | Widely used in consumer products Estimated to have moderate releases to the environment | 3 | High environmental persistence Low bioaccumulation potential | 2 | Consumer Industrial | Not yet initiated | 81-33-4 |

The hazard criteria used for the 2012 TSCA Work Plan Chemicals is described in the Methodology (U.S. EPA, 2012c). Chemicals were scored on the basis of readily available data, and no judgment was made concerning completeness or robustness of the available data set for a given chemical.

In 2012, C.I. Pigment Violet 29 was given the highest hazard score of 3 based on aquatic toxicity. The score was based on a predicted, modeled fish acute $LC_{50}$ value of 4.6 mg/l reported in Ecological Categorization Results, Canadian Domestic Substances List (DSL) (Environment Canada, 2006).

Prior to the 2014 TSCA Work Plan update, Canada had updated their Ecological Categorization Results (OECD, 2017) indicating that C.I. Pigment Violet 29 is not categorized as inherently toxic to aquatic organisms. However, EPA's updates for the 2014 Work Plan were based only on newer data for exposure, i.e., 2016 TRI and 2016 CDR data. EPA did not update the hazard ratings for any chemicals for the 2014 Work Plan update; therefore, C.I. Pigment Violet 29 remained with a high hazard score.

C.I. Pigment Violet 29 is listed on the Canadian Inventory of the 23,000 substances on the Domestic Substances List (DSL) but the Ecological Risk Classification for C.I. Pigment Violet 29 did not meet the

criteria for categorisation as a prioritized substance for further assessment. The determination for C.I. Pigment Violet 29 and seven other similar pigments was made using a combination of QSAR modeling and hazard data for analogous pigments with low solubility (Pigment Red 149; CAS RNs 4948-15-6). The conclusion of this screening was consistent with EPA's findings and indicated that because of low toxicity and low solubility, C.I. Pigment Violet 29 did not meet the criteria for further assessment and the potential hazard is low (Environment Canada, 2006).

In 2012, C.I. Pigment Violet 29 was given the highest exposure score of 3 based on findings in consumer products and moderate release to the environment. Data weighed to determine the score were the production volume in CDR 2012's reporting year (520,916 pounds per year), number of use sites (1), the Industrial Function Category (pigments) and the reported commercial uses and use in consumer products. Expert judgment, generic scenarios, experience with new and existing chemical assessments and exposure scenarios were drawn on to derive the final exposure score of 3. Updated data from the 2016 CDR had no effect on the exposure score. The current Problem Formulation for C.I. Pigment Violet 29 uses more specific exposure data and should be regarded as more accurate compared to the scores created in the 2012 and 2014 Work Plan process.

## A-2 Federal Laws and Regulations

**Table_Apx A-4. Federal Laws and Regulations**

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| **EPA Regulations** | | |
| TSCA – Section 6(b) | EPA is directed to identify and begin risk evaluations on 10 chemical substances drawn from the 2014 update of the TSCA Work Plan for Chemical Assessments. | C.I. Pigment Violet 29 is on the initial list of chemicals to be evaluated for unreasonable risk under TSCA (81 FR 91927, December 19, 2016). |
| TSCA – Section 8(a) | The TSCA § 8(a) CDR Rule requires manufacturers (including importers) to give EPA basic exposure-related information on the types, quantities and uses of chemical substances produced domestically and imported into the United States. | C.I. Pigment Violet 29 manufacturing (including importing), processing and use information is reported under the CDR Rule (76 FR 50816, August 16, 2011). |
| TSCA – Section 8(b) | EPA must compile, keep current and publish a list (the TSCA Inventory) of each chemical substance manufactured, (including imported) or processed, in the United States. | C.I. Pigment Violet 29 was on the initial TSCA Inventory and therefore was not subject to EPA's new chemicals review process under TSCA section 5 |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | | (42 FR 64572, December 23, 1977). |
| **Other Federal Regulations** | | |
| Food and Drug Administration (FDA) | Chemicals that come in contact with food must first be reviewed by the FDA for safety. In 1998 BASF submitted a petition for C.I. Pigment Violet 29 to be a food additive. | C.I. Pigment Violet 29 is approved to be in finished articles that come in contact with food. It should not to exceed 1% by weight of polymers and should follow specific conditions of use (21 CFR 178.3297). C.I. Pigment Violet 29 is not listed as an approved food additive. |

## A-3 International Laws and Regulations

**Table_Apx A-5. International Laws and Regulations**

| Country/Organization | Requirements and Restrictions |
|---|---|
| **Australia** | C.I. Pigment Violet 29 is on the Australian Inventory for Chemical Substances (AICS), a database of chemicals available for industrial use in Australia. There are no regulatory obligations or conditions cited for C.I. Pigment Violet 29 [1] |
| **Canada** | C.I. Pigment Violet 29 is on the public portion of the Domestic Substances List (DSL). The DSL is an inventory of approximately 23,000 substances manufactured, imported or used in Canada on a commercial scale. Substances not appearing on the DSL are considered to be new to Canada and are subject to notification.[2] |
| **China** | C.I. Pigment Violet 29 is on the non-confidential Inventory of Existing Chemical Substances Produced or Imported in China (IECSC). The inventory was last updated on January 31, 2013.[3] There are no restrictions associated with being on the Chinese inventory. |

[1] Australian Government. National Industrial Chemicals Notification and Assessment Scheme. Accessed March 14, 2017. https://www.nicnas.gov.au/search/chemical?id=1189.

[2] Government of Canada. Environment and Climate Change Canada. Search Engine for Chemicals and Polymers. Accessed March 14, 2017. http://www.ec.gc.ca/lcpe-cepa/eng/substance/chemicals_polymers.cfm.

[3] Chemical Inspection & Regulation Service. The Inventory of Existing Chemical Substance in China – IECSC (2013 and updates). April 20, 2016. Accessed October 11, 2017. http://www.cirs-reach.com/news-and-articles/the-inventory-of-existing-chemical-substance-in-china-iecsc-2013-and-updates.html.

| Country/Organization | Requirements and Restrictions |
|---|---|
| **European Union** | C.I. Pigment Violet 29 is on the European Inventory of Existing Commercial Chemical Substances (EINECS) List, which includes chemical substances deemed to be on the European Community market between January 1, 1971 and September 18, 1981.[4] Based on information provided in the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) dossier, C.I. Pigment Violet 29 is not classified as a hazard on the Classification and Labelling list. |
| **Japan** | In accordance with the provisions of Chemical Substances Control Law, C.I. Pigment Violet 29 is exempt from the new chemical notification requirement and listed as Low Molecular Heterocyclic Organic Compound on the existing chemical substances list.[5] |
| **Korea** | C.I. Pigment Violet 29 is on the Korea Existing Chemicals Inventory because it is a chemical that was domestically commercialized prior to February 2, 1991 and was designated and published by the Minister of Environment in consultation with the Minister of Labor.[6] There are no restrictions associated with being on the Korean inventory. |
| **New Zealand** | C.I. Pigment Violet 29 was added to the New Zealand Inventory (NZloC) on January 12, 2006 with the approval status that it may be used as a component in a product covered by a group standard, but it is not approved for use as a chemical in its own right. There are no restrictions or exclusions associated with C.I. Pigment Violet 29.[7] |
| **Philippines** | C.I. Pigment is on the Philippines Inventory of Chemicals and Chemical Substances (PICCS). PICCS was developed to provide government, industry and the public with a core inventory of all existing chemicals and chemical substances in the country and is updated annually.[8] There are no restrictions associated with being on the Philipino inventory. |

[4] ChemSafetyPRO. EU Chemical Inventory: EINECS, ELINCS and NLP. January 18, 2017. Accessed March 14, 2017. http://www.chemsafetypro.com/Topics/EU/EU_Chemical_Inventory_EINECS_ELINCS_NLP.html.

[5] NITE Chemical Risk Information Platform (NITE-CHRIP). Accessed March 14, 2017. http://www.nite.go.jp/en/chem/chrip/chrip_search/cmpInfDsp?cid=C010-529-04A&bcPtn=0&shMd=0&txNumSh=ODEtMzMtNA==&ltNumTp=1&txNmSh=&ltNmTp=&ltNmMh=1&txNmSh1=&ltNmTp1=&txNmSh2=&ltNmTp2=&txNmSh3=&ltNmTp3=&txMlSh=&ltMlMh=0&ltScDp=0&ltPgCtSt=100&rbDp=0&txScSML=&ltScTp=1&txUpScFl=null&hdUpScPh=&hdUpHash=&rbScMh=1&txScNyMh=&txMlWtSt=&txMlWtEd=&err

[6] Chemical Inspection & Regulation Service. Korea Existing Chemicals Inventory. December 20, 2016. Accessed October 11, 2017. http://www.cirs-reach.com/KoreaTCCA/Korea_Existing_Chemicals_Inventory_KECI.html.

[7] Environmental Protection Authority. Anthra[2,1,9-def:6,5,10-d'e'f']diisoquinoline-1,3,8,10(2H,9H)-tetrone. Accessed October 11, 2017. http://www.epa.govt.nz/search-databases/Pages/nzioc-details.aspx?SubstanceID=35898.

[8] Republic of the Philippines Chemical Management Section. Philippine Inventory of Chemicals and Chemical Substances. Accessed October 11, 2017. http://chemical.emb.gov.ph/?page_id=138.

| Country/Organization | Requirements and Restrictions |
|---|---|
| **Taiwan** | C.I. Pigment Violet 29 in on the National Existing Chemical Inventory in Taiwan. There are no restrictions associated with being on the Taiwanese inventory.[9] |
| **Vietnam** | C.I. Pigment Violet 29 is on the draft (March 2017) Vietnam National Existing Chemical Inventory. There are no restrictions associated with being on the Vietnamese inventory.[10] |

[9] Occupational Safety and Health Administration, Ministry of Labor. TCSI Search. Accessed October 11, 2017. https://csnn.osha.gov.tw/content/home/Substance_Result.aspx?enc=XpkoFr9qGvTvISX6V8jgsQ==.
[10] ChemSafetyPRO. Vietnam National Existing Chemical Inventory. October 28, 2016. Accessed October 11, 2017. http://www.chemsafetypro.com/Topics/Vietnam/Vietnam_National_Existing_Chemical_Inventory.html.

# Appendix B. LIST OF ON-TOPIC REFERENCES EXCLUDED FROM FURTHER CONSIDERATION

The following references were listed in their pertinent sections in the C.I. Pigment Violet 29 Bibliography document.

***Engineering/Occupational Exposure***

The following *on-topic* references were excluded from further consideration during a second title/abstract screening:


Guillermet, O; Mossoyan-Deneux, M; Giorgi, M; Glachant, A; Mossoyan, JC. (2006). Structural study of vapour phase deposited 3,4,9,10-perylene tetracarboxylicacid diimide: Comparison between single crystal and ultra thin films grown on Pt(100). Thin Solid Films. 514: 25-32. http://www.sciencedirect.com/science/article/pii/S0040609006002586.

Kozma, E; Catellani, M. (2013). Perylene diimides based materials for organic solar cells. Dyes and Pigments. 98: 160-179. http://www.sciencedirect.com/science/article/pii/S014372081300034X.

Ling, MM; Erk, P; Gomez, M; Koenemann, M; Locklin, J; Bao, Z. (2007). Air-stable n-channel organic semiconductors based on perylene diimide derivatives without strong electron withdrawing groups. Adv Mater Deerfield. 19: 1123-1127. http://onlinelibrary.wiley.com/doi/10.1002/adma.200601705/abstract.


***OPPT Risk Assessment, Problem Formulation or Scope Document***

The following *on-topic* references were excluded from further consideration during a second title/abstract screening because they pertain to pigments other than C.I. Pigment Violet 29:


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# Appendix C. PHYSICAL AND CHEMICAL PROPERTIES

**Table_Apx C-1**: Physical and Chemical Properties for C.I. Pigment Violet 29

| Test substance | Endpoint | Results | Name of test material/Analytical purity | Test Guideline/comments | Source |
|---|---|---|---|---|---|
| C.I. Pigment Violet 29 | Melting point | >400 °C | Paliogen Violet 5011 [a]/ >98-99% | OECD Guideline 102/No melting point found below 400 °C | (ECHA, 2017b) |
| C.I. Pigment Violet 29 | Vapor Pressure | <0 hPa at 20 °C | Paliogen Violet 5011/ >98-99% | OECD Guideline 104 | (ECHA, 2017b) |
| C.I. Pigment Violet 29 | Water Solubility | 0.01 mg/L at 20 °C | Paliogen Violet 5011/ >98-99% | OECD Guideline 105 | (ECHA, 2017b) |
| C.I. Pigment Violet 29 | Density | 1.584 g/cm$^3$ at 20 °C | Paliogen Violet 5011/ >98-99% | OECD Guideline 109/ relative density | (ECHA, 2017b) |
| C.I. Pigment Violet 29 | Octanol/water Partition Coefficient | <0.85 at 23 °C (measured) 3.76 (estimated) | Paliogen Violet 5011/ >98-99% | Calculated on the basis of the solubility in water and octanol determined experimentally | (ECHA, 2017b) (U.S. EPA, 2012b) |
| C.I. Pigment Violet 29 | Solubility in n-octanol | <0.07 mg/L at at 20 °C | Paliogen Violet 5011/ >98-99% | Not stated | (ECHA, 2017b), (BASF, 1998a) |

[a] BASF's trade name for C.I. Pigment Violet 29.

# Appendix D. ENVIRONMENTAL FATE STUDY SUMMARIES

**Table_Apx D-1:** Environmental Fate Studies for C.I. Pigment Violet 29

| Test substance | Study type | Endpoint | Description of test result/comments | Source |
|---|---|---|---|---|
| C.I. Pigment Violet 29 | OECD 301F -Biodegradability: Manometric Respirometry Test) | % Biodegradation | 0-10% (%BOD/ThOD) biodegradation after 28 days. | (ECHA, 2017b)<br><br>EPA has received the full study report from the data owner(s) and this report is under review |
| C.I. Pigment Violet 29 | OECD 305; Bioaccumulation; 8-weeks bioaccumulation study | Bioaccumulation factor (BCF and BAF) | No bioaccumulation from the 8-weeks bioaccumulation study. EPA EPI Suite estimate has similar result: low bioaccumulation (BCF=140; BAF=50) | Private data owner(s)<br><br>EPA has received the full study report from the data owner(s) and this report is under review |
| C.I. Pigment Violet 29 | OECD 209; Activated Sludge, Respiration inhibition test study | $EC_{20}$ and $EC_{50}$ | Has low toxicity to the activated sludge process in the receiving wastewater treatment plant ($EC_{20}$ ca.1.8 mg/L, EC50 ca. 6.5 mg/L). | Private data owner(s)<br><br>EPA has received the full study report from the data owner(s) and this report is under review |

# Appendix E. ENVIRONMENTAL HAZARD STUDY SUMMARIES

## E-1 Toxicity to Aquatic Organisms

### E-1-1 Aquatic Plant Toxicity

**Table_Apx E-1: Aquatic Plant Toxicity Study for C.I. Pigment Violet 29**

| Test substance | Study type | Species | Endpoint | Comments | Source |
|---|---|---|---|---|---|
| C.I. Pigment Violet 29 | OECD-201; Aquatic vascular plant: 7 days, static renewal | Duckweed (*Lemna gibba*) | NES (based on growth [frond number and dry weight]) | Nominal test concentrations: 0 (control), 1, 3.2, 10, 32, 100 mg/L based on loading<br><br>Measured test concentration: 0.007 mg/L (highest)<br><br>Test solution preparation: "The control and each test concentration was filtrated through a conditioned cellulose acetate membrane (Filter Sartorius, 0.20 µm pores). The concentrations 1.0 and 3.2 mg/L were prepared by dilution from the concentration 10.0 mg/L before the filtration. Before the dilution was made, the 10 mg/L concentration was checked carefully for homogeneous distribution of the test substance and for presence of precipitated test material. The test solution was clear and without precipitates. The test solution for the control was treated in the same way as the mixtures for the test concentrations: it was stirred for 72 hours, conditioned at 20 °C and was filtrated in the same way as the test concentrations to exclude any influences from the preparation of the test solutions. The preparation of the test solutions as described resulted in homogeneous solution, *i.e.*, Water | (ECHA, 2017b)<br><br>EPA has received the full study report from the data owner(s) and this report is under review |

| Test substance | Study type | Species | Endpoint | Comments | Source |
|---|---|---|---|---|---|
| | | | | Accommodated Fraction (WAF) which were used for exposure." (ECHA, 2017b)<br><br>Analytical measurements: "In fresh solutions the measured concentrations of test item were between 0.06 – 0.07 mg/L. The measured values did not correlate with the loading, which demonstrates that the measured concentrations were at the solubility limit in the test medium under test conditions. In 48 and 72 hour old solutions the concentration of test item was between 0.067 – 0.071 mg/L." (ECHA, 2017b) | |
| Abbreviation: NES = no effects at saturation | | | | | |

## E-1-2 Aquatic Invertebrate Toxicity

**Table_Apx E-2: Aquatic Invertebrate Toxicity Study for C.I. Pigment Violet 29**

| Test substance | Study type | Species | Endpoint | Comments | Source |
|---|---|---|---|---|---|
| C.I. Pigment Violet 29 | OECD-202; Acute freshwater invertebrate: 48 hours, static, limit | *Daphnia magna* | NES | Nominal test concentration: 0 (control), 100 mg/L<br><br>Measured test concentration: - (control), 0.0065 mg/L<br><br>Test solution preparation: "100.3 mg of test item was weighed into a glass flask and mixed with Elendt medium up to 1L. The stock solution was mixed thoroughly in an incubator at a temperature of 40 °C for 3 days with stirring resulting in a homogeneous, intensive grey mixture with a concentration of 100 mg/L. The stock solution was conditioned at a temperature of 20°C with continuous stirring. Next the control and the test concentration were filtered over a 0.20 µm membrane disc. After the filtration a clear and transparent solution was observed in the concentration of 100.0 mg/L. The filter was previously saturated with the test mixture." (ECHA, 2017b) | (ECHA, 2017b)<br><br>EPA has received the full study report from the data owner(s) and this report is under review |
| Abbreviation: NES = no effects at saturation | | | | | |

## E-1-3 Fish Toxicity

**Table_Apx E-3: Fish Toxicity Study for C.I. Pigment Violet 29**

| Test substance | Study type | Species | Endpoint | Comments | Source |
|---|---|---|---|---|---|
| C.I. Pigment Violet 29 | OECD-203; Acute freshwater fish: 96 hours, static | Zebrafish (*Brachydanio rerio*) | NES | Purity: >95%<br><br>Nominal test concentrations: 0 (control), 5000 mg/L<br><br>Test solution preparation: "The test substance was mixed with the test medium and homogenized using an ultra turrax. Evidence of undissolved material (e.g. precipitate, surface film, etc): floating particles of test substance were visible." (ECHA, 2017b) | (ECHA, 2017b)<br><br>EPA has received the full study report from the data owner(s) and this report is under review |
| Abbreviation: NES = no effects at saturation | | | | | |

# Appendix F. HUMAN HEALTH HAZARD STUDY SUMMARIES

## F-1 Acute Toxicity Studies

**Table_Apx F-1: Acute Toxicity Studies for C.I. Pigment Violet 29**

| Test substance | Study type | Species | Endpoint | Description of effects/comments | Source |
|---|---|---|---|---|---|
| C.I. Pigment Violet 29 | OECD-401; Acute oral, single dose by gavage, limit | Sprague-Dawley rat | $LD_{50}$ > 10,000 mg/kg-bw | No mortality or macroscopic abnormalities at necropsy; systemic dark red coloring of the skin and dark red coloring of the feces | (ECHA, 2017b)<br><br>EPA has received the full study report from the data owner(s) and this report is under review |
| C.I. Pigment Violet 29 | OECD 403-Acute Inhalation Toxicity | Wistar Rat | $LC_{50}$> 5.2 mg/L air | No mortality observed. Sublethal effects were irregular, accelerated and/or intermittent respiration, flight behaviour and discoloured fur. From day 7 of the observation period onward, no abnormalities, except discoloured fur, were detected in the animal | (ECHA, 2017b)<br><br>EPA has received the full study report from the data owner(s) and this report is under review |
| C.I. Pigment Violet 29 | OECD 402-Acute Dermal Toxicity | Sprague-Dawley Rat | $LD_{50}$ > 2,500 mg/kg-bw | No mortality, no abnormal findings, red-brown staining at the application site observed. | (ECHA, 2017b)<br><br>EPA has received the full study report from the data owner(s) and this report is under review |

## F-2 Repeated-Dose Toxicity Studies

There were no repeated-dose toxicity studies found for C.I. Pigment Violet 29.

## F-3 Reproductive and Developmental Toxicity Studies

**Table_Apx F-2: Reproductive and Developmental Study for C.I. Pigment Violet 29**

| Test substance | Study type | Species | Endpoint | Description of effects/comments | Source |
|---|---|---|---|---|---|
| C.I. Pigment Violet 29 | OECD-421; Reproductive/ developmental screening via gavage (exposure: premating period of 2 weeks and a mating period [max. of 2 weeks] in both sexes, approximately 1 week post-mating in males, and the entire gestation period as well as 4 days of lactation in females) | Wistar rat | NOAEL = 1000 mg/kg-bw/day (highest dose tested) | No test substance-related, adverse findings were noted; black discolored feces from study day 1 until the end of the study in all male and female animals at 300 mg/kg-bw/day and 1000 mg/kg-bw/day; macroscopically black discoloration of the content of the digestive tract in numerous animals | (ECHA, 2017b)<br><br>EPA has received the full study report from the data owner(s) and this report is under review |

## F-4 Skin Irritation and Sensitization Studies

**Table_Apx F-3: Skin Irritation and Sensitization Studies for C.I. Pigment Violet 29**

| Test substance | Study type | Species | Endpoint | Description of effects/comments | Source |
|---|---|---|---|---|---|
| C.I. Pigment Violet 29 | OECD- 404; Skin irritation: occlusive | Weiber Wiener rabbit | Not irritating | | (ECHA, 2017b)<br><br>EPA has received the full study reports from the data owner(s) and these reports are under review |
| C.I. Pigment Violet 29 | OECD-405; Eye irritation | Rabbit | Not irritating | | |
| C.I. Pigment Violet 29 | OECD- 404; Skin irritation: occlusive | Weiber Wiener rabbit | Not irritating | | |
| C.I. Pigment Violet 29 | OECD-405; Eye irritation | Weiber Wiener rabbit | Not irritating | | |
| C.I. Pigment Violet 29 | OECD-429; Skin sensitization: mouse local lymphocyte assay | Male CBA/Ca mouse | Negative | | |

## F-5 Genotoxicity and Cancer Studies

**Table_Apx F-4: Genotoxicity Studies for C.I. Pigment Violet 29**

| Test substance | Study type | Species | Endpoint | Description of effects/comments | Source |
|---|---|---|---|---|---|
| C.I. Pigment Violet 29 | OECD-471; Genotoxicity – gene mutation (*in vitro*) | *Salmonella typhimurium* TA 100, TA 1535, TA 1537, TA 1538, TA 98 and *E. coli* WP2uvrA | Negative | | (ECHA, 2017b), (BASF, 1998a) EPA has received the full study report from the data owner(s) and this report is under review |
| C.I. Pigment Violet 29 | OECD-476; Genotoxicity – gene mutation (*in vitro*) | Chinese hamster lung fibroblasts (V79) Target gene: HPRT | Negative | | (ECHA, 2017b) EPA has received the full study report from the data owner(s) and this report is under review |

# APPENDIX G. INCLUSION AND EXCLUSION CRITERIA FOR FULL TEXT SCREENING

As indicated in Section 1.2, the *Pigment Violet 29 (CASRN: 81-33-4) Bibliography: Supplemental File for the TSCA Scope Document* did not identify *on-topic* literature search results for C.I. Pigment Violet 29 (U.S. EPA, 2017a). The exceptions are those relevant studies on C.I. Pigment Violet 29 that were identified in the ECHA Database and the two studies from Food Additive Petition (FAP) 8B4626 (BASF, 1998a). The *Pigment Violet 29 (CASRN: 81-33-4) Bibliography: Supplemental File for the TSCA Scope Document* also identified twenty other references previously cited in OPPT's documents. Based on a comment received [(EPA-HQ-2016-0725-0039) (CPMA, 2017b)], EPA conducted a second title/abstract screening and determined that some of these references were not relevant to C.I. Pigment Violet 29. As such, with the exception of the ECHA and FAP studies, these references were excluded from further consideration for C.I. Pigment Violet 29.

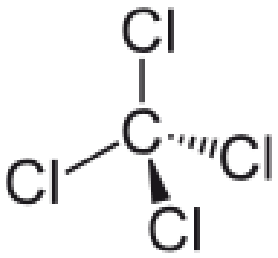
As no new *on topic references* were identified during problem formulation, EPA did not develop additional inclusion/exclusion criteria for C.I. Pigment Violet 29 to guide full text screening activities. EPA/OPPT's initial methods, approaches and procedures for identifying, compiling, and screening publicly available information supporting the TSCA risk evaluation for C.I. Pigment Violet 29 can be found in the *Strategy for Conducting Literature Searches for Pigment Violet 29 (PV29): Supplemental Document to the TSCA Scope Document*. If new information is received by the Agency after the publication of the TSCA Problem Formulation, EPA plans to use the initial eligibility criteria already published in the *Strategy for Conducting Literature Searches for Pigment Violet 29 (PV29): Supplemental Document to the TSCA Scope Document* to conduct the title and abstract screening. If necessary, EPA will make refinements to the inclusion and exclusion criteria and include them in the Risk Evaluation.

EPA Document# EPA-740-R1-7020
May 2018
Office of Chemical Safety and
Pollution Prevention

United States
Environmental Protection Agency

# Problem Formulation of the Risk Evaluation for Carbon Tetrachloride (Methane, Tetrachloro-)

## CASRN: 56-23-5




*May 2018*

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# ACKNOWLEDGMENTS

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**Docket**
Supporting information can be found in public docket: EPA-HQ-OPPT-2016-0733.

**Disclaimer**
Reference herein to any specific commercial products, process or service by trade name, trademark, manufacturer or otherwise does not constitute or imply its endorsement, recommendation or favoring by the U.S. Government.

# ABBREVIATIONS

| | |
|---|---|
| °C | Degrees Celsius |
| AAL | Allowable Ambient Levels |
| atm | Atmosphere(s) |
| ATSDR | Agency for Toxic Substances and Disease Registries |
| AWQC | Ambient Water Quality Criteria |
| BCF | Bioconcentration Factor |
| BUN | Blood Urea Nitrogen |
| CAA | Clean Air Act |
| CASRN | Chemical Abstract Service Registry Number |
| CBI | Confidential Business Information |
| CDR | Chemical Data Reporting |
| CEHD | Chemical Exposure Health Data |
| CERCLA | Comprehensive Environmental Response, Compensation and Liability Act |
| CFC | Chlorofluorocarbon |
| $cm^3$ | Cubic Centimeter(s) |
| CNS | Central Nervous System |
| COC | Concentration of Concern |
| CoRAP | Community Rolling Action Plan |
| CPSC | Consumer Product Safety Commission |
| $CS_2$ | Carbon Disulfide |
| CSATAM | Community-Scale Air Toxics Ambient Monitoring |
| CSCL | Chemical Substances Control Law |
| CYP450 | Cytochrome P450 |
| CWA | Clean Water Act |
| DNA | Deoxyribonucleic Acid |
| DT50 | Dissipation Time for 50% of the compound to dissipate |
| EC | European Commission |
| ECHA | European Chemicals Agency |
| EDC | Ethylene Dichloride |
| EPA | Environmental Protection Agency |
| EPCRA | Emergency Planning and Community Right-to-Know Act |
| ESD | Emission Scenario Document |
| EU | European Union |
| FDA | Food and Drug Administration |
| FFDCA | Federal Food, Drug and Cosmetic Act |
| FHSA | Federal Hazardous Substance Act |
| FIFRA | Federal Insecticide, Fungicide, and Rodenticide Act |
| g | Gram(s) |
| HAP | Hazardous Air Pollutant |
| HCFC | Hydrochlorofluorocarbons |
| HCl | Hydrochloric Acid |
| HFC | Hydrofluorocarbon |
| HFO | Hydrofluoroolefin |
| IDLH | Immediately Dangerous to Life and Health |
| IMAP | Inventory Multi-Tiered Assessment and Prioritisation |
| IRIS | Integrated Risk Information System |
| ISHA | Industrial Safety and Health Act |

| | |
|---|---|
| km | Kilometer(s) |
| L | Liter(s) |
| lb | Pound |
| log $K_{oc}$ | Logarithmic Soil Organic Carbon:Water Partitioning Coefficient |
| log $K_{ow}$ | Logarithmic Octanol:Water Partition Coefficient |
| $m^3$ | Cubic Meter(s) |
| MACT | Maximum Achievable Control Technology |
| MCL | Maximum Contaminant Level |
| MCLG | Maximum Contaminant Level Goal |
| mg | Milligram(s) |
| mmHg | Millimeter(s) of Mercury |
| MP | Montreal Protocol |
| mPa·s | Millipascal(s)-Second |
| NAICS | North American Industrial Classification System |
| NATA | National Air Toxics Assessment |
| NATTS | National Air Toxics Trends Stations |
| NEI | National Emissions Inventory |
| NESHAP | National Emission Standards |
| NHANES | National Health and Nutrition Examination Survey |
| NIOSH | National Institute of Occupational Safety and Health |
| NPDWR | National Primary Drinking Water Regulations |
| NTP | National Toxicology Program |
| NWQMC | National Water Quality Monitoring Council |
| OCSPP | Office of Chemical Safety and Pollution Prevention |
| ODS | Ozone Depleting Substance |
| OECD | Organisation for Economic Co-operation and Development |
| OELs | Occupational Exposure Limits |
| ONU | Occupational Non-Users |
| OPPT | Office of Pollution Prevention and Toxics |
| OSHA | Occupational Safety and Health Administration |
| OW | Office of Water |
| PCE | Perchloroethylene |
| PEL | Permissible Exposure Level |
| PESS | Potentially Exposed or Susceptible Subpopulations |
| POD | Point of Departure |
| POTW | Publicly Owned Treatment Works |
| ppm | Part(s) per Million |
| PDM | Probabilistic Dilution Model |
| QC | Quality Control |
| REACH | Registration, Evaluation, Authorisation and Restriction of Chemicals |
| RCRA | Resource Conservation and Recovery Act |
| RIE | Reactive Ion Etching |
| SDS | Safety Data Sheet |
| SDWA | Safe Drinking Water Act |
| SIAP | Screening Information Dataset Initial Assessment Profile |
| SIDS | Screening Information Dataset |
| STEL | Short-term Exposure Limit |
| STORET | STORage and RETrieval |

| | |
|---|---|
| SYR | Six-year Review |
| TCCR | Transparent, Clear, Consistent and Reasonable |
| TCLP | Toxicity Characteristic Leaching Procedure |
| TRI | Toxics Release Inventory |
| TSCA | Toxic Substances Control Act |
| TURA | Toxic Use Reduction Act |
| TWA | Time-Weighted Average |
| UATMP | Urban Air Toxics Monitoring Program |
| U.S. | United States |
| USGS | United States Geological Survey |
| VOC | Volatile Organic Compounds |
| WHO | World Health Organisation |
| WQP | Water Quality Portal |

# EXECUTIVE SUMMARY

TSCA § 6(b)(4) requires the U.S. Environmental Protection Agency (EPA) to establish a risk evaluation process. In performing risk evaluations for existing chemicals, EPA is directed to "determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of costs or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator under the conditions of use." In December of 2016, EPA published a list of 10 chemical substances that are the subject of the Agency's initial chemical risk evaluations (81 FR 91927), as required by TSCA § 6(b)(2)(A). Carbon tetrachloride was one of these chemicals.

TSCA § 6(b)(4)(D) requires that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use and potentially exposed or susceptible subpopulations (PESS) that the Administrator expects to consider. In June 2017, EPA published the Scope of the Risk Evaluation for carbon tetrachloride. As explained in the scope document, because there was insufficient time for EPA to provide an opportunity for comment on a draft of the scope, as EPA intends to do for future scope documents, EPA is now publishing and taking public comment on a problem formulation document to refine the current scope, as an additional interim step prior to publication of the draft risk evaluation for carbon tetrachloride. Comments on this problem formulation document will inform the development of the draft risk evaluation.

This problem formulation document refines the conditions of use, exposures and hazards presented in the scope of the risk evaluation for carbon tetrachloride and presents refined conceptual models and analysis plans that describe how EPA expects to evaluate the risk for carbon tetrachloride.

Carbon tetrachloride is a high production volume solvent. The Montreal Protocol and Title VI of the Clean Air Act (CAA) Amendments of 1990 led to a phase-out of carbon tetrachloride production in the United States for most non-feedstock domestic uses in 1996 and the Consumer Product Safety Commission (CPSC) banned the use of carbon tetrachloride in consumer products (excluding unavoidable residues not exceeding 10 ppm atmospheric concentration) in 1970. Currently, carbon tetrachloride is used as a feedstock in the production of hydrochlorofluorocarbons (HCFCs), hydrofluorocarbons (HFCs) and hydrofluoroolefins (HFOs). EPA has identified information on the regulated use of carbon tetrachloride as a process agent in the manufacturing of petrochemicals-derived and agricultural products and other chlorinated compounds such as chlorinated paraffins, chlorinated rubber and others that may be used downstream in the formulation of solvents for degreasing and cleaning, adhesives, sealants, paints, coatings, rubber, cement and asphalt formulations. The use of carbon tetrachloride for non-feedstock uses (i.e., process agent, laboratory chemical) is regulated in accordance with the Montreal Protocol.

Recent data on environmental releases from the Toxics Release Inventory (TRI), indicate that approximately 153,000 pounds of carbon tetrachloride were released to the environment in 2015. Most of the reported environmental releases for carbon tetrachloride were air emissions (fugitive and point source air emissions).

This document presents the potential exposures that may result from the conditions of use of carbon tetrachloride. Exposure may occur through inhalation and oral and dermal pathways, due to carbon tetrachloride's widespread presence in a variety of environmental media such as air, drinking water, groundwater, and surface water. Exposures to the general population may occur from industrial, and/or commercial uses; industrial releases to air, water or land; and other conditions of use. Workers and

occupational non-users (ONU) may be exposed to carbon tetrachloride during a variety of conditions of use, such as manufacturing, processing and industrial and commercial uses, including manufacturing of refrigerants and other chlorinated compounds. EPA expects that the highest exposures to carbon tetrachloride generally involve workers in industrial and commercial settings. EPA considers workers and ONU to be PESS. EPA will evaluate whether groups of individuals may be exposed via pathways that are distinct due to unique characteristics (e.g., life stage, behaviors, activities, duration) that increase exposure, and whether groups of individuals have heightened susceptibility, and should therefore be considered PESS for purposes of the risk evaluation.

Carbon tetrachloride has been the subject of numerous health hazard reviews including EPA's Integrated Risk Information System (IRIS) Toxicological Review and Agency for Toxic Substances and Disease Registry's (ATSDR's) Toxicological Profile. EPA plans to evaluate all potential hazards for carbon tetrachloride, including any found in recent literature. Human health hazards of carbon tetrachloride that have been identified by EPA previously include liver toxicity, renal toxicity and cancer. Carbon tetrachloride hazards to fish, aquatic invertebrates, aquatic plants, sediment invertebrates and amphibians have previously been assessed by EPA or other organizations.

The revised conceptual models presented in this problem formulation identify conditions of use; exposure pathways (e.g., media); exposure routes (e.g., inhalation, dermal, oral); PESS; and hazards EPA expects to consider in the risk evaluation. The initial conceptual models provided in the scope document were revised during problem formulation based on evaluation of reasonably available information for physical and chemical properties, fate, exposures, hazards, and conditions of use, and based upon consideration of other statutory and regulatory authorities. In each problem formulation document for the first 10 chemical substances, EPA also refined the activities, hazards, and exposure pathways that will be included in and excluded from the risk evaluation.

EPA's overall objectives in the risk evaluation process are to conduct timely, relevant, high-quality, and scientifically credible risk evaluations within the statutory deadlines, and to evaluate the conditions of use that raise greatest potential for risk.  82 FR 33726, 33728 (July 20, 2017).

# 1 INTRODUCTION

This document presents for comment the problem formulation of the risk evaluation to be conducted for carbon tetrachloride under the Frank R. Lautenberg Chemical Safety for the 21st Century Act. The Frank R. Lautenberg Chemical Safety for the 21st Century Act amended the Toxic Substances Control Act (TSCA), the Nation's primary chemicals management law, on June 22, 2016. The new law includes statutory requirements and deadlines for actions related to conducting risk evaluations of existing chemicals.

In December of 2016, EPA published a list of 10 chemical substances that are the subject of the Agency's initial chemical risk evaluations (81 FR 91927), as required by TSCA § 6(b)(2)(A). These 10 chemical substances were drawn from the 2014 update of EPA's TSCA Work Plan for Chemical Assessments, a list of chemicals that EPA identified in 2012 and updated in 2014 (currently totaling 90 chemicals) for further assessment under TSCA. EPA's designation of the first 10 chemical substances constituted the initiation of the risk evaluation process for each of these chemical substances, pursuant to the requirements of TSCA § 6(b)(4).

TSCA § 6(b)(4)(D) requires that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use and PESS that the Administrator expects to consider, within 6 months after the initiation of a risk evaluation. The scope documents for all first 10 chemical substances were issued on June 22, 2017. The first 10 problem formulation documents are a refinement of what was presented in the first 10 scope documents. TSCA § 6(b)(4)(D) does not distinguish between scoping and problem formulation, and requires EPA to issue scope documents that include information about the chemical substance, including the hazards, exposures, conditions of use, and the PESS that the Administrator expects to consider in the risk evaluation. In the future, EPA expects scoping and problem formulation to be completed prior to the issuance of scope documents and intends to issue scope documents that include problem formulation.

As explained in the scope document, because there was insufficient time for EPA to provide an opportunity for comment on a draft of the scope, as EPA intends to do for future scope documents, EPA is publishing and taking public comment on a problem formulation document to refine the current scope, as an additional interim step prior to publication of the draft risk evaluation for carbon tetrachloride. Comments received on this problem formulation document will inform development of the draft risk evaluation.

The Agency defines problem formulation as the analytical phase of the risk assessment in which "the purpose for the assessment is articulated, the problem is defined, and a plan for analyzing and characterizing risk is determined" (see Section 2.2 of the Framework for Human Health Risk Assessment to Inform Decision Making). The outcomes of problem formulation are a conceptual model(s) and an analysis plan. The conceptual model describes the linkages between stressors and adverse human health effects, including the stressor(s), exposure pathway(s), exposed life stage(s) and population(s), and endpoint(s) that will be addressed in the risk evaluation (U.S. EPA, 2014). The analysis plan follows the development of the conceptual model(s) and is intended to describe the approach for conducting the risk evaluation, including its design, methods and key inputs and intended outputs as described in the EPA Human Health Risk Assessment Framework (U.S. EPA, 2014). The problem formulation documents refine the initial conceptual models and analysis plans that were provided in the scope documents.

First, EPA has removed from the risk evaluation any activities and exposure pathways that EPA has concluded do not warrant inclusion in the risk evaluation. For example, for some activities that were listed as "conditions of use" in the scope document, EPA has insufficient information following the further investigations during problem formulation to find they are circumstances under which the chemical is actually "intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of."

Second, EPA also identified certain exposure pathways that are under the jurisdiction of regulatory programs and associated analytical processes carried out under other EPA-administered environmental statutes – namely, the Clean Air Act (CAA), the Safe Drinking Water Act (SDWA), the Clean Water Act (CWA), and the Resource Conservation and Recovery Act (RCRA) – and which EPA does not expect to include in the risk evaluation.

As a general matter, EPA believes that certain programs under other Federal environmental laws adequately assess and effectively manage the risks for the covered exposure pathways. To use Agency resources efficiently under the TSCA program, to avoid duplicating efforts taken pursuant to other Agency programs, to maximize scientific and analytical efforts, and to meet the three-year statutory deadline, EPA is planning to exercise its discretion under TSCA 6(b)(4)(D) to focus its analytical efforts on exposures that are likely to present the greatest concern and consequently merit a risk evaluation under TSCA, by excluding, on a case-by-case basis, certain exposure pathways that fall under the jurisdiction of other EPA-administered statutes.[1] EPA does not expect to include any such excluded pathways as further explained below in the risk evaluation. The provisions of various EPA-administered environmental statutes and their implementing regulations represent the judgment of Congress and the Administrator, respectively, as to the degree of health and environmental risk reduction that is sufficient under the various environmental statutes.

Third, EPA identified any conditions of use, hazards, or exposure pathways which were included in the scope document and that EPA expects to include in the risk evaluation but which EPA does not expect to further analyze in the risk evaluation. EPA expects to be able to reach conclusions about particular conditions of use, hazards or exposure pathways without further analysis and therefore plans to conduct no further analysis on those conditions of use, hazards or exposure pathways in order to focus the Agency's resources on more extensive or quantitative analyses. Each risk evaluation will be "fit-for-purpose," meaning not all conditions of use will warrant the same level of evaluation and the Agency may be able to reach some conclusions without comprehensive or quantitative risk evaluations. 82 FR 33726, 33734, 33739 (July 20, 2017).

EPA received comments on the published scope document for carbon tetrachloride and has considered the comments specific to carbon tetrachloride in this problem formulation document. EPA is soliciting public comment on this problem formulation document and when the draft risk evaluation is issued the Agency intends to respond to comments that are submitted. In its draft risk evaluation, EPA may revise the conclusions and approaches contained in this problem formulations, including the conditions of use and pathways covered and the conceptual models and analysis plans, based on comments received.

[1] As explained in the final rule for chemical risk evaluation procedures, "EPA may, on a case-by case basis, exclude certain activities that EPA has determined to be conditions of use in order to focus its analytical efforts on those exposures that are likely to present the greatest concern, and consequently merit an unreasonable risk determination." [82 FR 33726, 33729 (July 20, 2017)]

## 1.1 Regulatory History

EPA conducted a search of existing domestic and international laws, regulations and assessments pertaining to carbon tetrachloride. EPA compiled this summary from data available from federal, state, international and other government sources, as cited in Appendix A. EPA evaluated and considered the impact of existing laws and regulations (e.g., regulations on landfill disposal, design, and operations) in the problem formulation step to determine what, if any, further analysis might be necessary as part of the risk evaluation. Consideration of the nexus between these existing regulations and TSCA conditions of use may additionally be made as detailed/specific conditions of use and exposure scenarios are developed in conducting the analysis phase of the risk evaluation.

***Federal Laws and Regulations***

Carbon tetrachloride is subject to federal statutes or regulations, other than TSCA, that are implemented by other offices within EPA and/or other federal agencies/departments. A summary of federal laws, regulations and implementing authorities is provided in Appendix A.

***State Laws and Regulations***

Carbon tetrachloride is subject to state statutes or regulations implemented by state agencies or departments. A summary of state laws, regulations and implementing authorities is provided in Appendix A.

***Laws and Regulations in Other Countries and International Treaties or Agreements***

Carbon tetrachloride is subject to statutes or regulations in countries other than the United States and/or international treaties and/or agreements. A summary of these laws, regulations, treaties and/or agreements is provided in Appendix A.

## 1.2 Assessment History

EPA has identified assessments conducted by other EPA Programs and other organizations (see Table 1-1). Depending on the source, these assessments may include information on conditions of use, hazards, exposures and PESS. Table 1-1 shows the assessments that have been conducted. EPA found an additional assessment for carbon tetrachloride by the National Industrial Chemicals Notification and Assessment Scheme (Australia) during the problem formulation and the assessment history table has been updated accordingly.

In addition to using this information, EPA intends to conduct a full review of the relevant data/information collected in the initial comprehensive search (see *Carbon tetrachloride (CASRN 56-23-5) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0733) following the literature search and screening strategies documented in the *Strategy for Conducting Literature Searches for Carbon Tetrachloride: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0733. This will ensure that EPA considers data/information that has been made available since these assessments were conducted.

**Table 1-1. Assessment History of Carbon Tetrachloride**

| Authoring Organization | Assessment |
|---|---|
| **EPA assessments** | |
| U.S. EPA, Office of Water (OW) | Update of Human Health Ambient Water Quality Criteria: Carbon Tetrachloride 56-23-5, EPA-HQ-OW-2014-0135-0182 (2015b) |
| U.S. EPA, Integrated Risk Information System (IRIS) | Toxicological Review of Carbon Tetrachloride In Support of Summary Information on IRIS (2010) |
| U.S. EPA, Office of Drinking Water | Carbon Tetrachloride Health Advisory, Office of Drinking Water US Environmental Protection Agency (1987) |
| **Other U.S.-based organizations** | |
| Agency for Toxic Substances and Disease Registry (ATSDR) | Toxicological Profile for Carbon Tetrachloride (2005) |
| California Environment Protection Agency, Office of Environmental Health Hazard Assessment | Public Health Goal for Carbon Tetrachloride (2000) |
| **International** | |
| Health Canada | Guidelines for Canadian Drinking Water Quality, Guideline Technical Document, Carbon Tetrachloride (2010) |
| Organisation for Economic Co-operation and Development's Screening Information Dataset (OECD SIDS), Co-CAM, 10-12 | SIDS SIAP for Carbon Tetrachloride (2011) |
| World Health Organisation (WHO) | Carbon Tetrachloride in Drinking Water, Background document for development of WHO Guidelines for Drinking -water Quality (2004) |
| National Industrial Chemicals Notification and Assessment Scheme (Australia) | Environment Tier II Assessment for Methane, Tetrachloro- (2017, last update) |

## 1.3 Data and Information Collection

EPA/OPPT generally applies a systematic review process and workflow that includes: (1) data collection; (2) data evaluation; and (3) data integration of the scientific data used in risk evaluations developed under TSCA. Scientific analysis is often iterative in nature as new knowledge is obtained. Hence, EPA/OPPT expects that multiple refinements regarding data collection may occur during the process of risk evaluation.

***Data Collection: Data Search***

EPA/OPPT conducted chemical-specific searches for data and information on: physical and chemical properties; environmental fate and transport; conditions of use information; environmental exposures, human exposures, including potentially exposed or susceptible subpopulations (PESS) identified by virtue of greater exposure; ecological hazard; and human health hazard, including PESS identified by virtue of greater susceptibility.

EPA/OPPT designed its initial data search to be broad enough to capture a comprehensive set of sources containing data and/or information potentially relevant to the risk evaluation. Generally, the search was not limited by date and was conducted on a wide range of data sources, including but not limited to: peer-reviewed literature and gray literature (e.g., publicly-available industry reports, trade association resources, government reports). When available, EPA/OPPT relied on the search strategies from recent assessments, such as EPA IRIS assessments and the National Toxicology Program's (NTP) *Report on Carcinogens*, to identify relevant references and supplemented these searches to identify relevant information published after the end date of the previous search to capture more recent literature. The *Strategy for Conducting Literature Searches for Carbon Tetrachloride: Supplemental File for the TSCA Scope Document,* EPA-HQ-OPPT-2016-0733 provides details about the data sources and search terms that were used in the initial search.

***Data Collection: Data Screening***

Following the data search, references were screened and categorized using selection criteria outlined in the *Strategy for Conducting Literature Searches for Carbon Tetrachloride*: *Supplemental File for the TSCA Scope Document,* EPA-HQ-OPPT-2016-0733. Titles and abstracts were screened against the criteria as a first step with the goal of identifying a smaller subset of the relevant data to move into the subsequent data extraction and data evaluation steps. Prior to full-text review, EPA/OPPT anticipates refinements to the search and screening strategies, as informed by an evaluation of the performance of the initial title/abstract screening and categorization process.

The categorization scheme (or tagging structure) used for data screening varies by scientific discipline (i.e., physical and chemical properties; environmental fate and transport; use/conditions of use information; human and environmental exposures, including PESS identified by virtue of greater exposure; human health hazard, including PESS identified by virtue of greater susceptibility; and ecological hazard). However, within each data set, there are two broad categories or data tags: (1) o*n-topic* references or (2) *off-topic* references. *On-topic* references are those that may contain data and/or information relevant to the risk evaluation. O*ff-topic* references are those that do not appear to contain data or information relevant to the risk evaluation. The *Strategy for Conducting Literature Searches for Carbon Tetrachloride: Supplemental File for the TSCA Scope Document,* EPA-HQ-OPPT-2016-0733 discusses the inclusion and exclusion criteria that EPA/OPPT used to categorize references as *on-topic* or *off-topic*.

Additional data screening using sub-categories (or sub-tags) was also performed to facilitate further sorting of data/information - for example, identifying references by source type (e.g., published peer-reviewed journal article, government report); data type (e.g., primary data, review article); human health hazard (e.g., liver toxicity, cancer, reproductive toxicity); or chemical-specific and use-specific data or information. These sub-categories are described in the supplemental document, *Strategy for Conducting Literature Searches for Carbon Tetrachloride: Supplemental File for the TSCA Scope Document,* EPA-HQ-OPPT-2016-0733 and will be used to organize the different streams of data during the stages of data evaluation and data integration steps of systematic review.

Results of the initial search and categorization can be found in the *Carbon tetrachloride (CASRN 56-23-5) Bibliography: Supplemental File for the TSCA Scope Document,* EPA-HQ-OPPT-2016-0733. This document provides a comprehensive list (bibliography) of the sources of data identified by the initial search and the initial categorization for *on-topic* and *off-topic* references. Because systematic review is an iterative process, EPA/OPPT expects that some references may move from the *on-topic* to the *off-*

*topic* categories, and vice versa. Moreover, targeted supplemental searches may also be conducted to address specific needs for the analysis phase (e.g., to locate specific data needed for modeling); hence, additional *on-topic* references not initially identified in the initial search may be identified as the systematic review process proceeds.

## 1.4 Data Screening During Problem Formulation

EPA/OPPT is in the process of completing the full text screening of the on-topic references identified in the *Carbon tetrachloride (CASRN 56-23-5) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0733. Details about the screening process at the full-text level are provided in the *Application of Systematic Review in TSCA Risk Evaluations* document (U.S. EPA, 2018). Appendix H provides the inclusion and exclusion criteria applied at the full text screening. Since full text screening commenced right after the publication of the TSCA Scope document, the criteria were set to be broad to capture relevant information that would support the risk evaluation. Thus, the inclusion and exclusion criteria for full text screening do not reflect the refinements to the conceptual model and analysis plan resulting from problem formulation. As part of the iterative process, EPA is in the process of refining the results of the full text screening to incorporate the changes in information/data needs to support the risk evaluation.

These refinements include changes to the inclusion and exclusion criteria to better support the risk evaluation and will likely reduce the number of data/information sources that will undergo evaluation.

Following the screening process, the quality of the included studies will be assessed using the evaluation strategies that are described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018). EPA/OPPT is in the process of completing the full text screening of the on-topic references identified in the *Carbon tetrachloride (CASRN 56-23-5) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0733. Details about the screening process and criteria at the full-text level are provided in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018). Following the screening process, the quality of the included studies will be assessed using the evaluation strategies that are described in the supplemental document on systematic review.

A review of the *on topic* human health references after the title and abstract screening revealed a large number of animal studies that were likely to be of limited use for the following reasons: (1) The aim of the study was to induce a disease state in an animal (e.g., cirrhosis, fibrosis, organ damage: liver, kidney, testes and others) rather than evaluate the effects of carbon tetrachloride exposure in animals and/or (2) Exposure was via injection. In order to refine the search results for full-text screening, the inclusion/exclusion criteria were revised to remove these studies from the “on topic” pool. Appendix B describes the process used to re-screen the references identified as “on topic” in the first screening round, including prioritizing the literature for screening and the re-categorization criteria applied during the re-screening and tagging.

# 2 PROBLEM FORMULATION

As required by TSCA, the scope of the risk evaluation identifies the conditions of use, hazards, exposures and PESS that the Administrator expects to consider. To communicate and visually convey the relationships between these components, EPA included in the scope document an initial life cycle diagram and initial conceptual models that describe the actual or potential relationships between carbon tetrachloride and human and ecological receptors. During the problem formulation, EPA has revised the life cycle diagram and conceptual models based on further data gathering and analysis as presented in this problem formulation document. A revised analysis plan is also included, which identifies, to the extent feasible, the approaches and methods that EPA may use to assess exposures, effects (hazards) and risks under the conditions of use of carbon tetrachloride.

## 2.1 Physical and Chemical Properties

Physical-chemical properties influence the environmental behavior and the toxic properties of a chemical, thereby informing the potential conditions of use, exposure pathways and routes and hazards that EPA intends to consider. For scope development, EPA considered the measured or estimated physical-chemical properties set forth in Table 2-1; EPA found no additional information during problem formulation that would change these values.

**Table 2-1. Physical and Chemical Properties of Carbon Tetrachloride**

| Property | Value [a] | References |
|---|---|---|
| Molecular formula | $CCl_4$ | |
| Molecular weight | 153.82 | |
| Physical form | Colorless liquid, sweet, aromatic and ethereal odor resembling chloroform | (Merck, 1996); (U.S. Coast Guard, 1985) |
| Melting point | -23°C | (Lide, 1999) |
| Boiling point | 76.8°C | (Lide, 1999) |
| Density | 1.46 g/cm$^3$ at 20°C | (Boublík et al., 1984) |
| Vapor pressure | 115 mm Hg at 25°C | (Lide, 1999) |
| Vapor density | 5.32 (relative to air) | (Boublík et al., 1984) |
| Water solubility | 793 mg/L at 25°C | (Horvath, 1982) |
| Octanol:water partition coefficient (log $K_{ow}$) | 2.83[b] | (Hansch et al., 1995) |
| Henry's Law constant | 0.0276 atm m$^3$/mole | (Leighton and Calo, 1981) |
| Flash point | None | (U.S. Coast Guard, 1985) |
| Autoflammability | Not readily available | |
| Viscosity | 2.03 mPa·s at -23°C | (Daubert and Danner, 1989) |
| Refractive index | 1.4607 at 20°C | (Merck, 1996) |

| Property | Value [a] | References |
|---|---|---|
| Diaelectric constant | 2.24 at 20°C | (Norbert and Dean, 1967) |
| [a] Measured unless otherwise noted. [b] Estimated value based on modeling | | |

## 2.2 Conditions of Use

TSCA § 3(4) defines the conditions of use as ‘‘the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of.’’

### 2.2.1 Data and Information Sources

In the scope documents, EPA identified, based on reasonably available information, the conditions of use for the subject chemicals. As further described in the document, EPA searched a number of available data sources (e.g., *Use and Market Profile for Carbon Tetrachloride*, EPA-HQ-OPPT-2016-0733). Based on this search, EPA published a preliminary list of information and sources related to chemical conditions of use (see *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: Carbon Tetrachloride*, EPA-HQ-OPPT-2016-0733-0003) prior to a February 2017 public meeting on scoping efforts for risk evaluations convened to solicit comment and input from the public. EPA also convened meetings with companies, industry groups, chemical users and other stakeholders to aid in identifying conditions of use and verifying conditions of use identified by EPA. The information and input received from the public and stakeholder meetings and public comments has been incorporated into this problem formulation document to the extent appropriate, as indicated in Table 2-3. Thus, EPA believes the identified manufacture, processing, distribution, use and disposal activities constitute the intended, known, and reasonably foreseeable activities associated with the subject chemical, based on reasonably available information.

### 2.2.2 Identification of Conditions of Use

To determine the current conditions of use of carbon tetrachloride and inversely, activities that do not qualify as conditions of use, EPA conducted extensive research and outreach. This included EPA’s review of published literature and online databases including the most recent data available from EPA’s Chemical Data Reporting program (CDR) and Safety Data Sheets (SDSs). EPA also reviewed Montreal Protocol’s (MP) directives and related reports (WCRP, 2016) with information on domestic and international regulation and monitoring of carbon tetrachloride use and emissions. EPA also received comments on the Scope of the Risk Evaluation for carbon tetrachloride (U.S. EPA, 2017e) that were used to determine the conditions of use. In addition, EPA convened meetings with companies, industry groups, chemical users, states, environmental groups, and other stakeholders to aid in identifying conditions of use and verifying conditions of use identified by EPA.

EPA has removed from the risk evaluation any activities that EPA has concluded do not constitute conditions of use – for example, because EPA has insufficient information to find certain activities are circumstances under which the chemical is actually “intended, known, or reasonably foreseen to be manufactured processed, distributed in commerce, used, or disposed of.” EPA has also identified any conditions of use that EPA does not expect to include in the risk evaluation. As explained in the final rule for Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act, TSCA section 6(b)(4)(D) requires EPA to identify "the hazards, exposures, conditions of use, and the PESS that the Administrator expects to consider in a risk evaluation," suggesting that EPA may exclude certain activities that EPA has determined to be conditions of use on a case-by-case basis. (82 FR 33736, 33729; July 20, 2017). For example, EPA may exclude conditions of use that the Agency has sufficient

basis to conclude would present only de minimis exposures or otherwise insignificant risks (such as use in a closed system that effectively precludes exposure or use as an intermediate).

The activities that EPA no longer believes are conditions of use or that were otherwise excluded during problem formulation are described in Section 2.2.2.1. The conditions of use included in the scope of the risk evaluation are summarized in Section 2.2.2.2.

#### 2.2.2.1 Categories and Subcategories Determined Not to be Conditions of Use or Otherwise Excluded During Problem Formulation

For carbon tetrachloride, EPA has conducted public outreach and literature searches to collect information about carbon tetrachloride's conditions of use and has reviewed reasonably available information obtained or possessed by EPA concerning activities associated with carbon tetrachloride. As a result of that analysis, EPA has identified activities not currently associated with carbon tetrachloride and therefore determined not to be conditions of use. In addition, there are conditions of use for which EPA has sufficient basis to conclude would present only de minimis exposures or otherwise insignificant risks and that do not warrant further evaluation. Consequently, EPA will not consider or evaluate these activities and conditions of use or associated hazards or exposures in the risk evaluation for carbon tetrachloride. These activities and conditions of use consist of incorporation of carbon tetrachloride into an article (activity that is not a condition of use), and industrial/commercial/consumer uses of carbon tetrachloride in commercially available aerosol and non-aerosol adhesives/sealants, paints/coatings, and cleaning/degreasing solvent products (conditions of use with de minimis exposure).

Domestic production and importation of carbon tetrachloride is currently prohibited under regulations implementing the Montreal Protocol (MP) and CAA Title VI, except when transformed (used and entirely consumed, except for trace quantities, in the manufacture of other chemicals for commercial purposes), destroyed (including destruction after use as a catalyst or stabilizer), or used for essential laboratory and analytical uses. *See* 40 CFR Part 82; *see also* 60 FR 24970, 24971 (May 10, 1995). Based on information obtained by EPA, there are no approved consumer uses for carbon tetrachloride. There are current regulatory actions that prohibit the direct use of carbon tetrachloride as reactant or additive in the formulation of commercially available products for industrial/commercial/consumer uses (including aerosol and non-aerosol adhesives/sealants, paints/coatings, and cleaning/degreasing solvent products), besides as a laboratory chemical. The use of carbon tetrachloride (and mixtures containing it) in household products has also been banned by CPSC since 1970, with the exception of "unavoidable manufacturing residues of carbon tetrachloride in other chemicals that under reasonably foreseen conditions of use do not result in an atmospheric concentration of carbon tetrachloride greater than 10 parts per million." 16 CFR 1500.17(a)(2).

The domestic and international use of carbon tetrachloride as a process agent is addressed under the Montreal Protocol (MP) side agreement, Decision X/14: Process Agents (UNEP/Ozone Secretariat, 1998). This decision lists a limited number of specific manufacturing uses of carbon tetrachloride as a process agent (non-feedstock use) in which carbon tetrachloride may not be destroyed in the production process. Based on the process agent applications, carbon tetrachloride is used in the manufacturing of other chlorinated compounds that may be subsequently added to commercially available products (i.e., solvents for cleaning/degreasing, adhesives/sealants, and paints/coatings). Given the high volatility of carbon tetrachloride and the extent of reaction and efficacy of the separation/purification process for purifying final products, EPA expects insignificant or unmeasurable concentrations of carbon tetrachloride in the manufactured chlorinated substances in the commercially available products. In its regulations on the protection of stratospheric ozone at 40 CFR part 82, EPA excludes from the definition of controlled substance the inadvertent or coincidental creation of insignificant quantities of a listed

substance (including carbon tetrachloride) resulting from the substance's use as a process agent (40 CFR 82.3). These expectations and current regulations are consistent with public comments received by EPA, EPA-HQ-OPPT-2016-0733-0005 and EPA-HQ-OPPT-2016-0733-0017, stating that carbon tetrachloride may be present in a limited number of industrial products with chlorinated ingredients at a concentration of less than 0.003% by weight.

Based on the information identified by EPA, carbon tetrachloride is not a direct reactant or additive in the formulation of solvents for cleaning and degreasing, adhesives and sealants or paints and coatings. Because industrial, commercial, and consumer use of such products (solvents for cleaning/degreasing, adhesives/sealants, and paints/coatings) would present only de minimis exposure or otherwise insignificant risk, EPA has determined that these conditions of use do not warrant evaluation, and EPA does not expect to consider or evaluate these conditions of use or associated hazards or exposures in the risk evaluation for carbon tetrachloride. Based on information obtained by EPA and the household products ban at 16 CFR 1500.17(a)(2), there are no other approved consumer uses for carbon tetrachloride. Therefore, as a general matter, EPA does not expect to analyze consumer exposures or associated hazards in the risk evaluation for carbon tetrachloride, and accordingly the initial conceptual model for consumer activities and uses presented in the Scope of the Risk Evaluation for Carbon Tetrachloride (U.S. EPA, 2017e) does not appear in this problem formulation document.

In addition, EPA has determined that there is insufficient information to support the classification of one activity which was identified as a "condition of use" in the Scope document. TSCA defines a chemical's "conditions of use" as "the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of." 15 USC 2602(4). As explained in the final rule for Procedures for Chemical Risk Evaluation under the Amended Toxic Substances Control Act, TSCA grants EPA discretion to determine the circumstances that are appropriately considered to be "conditions of use." 82 FR at 33729. As noted above, EPA has conducted public outreach and literature searches to collect information about carbon tetrachloride's conditions of use and has reviewed reasonably available information obtained or possessed by EPA concerning activities associated with carbon tetrachloride. As a result of that analysis, EPA has determined there is insufficient information to support a finding that one activity which was listed as a condition of use in the Scope document for carbon tetrachloride actually constitutes a circumstance under which carbon tetrachloride "is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of." This activity consists of incorporation into articles. Incorporation into an article refers to processing in which the chemical becomes an integral component of an article (as defined at 40 CFR 704.3) that is distributed for industrial, trade or consumer use. EPA has not identified information during problem formulation indicating that carbon tetrachloride is incorporated into articles (see EPA-HQ-OPPT-2016-0733-0003). Consequently, EPA will not consider or evaluate incorporation into articles, or any associated hazards or exposures, in the risk evaluation for carbon tetrachloride.

**Table 2-2. Categories and Subcategories Determined Not to be Conditions of Use or Otherwise Excluded During Problem Formulation**

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| Processing | Processing-Incorporation into Article | Incorporation into Article | (U.S. EPA, 2016b)<br>* not confirmed as a current use |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| Industrial/commercial/ consumer use | Solvents for Cleaning and Degreasing | Machinery cleaning | Use document, EPA-HQ-OPPT-2016-0733-0003;<br>Public comment, EPAHQ-OPPT-2016-07330011<br>* de minimis exposure. |
| | | Textile cleaning | Use document, EPA-HQhttps://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0733-0003OPPT-2016-0733-0003<br>* de minimis exposure |
| | | Brake cleaning | Use document, EPA-HQhttps://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0733-0003OPPT-2016-0733-0003<br>* de minimis exposure |
| | Adhesives and Sealants | Rubber cement | Use document, EPA-HQhttps://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0733-0003OPPT-2016-0733-0003<br>* de minimis exposure |
| | | Arts and crafts | Use document, EPA-HQ-OPPT-2016-0733-0003;<br>Public comment, EPAHQ-OPPT-2016-07330015<br>* de minimis exposure |
| | | Asphalt | Use document, EPA-HQhttps://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0733-0003OPPT-2016-0733-0003<br>* de minimis exposure |
| | | Industrial adhesives | Use document, EPA-HQ-OPPT-2016-0733-0003;<br>Public comments, EPA-HQ-OPPT-2016-0733-0011, EPA-HQ-OPPT2016-0733-0012, and EPA-HQ-OPPT-20160733-0015<br>* de minimis exposure |
| | Paints and Coatings | Paints and coatings | Use document, EPA-HQhttps://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0733-0003OPPT-2016-0733-0003<br>* de minimis exposure |

#### 2.2.2.2 Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation

Table 2-3 summarizes each life cycle stage and the corresponding categories and subcategories of conditions of use for carbon tetrachloride that EPA expects to consider in the risk evaluation. Using the 2016 CDR, EPA identified industrial processing or use activities, industrial function categories and commercial and consumer use product categories. EPA identified the subcategories by supplementing CDR data with other published literature and information obtained through stakeholder consultations. For risk evaluations, EPA intends to consider each life cycle stage (and corresponding use categories and subcategories) and assess relevant potential sources of release and human exposure associated with that life cycle stage. Beyond the uses identified in the Scope of the Risk Evaluation for carbon tetrachloride (U.S. EPA, 2017e), EPA has received no additional information identifying additional current conditions of use for carbon tetrachloride from public comment and stakeholder meetings.

**Table 2-3. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation**

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| Manufacture | Domestic Manufacture | Domestic manufacture | (U.S. EPA, 2016b) |
| | Import | Import | (U.S. EPA, 2016b) |
| Processing | Processing as a Reactant/ Intermediate | Hydrochlorofluorocarbons (HCFCs), Hydrofluorocarbon (HFCs) and Hydrofluoroolefin (HFOs) | Use document, EPA-HQ-OPPT-2016-0733-0003; Public comments, EPA-HQ-OPPT-2016-0733-0007, EPA-HQ-OPPT-2016-0733-0008, EPA-HQ-OPPT-2016-0733-0016 and EPA-HQ-OPPT-2016-0733-0064; (U.S. EPA, 2016b) |
| | | Perchloroethylene (PCE) | Use document, EPA-HQ-OPPT-2016-0733-0003; Public comments, EPA-HQ-OPPT-2016-0733-0007 and EPA-HQ-OPPT-2016-0733-0008; (U.S. EPA, 2016b) |
| | | Reactive ion etching (i.e., semiconductor manufacturing) | Use document, EPA-HQ-OPPT-2016-0733-0003; Public comment, EPA-HQ-OPPT-2016-0733-0063 |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| | Incorporation into Formulation, Mixture or Reaction Products | Petrochemicals-derived manufacturing; Agricultural products manufacturing; Other basic organic and inorganic chemical manufacturing. | (U.S. EPA, 2016b); Use document, EPA-HQ-OPPT-2016-0733-0003; (U.S. EPA, 2016a); (UNEP/Ozone Secretariat, 1998); Public comment, EPA-HQ-OPPT-2016-0733-0064 |
| | Processing - repackaging | Laboratory Chemicals | (U.S. EPA, 2016a) |
| | Recycling | Recycling | (U.S. EPA, 2016b), (U.S. EPA, 2016a) |
| Distribution in commerce | Distribution | Distribution in commerce | (U.S. EPA, 2016a); Use document, EPA-HQ-OPPT-2016-0733-0003. |
| Industrial/commercial use | Petrochemicals-derived Products Manufacturing | Processing aid | Use document, EPA-HQ-OPPT-2016-0733-0003; (U.S. EPA, 2016b); (UNEP/Ozone Secretariat, 1998) |
| | | Additive | Use document, EPA-HQ-OPPT-2016-0733-0003; Public comment, EPA-HQ-OPPT-2016-0733-0012; (U.S. EPA, 2016a); (UNEP/Ozone Secretariat, 1998) |
| | Agricultural Products Manufacturing | Processing aid | (U.S. EPA, 2016b), Use document, EPA-HQ-OPPT-2016-0733-0003; Public comments, EPA-HQ-OPPT-2016-0733-0007 and EPA-HQ-OPPT-2016-0733-0008; (UNEP/Ozone Secretariat, 1998) |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| | Other Basic Organic and Inorganic Chemical Manufacturing | Manufacturing of chlorinated compounds used in solvents for cleaning and degreasing | Use document, EPA-HQ-OPPT-2016-0733-0003; Public comments, EPA-HQ-OPPT-2016-0733-0011, EPA-HQ-OPPT-2016-0733-0012 and EPA-HQ-OPPT-2016-0733-0015; (UNEP/Ozone Secretariat, 1998) |
| | | Manufacturing of chlorinated compounds used in adhesives and sealants | Use document, EPA-HQ-OPPT-2016-0733-0003; Public comments, EPA-HQ-OPPT-2016-0733-0011, EPA-HQ-OPPT-2016-0733-0024, EPA-HQ-OPPT-2016-0733-0012, and EPA-HQ-OPPT-2016-0733-0015; (UNEP/Ozone Secretariat, 1998) |
| | | Manufacturing of chlorinated compounds used in paints and coatings | Use document, EPA-HQ-OPPT-2016-0733-0003 Public comment, EPA-HQ-OPPT-2016-0733-0024; (UNEP/Ozone Secretariat, 1998) |
| | | Manufacturing of inorganic chlorinated compounds (i.e., elimination of nitrogen trichloride in the production of chlorine and caustic) | Public comment, EPA-HQ-OPPT-2016-0733-0027; (UNEP/Ozone Secretariat, 1998) |
| | | Manufacturing of chlorinated compounds used in asphalt | Use document, EPA-HQ-OPPT-2016-0733-0003; (UNEP/Ozone Secretariat, 1998) |
| | | Manufacturing of Pharmaceuticals | (UNEP/Ozone Secretariat, 1998) |
| | Other Uses | Processing aid (i.e., metal recovery). | Use document, EPA-HQ-OPPT-2016-0733-0003 |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| | | Specialty uses (i.e., aerospace industry) | Public comment, EPA-HQ-OPPT-2016-0733-0063 |
| | Laboratory Chemicals | Laboratory chemical | Use document, EPA-HQ-OPPT-2016-0733-0003; (U.S. EPA, 2016b), Public comments, EPA-HQ-OPPT-2016-0733-0007; EPA-HQ-OPPT-2016-0733-0013 and EPA-HQ-OPPT-2016-0733-0063 |
| Disposal | Disposal | Industrial pre-treatment | U.S. EPA, 2017d |
| | | Industrial wastewater treatment | U.S. EPA, 2017d |
| | | Publicly owned treatment works (POTW) | U.S. EPA, 2017d |
| | | Underground injection | U.S. EPA, 2017d |
| | | Municipal landfill | U.S. EPA, 2017d |
| | | Hazardous landfill | U.S. EPA, 2017d |
| | | Other land disposal | U.S. EPA, 2017d |
| | | Municipal waste incinerator | U.S. EPA, 2017d |
| | | Hazardous waste incinerator | U.S. EPA, 2017d |
| | | Off-site waste transfer | U.S. EPA, 2017d |

[a] These categories of conditions of use appear in the Life Cycle Diagram, reflect CDR codes and broadly represent conditions of use of carbon tetrachloride in industrial and/or commercial settings.
[b] These subcategories reflect more specific uses of carbon tetrachloride.

#### 2.2.2.3 Overview of Conditions of Use and Lifecycle Diagram

The life cycle diagram provided in Figure 2-1 depicts the conditions of use that are considered within the scope of the risk evaluation during various life cycle stages including manufacturing, processing, use (industrial, commercial), distribution and disposal. Additions or changes to conditions of use based on additional information gathered or analyzed during problem formulation were described in Sections 2.2.2.1 and 2.2.2.2. The activities that EPA determined are out of scope during problem formulation are not included in the life cycle diagram. The information is grouped according to CDR processing codes and use categories (including functional use codes for industrial uses and product categories for industrial, commercial and consumer uses), in combination with other data sources (e.g., published literature and consultation with stakeholders), to provide an overview of conditions of use. EPA notes that some subcategories of use may be grouped under multiple CDR categories.

Use categories include the following: "industrial use" means use at a site at which one or more chemicals or mixtures are manufactured (including imported) or processed. "Commercial use" means the use of a chemical or a mixture containing a chemical (including as part of an article) in a commercial enterprise providing saleable goods or services (U.S. EPA, 2016b). This information has not changed from that provided in the Scope Document.

To understand conditions of use relative to one another and associated potential exposures under those conditions of use, the life cycle diagram includes the production volume associated with each stage of the life cycle, as reported in the 2016 CDR (U.S. EPA, 2017c, 2016b), when the volume was not claimed confidential business information (CBI). The 2016 CDR reporting data for carbon tetrachloride are provided in Table 2-4 for carbon tetrachloride from EPA's CDR database (U.S. EPA, 2017c).

**Table 2-4. Production Volume of Carbon Tetrachloride in Chemical Data Reporting (CDR) Reporting Period (2012 to 2015) [a]**

| Reporting Year | 2012 | 2013 | 2014 | 2015 |
|---|---|---|---|---|
| Total Aggregate Production Volume (lbs) | 129,145,698 | 116,658,281 | 138,951,153 | 142,582,067 |

[a] (U.S. EPA, 2017c). Internal communication. The CDR data for the 2016 reporting period is available via ChemView (https://java.epa.gov/chemview) (U.S. EPA, 2016b). Because of an ongoing CBI substantiation process required by amended TSCA, the CDR data available in the problem formulation is more specific than currently in ChemView.

Due to CBI claims in the 2016 CDR, EPA cannot provide the volumes associated with most life cycle stages (U.S. EPA, 2016b). Activities related to distribution (e.g., loading, unloading) will be considered throughout the carbon tetrachloride life cycle, rather than using a single distribution scenario.

Descriptions of the industrial or commercial use categories identified from the 2016 CDR are summarized below and included in the life cycle diagram (Figure 2-1). The descriptions provide a brief overview of the use category and Appendix C contains more detailed descriptions (e.g., process descriptions, worker activities, process flow diagrams, equipment illustrations) for each manufacture, processing, use and disposal category. The descriptions provided below are primarily based on the corresponding industrial function category and/or commercial product category descriptions from the 2016 CDR and can be found in EPA's *Instructions for Reporting 2016 TSCA Chemical Data Reporting* (U.S. EPA, 2016a).

The "**Petrochemicals-derived and Agricultural Products Manufacturing**" category encompasses chemical substances used for a variety of purposes at petrochemicals-derived and agricultural products manufacturing sites. This category includes the use of carbon tetrachloride as a process agent (i.e., processing aid for catalyst regeneration) in uses listed in the MP side agreement, Decision X/14: Process Agents, including manufacture of chlorosulphonated polyolefin, manufacture of styrene butadiene rubber, manufacture of endosulphan (insecticide), production of tralomethrine (insecticide), manufacture of 1-1, Bis (4-chlorophenyl) 2,2,2- trichloroethanol (dicofol insecticide) (see Appendix D).

The "**Other Basic Organic and Inorganic Chemical Manufacturing**" category encompasses chemical substances used to facilitate the manufacturing or production of a particular chemical. Process agents are not feedstocks, and may not be destroyed in a production process. Use of carbon tetrachloride as a process agent is specifically listed under the MP side agreement, Decision X/14: Process Agents. This category includes the use of carbon tetrachloride in the manufacturing of pharmaceuticals (i.e.,

ibuprofen) and the manufacturing of chlorinated compounds that are subsequently used in the formulation of solvents for cleaning and degreasing, adhesives and sealants and paints and coatings. The process agent applications of carbon tetrachloride as a process agent include manufacturing of chlorinated paraffins (e.g., plasticizer in rubber, paints, adhesives, sealants, plastics) and chlorinated rubber (e.g., additive in paints, adhesives). The category also includes the use of carbon tetrachloride in the manufacturing of inorganic chlorinated compounds, such as the use of carbon tetrachloride in the production of chlorine and caustic.

Figure 2-1 depicts the life cycle diagram of carbon tetrachloride from manufacture to the point of disposal. Activities related to distribution (e.g., loading, unloading) will be considered throughout the life cycle, rather than using a single distribution scenario.

As reflected in the life cycle diagram, intended, known and reasonably foreseen uses of carbon tetrachloride are primarily associated with industrial and commercial activities. As explained above, the Montreal Protocol and Title VI of the Clean Air Act (CAA) Amendments of 1990 led to a phase-out of carbon tetrachloride production in the United States for most non-feedstock domestic uses in 1996 and the CPSC banned the use of carbon tetrachloride in consumer products (excluding unavoidable residues not exceeding 10 ppm atmospheric concentration) in 1970.

EPA has identified use as a feedstock (Processing as Reactant/Intermediate) as the main use for carbon tetrachloride. However, there are other industrial/commercial uses that may still exist including: solvent for laboratory procedures (i.e., extraction solvent), and process agent in the manufacturing of petrochemicals-derived and agricultural products, and in the manufacturing of chlorinated compounds to be used in the formulation of solvents for degreasing and cleaning, in adhesives, sealants, paints, coatings, rubber cement and asphalt formulations [EPA-HQ-OPPT-2016-0733-0003 (U.S. EPA, 2017d)].

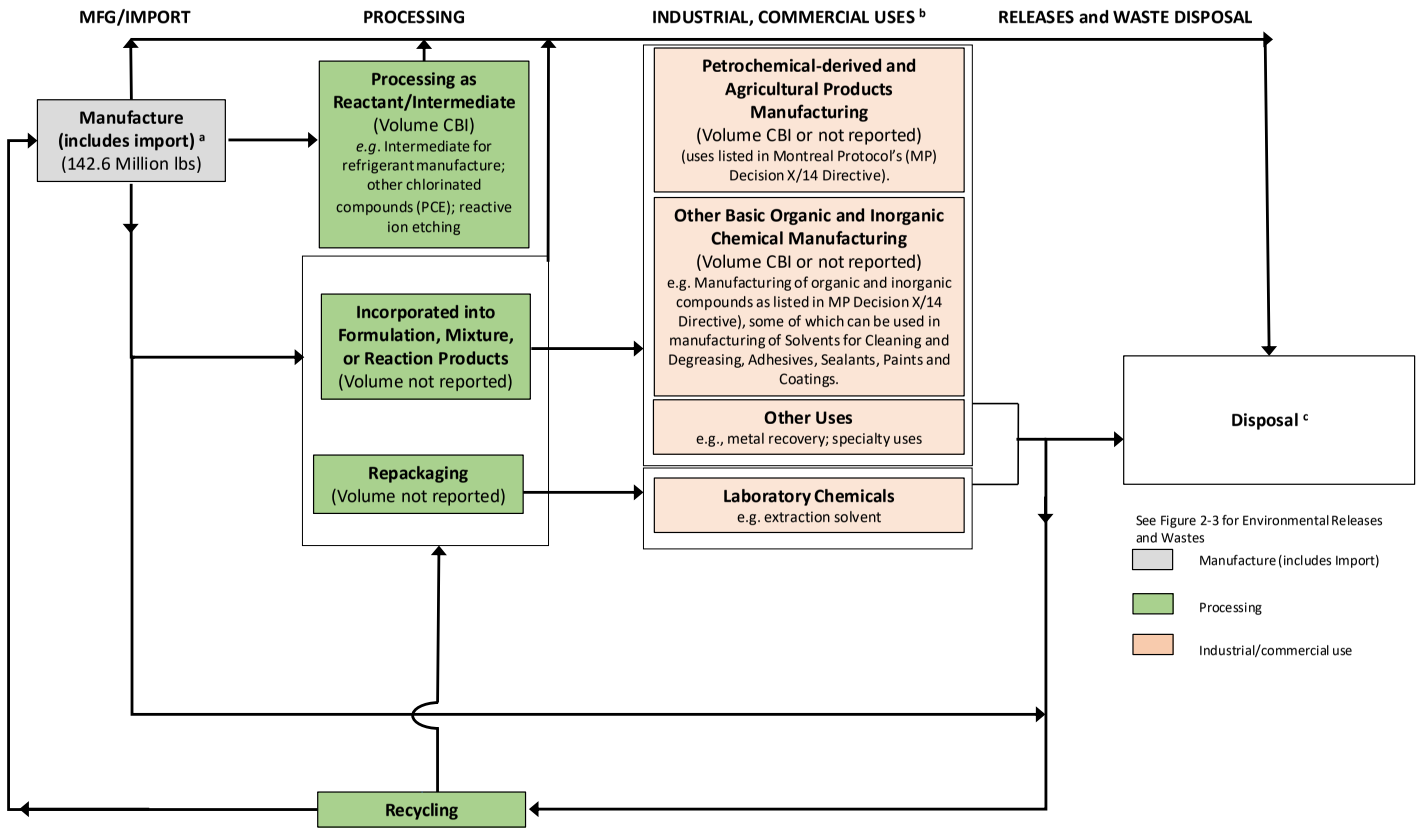


**Figure 2-1. Carbon Tetrachloride Life Cycle Diagram**

The life cycle diagram depicts the conditions of use that are within the scope of the risk evaluation during various life cycle stages including manufacturing, processing, use (industrial or commercial), distribution and disposal. The production volumes shown are for reporting year 2015 from the 2016 CDR reporting period (U.S. EPA, 2016b). Activities related to distribution (e.g., loading, unloading) will be considered throughout the carbon tetrachloride life cycle, rather than using a single distribution scenario.

[a] Due to CBI claims, EPA cannot differentiate between manufacturing and import sites.

[b] See Table 2-3 for additional uses not mentioned specifically in this diagram.

[c] Disposal refers to all of the following activities - Industrial pre-treatment, Industrial wastewater treatment, Publicly owned treatment works (POTW), Underground injection, Municipal landfill, Hazardous landfill, Other land disposal, Municipal waste incinerator, Hazardous waste incinerator, Off-site waste transfer

## 2.3 Exposures

For TSCA exposure assessments, EPA expects to evaluate exposures and releases to the environment resulting from the conditions of use applicable to carbon tetrachloride. Post-release pathways and routes will be described to characterize the relationship or connection between the conditions of use for carbon tetrachloride and the exposure to human receptors, including PESS, and ecological receptors. EPA will take into account, where relevant, the duration, intensity (concentration), frequency and number of exposures in characterizing exposures to carbon tetrachloride.

### 2.3.1 Fate and Transport

Environmental fate includes both transport and transformation processes. Environmental transport is the movement of the chemical within and between environmental media. Transformation occurs through the degradation or reaction of the chemical with other species in the environment. Hence, knowledge of the environmental fate of the chemical informs the determination of the specific exposure pathways and potential human and environmental receptors EPA expects to consider in the risk evaluation. Table 2-5 provides environmental fate data that EPA identified and considered in developing the scope for carbon tetrachloride. This information has not changed from that provided in the scope document.

During problem formulation, EPA considered volatilization during wastewater treatment, volatilization from lakes and rivers followed by upward diffusion in the troposphere, biodegradation rates, and soil organic carbon:water partition coefficient (log $K_{OC}$) were used when making changes, as described in Section 2.5 to the conceptual models. Systematic literature review is currently underway, so model results and basic principles were used to support the fate data used in problem formulation.

EPI Suite™ (U.S. EPA, 2012a) modules were used to predict volatilization of carbon tetrachloride from wastewater treatment plants, lakes, and rivers. The EPI Suite™ module that estimates chemical removal in sewage treatment plants ("STP" module) was run using default settings to evaluate the potential for carbon tetrachloride to volatilize to air or adsorb to sludge during wastewater treatment. The STP module estimates that about 90% of carbon tetrachloride in wastewater will be removed by volatilization and 2% by adsorption.

The EPI Suite™ module that estimates volatilization from lakes and rivers ("Volatilization" module) was run using default settings to evaluate the volatilization half-life of carbon tetrachloride in surface water. The volatilization module estimates that the half-life of carbon tetrachloride in a model river will be about 1.3 hours and the half-life in a model lake will be about 5 days.

The EPI Suite™ module that predicts biodegradation rates ("BIOWIN" module) was run using default settings to estimate biodegradation rates of carbon tetrachloride under aerobic conditions. Three of the models built into the BIOWIN module (BIOWIN 1, 2 and 6) estimate that carbon tetrachloride will not rapidly biodegrade in aerobic environments. These results support the biodegradation data presented in the scope document for carbon tetrachloride, which demonstrate limited biodegradation under aerobic conditions. However, BIOWIN 5 shows moderate biodegradation under aerobic conditions. On the other hand, the model that estimates anaerobic biodegradation (BIOWIN 7) predicts that carbon tetrachloride will biodegrade moderately under anaerobic conditions. Further, previous assessments of carbon

tetrachloride found that aerobic biodegradation was very slow and anaerobic biodegradation was moderate to rapid (ECHA, 2012; OECD, 2011; ATSDR, 2005; CalEPA, 2000).

Conversely, previous assessment of carbon tetrachloride by HSDB found rapid biodegradation in aerobic aquatic conditions (NLM, 2003). This may be largely due to fact that carbon tetrachloride exhibits toxicity to aquatic microorganisms in concentrations higher than 10 mg/L. In water, under aerobic conditions, a negative result has been reported for a ready biodegradability test according to OECD TG 301C MITI (I) (Ministry of International Trade and Industry, Japan) test method, toxicity to aerobic bacteria may have prevented biodegradation due to the high concentration used in this test (ECHA, 2012).

Based on the available environmental fate data, carbon tetrachloride is likely to biodegrade slowly under aerobic conditions with pathways that are environment- and microbial population-dependent. Anaerobic degradation has been observed to be faster than aerobic degradation under some conditions with acclimated microbial populations. Anaerobic biodegradation is expected to be a significant degradation mechanism in soil and ground water.

The log $K_{OC}$ reported in the carbon tetrachloride scoping document were measured values in the range of 1.69 – 2.16, while the estimated value range using EPI Suite™ is 1.6 – 2.5. These values are supported by the basic principles of environmental chemistry which states that the $K_{OC}$ is typically within one order of magnitude (one log unit) of the octanol:water partition coefficient ($K_{OW}$). Indeed, the log $K_{OW}$ reported for carbon tetrachloride in Table 2-1 is a measured value of 2.83, which is within the expected range. Further, the $K_{OC}$ could be approximately one order of magnitude larger than predicted by EPI Suite™ before sorption would be expected to significantly impact the mobility of carbon tetrachloride in groundwater. The log $K_{OC}$ and log $K_{OW}$ reported in previous assessments of carbon tetrachloride were in the range of 1.69 – 2.16 and 2.64 – 2.83 respectively [(ECHA, 2012; OECD, 2011; ATSDR, 2005)], and these values are associated with low sorption to soil and sediment.

**Table 2-5. Environmental Fate Characteristics of Carbon Tetrachloride**

| Property or Endpoint | Value [a] | References |
|---|---|---|
| Direct photodegradation | Minutes (atmospheric-stratospheric) | (OECD, 2011) |
| Indirect photodegradation | >330 years (atmospheric) | (OECD, 2011) |
| Hydrolysis half-life | 7000 years at 1 ppm | (OECD, 2011) |
| Biodegradation | 6 to 12 months (soil)[b]<br><br>7 days to 12 months (aerobic water, based on multiple studies)<br><br>3 days to 4 weeks (anaerobic water, based on multiple studies) | (OECD, 2011)<br>(ECHA, 2012)<br>(ATSDR, 2005)<br>(NLM, 2003) |
| Bioconcentration factor (BCF) | 30 bluegill sunfish<br>40 rainbow trout | (OECD, 2011) |
| Bioaccumulation factor (BAF) | 19 (estimated) | (U.S. EPA, 2012a) |
| Soil organic carbon:water partition coefficient (log $K_{oc}$) | 1.69-2.16 | (ECHA, 2012) |
| | 2.06 (weighted mean of two soils-silt loam and sandy loam) | (OECD, 2011) |

[a] Measured unless otherwise noted. [b] This figure (6 to 12 months) represents a half-life estimate based on the estimated aqueous aerobic biodegradation half-life of carbon tetrachloride.

Carbon tetrachloride shows minimal susceptibility to indirect photolysis by hydroxyl radicals in the troposphere, where its estimated tropospheric half-life exceeds 330 years. Ultimately, carbon tetrachloride diffuses upward into the stratosphere where it is photodegraded to form the trichloromethyl radical and chlorine atoms (OECD, 2011). Carbon tetrachloride is efficiently degraded by direct photolysis under stratospheric conditions and the $DT_{50}$ (Dissipation Time for 50% of the compound to dissipate) value is in the order of minutes. However, the troposphere to the stratosphere migration of carbon tetrachloride is very long and this migration time limits the dissipation. The rate of photodegradation increases at altitudes >20 km and beyond.

Carbon tetrachloride dissolved in water does not photodegrade or oxidize in any measurable amounts, with a calculated hydrolysis half-life of 7,000 years based on experimental data at a concentration of 1 ppm (OECD, 2011). Removal mechanisms from water could include volatilization due to the Henry's law constant and anaerobic degradation in subsurface environment.

Estimated and measured BCF and BAF values ranging from 19 – 40 indicates that carbon tetrachloride has low bioaccumulation potential in fish (U.S. EPA, 2012a; OECD, 2011).

### 2.3.2 Releases to the Environment

Releases to the environment from conditions of use (e.g., industrial and commercial processes) are one component of potential exposure and may be derived from reported data that are obtained through direct measurement, calculations based on empirical data and/or assumptions and models.

Under the Emergency Planning and Community Right-to-Know Act (EPCRA) Section 313 rule, carbon tetrachloride is a Toxics Release Inventory (TRI)-reportable substance effective January 1, 1987 (see Appendix A.1). EPA expects to consider data reported under the TRI program for evaluating exposure to carbon tetrachloride.

Table 2-6 provides production-related waste managed data (also referred to as waste managed) for carbon tetrachloride reported by industrial facilities to the TRI program for 2015 (U.S. EPA, 2017f). Table 2-7 provides more detailed information on the quantities released to air or water or disposed of on land.

**Table 2-6. Summary of Carbon Tetrachloride TRI Production-Related Waste Managed in 2015 (lbs)**

| Number of Facilities | Recycling | Energy Recovery | Treatment | Releases [a,b] | Total Production Related Waste |
|---|---|---|---|---|---|
| 47 | 5,954,066 | 5,638,154 | 15,196,739 | 151,690 | 26,940,648 |

Data source: 2015 TRI Data (updated March 2017) (U.S. EPA, 2017f).
[a] Terminology used in these columns may not match the more detailed data element names used in the TRI public data and analysis access points.
[b] Does not include releases due to one-time event not associated with production such as remedial actions or earthquakes.

Facilities are required to report if they manufacture (including import) or process more than 25,000 pounds of carbon tetrachloride, or if they otherwise use more than 10,000 pounds of carbon tetrachloride. In 2015, 47 facilities reported a total of 27 million pounds of carbon tetrachloride waste managed. Of this total, nearly 6 million pounds were recycled, 5.6 million pounds were recovered for energy, 15 million pounds were treated, and almost 152 thousand pounds were released into the environment.

Of these releases, the largest releases of nearly 105 thousand pounds were to air (fugitive and point source air emissions), a little under 500 pounds were released to water (surface water discharges), 50 thousand pounds were released to land (of which disposal to Resource Conservation and Recovery Act (RCRA) Subtitle C landfills is the primary disposal method), and under 200 pounds were released in other forms such as indefinite storage. Carbon tetrachloride migration to groundwater from RCRA Subtitle C landfills regulated by the state/local jurisdictions will likely be mitigated by landfill design (double liner, leachate capture) and requirements to adsorb liquids onto solid adsorbant and containerize prior to disposal.

**Table 2-7. Summary of Carbon Tetrachloride Toxics Release Inventory (TRI) Releases to the Environment in 2015 (lbs)**

| | | Air Releases | | | Land Releases | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Number of Facilities | Stack Air Releases | Fugitive Air Releases | Water Releases | Class I Under-ground Injection | RCRA Subtitle C Landfills | All other Land Disposal [a,b] | Other Releases [a] | Total Releases [c] |
| Subtotal | | 69,897 | 34,941 | | 19,608 | 27,300 | 401 | | |
| Totals | 47 | 104,838 | | 468 | 47,309 | | | 164 | 152,780 |

Data source: 2015 TRI Data (updated March 2017) (U.S. EPA, 2017f)
[a] Terminology used in these columns may not match the more detailed data element names used in the TRI public data and analysis access points.

| | Number of Facilities | Air Releases | | Water Releases | Land Releases | | | Other Releases [a] | Total Releases [c] |
|---|---|---|---|---|---|---|---|---|---|
| | | Stack Air Releases | Fugitive Air Releases | | Class I Under-ground Injection | RCRA Subtitle C Landfills | All other Land Disposal [a,b] | | |

[b] Upon further evaluation of these reports of other land disposal releases, it was found that the reports consist of misreported disposal values. The incorrect code uses or waste identification were used in the reports. Therefore these 401 lbs of released waste do not consist of carbon tetrachloride waste released by other land disposal.
[c] These release quantities do include releases due to one-time events not associated with production such as remedial actions or earthquakes.

While production-related waste managed shown in Table 2-6 excludes any quantities reported as catastrophic or one-time releases (TRI section 8 data), release quantities shown in Table 2-7 include both production-related and non-routine quantities (TRI section 5 and 6 data). As a result, release quantities may differ slightly and may further reflect differences in TRI calculation methods for reported release range estimates (U.S. EPA, 2016a).

During problem formulation, EPA further analyzed the TRI data and examined the definitions of elements in the TRI data to determine the level of confidence that a carbon tetrachloride release would result from other types of land disposal, as reported in Table 2-7, given that carbon tetrachloride waste is regulated as a hazardous waste under RCRA. In 2015, three facilities reported the disposal of a combined total of 401 lbs of carbon tetrachloride through *other land disposal.* Upon further investigation of these reports, EPA has found that these facilities used an incorrect TRI code during reporting or that the disposed waste did not actually consist of carbon tetrachloride waste. These incorrectly reported values cannot be removed from the TRI database until the facilities submit the corresponding revision reports. However, these uncorrected reports are not considered relevant for the purposes of this problem formulation.

### 2.3.3 Presence in the Environment and Biota

Monitoring studies or a collection of relevant and reliable monitoring studies provide(s) information that can be used in an exposure assessment. Monitoring studies that measure environmental concentrations or concentrations of chemical substances in biota provide evidence of exposure.

Monitoring and biomonitoring data were identified in EPA's data search for carbon tetrachloride. Though carbon tetrachloride's use has significantly decreased from a peak in the 1970's, its long half-life and previous ubiquitous use and disposal has resulted in the continued presence in various environmental media (ATSDR, 2005). Carbon tetrachloride is listed as a Hazardous Air Pollutant (HAP) and is included in several multi-year monitoring programs, with data collected across the nation in both urban and rural locations (U.S. EPA, 2017b, 1996). For example, carbon tetrachloride is included in all three ambient air monitoring programs, collectively known as the National Monitoring Programs: National Air Toxics Trends Stations (NATTS) network, Community-Scale Air Toxics Ambient Monitoring (CSATAM) Program and Urban Air Toxics Monitoring Program (UATMP). NATTS sites are based on preliminary air toxics programs such as the 1996 National Air Toxics Assessment (NATA).

According to the 2015 National Air Toxics Inventory, ambient air monitoring trends from 2003 to 2013 have shown that of the eight HAP monitored, only carbon tetrachloride average concentrations have slightly increased in the atmosphere over the 10-year period. This is likely primarily due to its extremely long half-life in the troposphere (U.S. EPA, 2015a).

Carbon tetrachloride is specifically regulated under the Safe Drinking Water Act (SDWA). Therefore, under the National Primary Drinking Water Regulations, carbon tetrachloride is designated as a volatile organic compound (VOC) contaminant and is monitored in drinking water (U.S. EPA, 2009). Nationally representative drinking water monitoring data are available through EPA's SDWA compliance monitoring. SDWA requires EPA to review each national primary drinking water regulation at least once every six years and revise as necessary. As part of the "Six-Year Review (SYR)," EPA evaluates any newly available data, information and technologies to determine if any regulatory revisions are needed. Internal analysis for SYR3 (2006-2011) data, not yet published, show that 118 systems of 55,735 systems (0.212%) have mean concentrations greater than the Minimum Reporting Level (MRL) of 0.5 µg/L. SYR 2 (1998-2005) data showed 650 systems or 1.289% of 50,446 systems had detects greater than 0.5 µg/L. Of those, over 75% of the detections were in groundwater (versus surface water systems). In addition, only 57 (0.113%) systems had detects of carbon tetrachloride greater than the Maximum Contaminant Level (MCL) of 5 µg/L. During SYR 2, EPA's Office of Water (OW) determined the Estimated Quantitation Level (EQL) to be 0.5 ug/L, which is the threshold for determining if the occurrence data showed a meaningful opportunity to improve health protection. The basis for the SYR 2 EQL for carbon tetrachloride is the modal MRL reported for each sample in the SYR 2 ICR dataset (https://wcms.epa.gov/dwsixyearreview/six-year-review-3-compliance-monitoring-data-2006-2011).

The U.S. Geological Survey (USGS) monitors organic compounds in ground water and has detected carbon tetrachloride in community water systems (USGS, 2007). EPA provides the public with storage and retrieval (STORET) data that maps monitoring sites and allows for download of sampling data of surface water monitoring sites. These data are searchable via the Water Quality Portal (WQP), a cooperative service sponsored by the USGS, the EPA and the National Water Quality Monitoring Council (NWQMC) (NWQMC, 2017). The portal contains data collected by over 400 state, federal, tribal and local agencies.

Biomonitoring data on carbon tetrachloride are collected in the National Health and Nutrition Examination Survey (NHANES) (CDC, 2017).

### 2.3.4 Environmental Exposures

The manufacturing, processing, use and disposal of carbon tetrachloride can result in releases to the environment. In this section, EPA presents exposures to aquatic and terrestrial organisms.

***Aquatic Environmental Exposures***

During problem formulation, EPA modeled industrial discharges to surface water to estimate surface water concentration using TRI and EPA NPDES permit Discharge Monitoring Report (DMR) data on the top 10 highest carbon tetrachloride releasing facilities. EPA used the Probabilistic Dilution Model (PDM) within E-FAST to estimate annual discharges for the facilities. In order to estimate a range of conservative surface water concentrations, the 2015 NPDES DMR data reporting carbon tetrachloride discharges were used as a high-end range of possible release days (i.e., 20 and 250 days/year) allowing the estimation of conservative carbon tetrachloride surface water concentrations (i.e., conservative exposure scenarios). Appendix E presents the first-tier estimate of surface water concentrations.

***Terrestrial Environmental Exposures***

Terrestrial species populations living near industrial and commercial facilities using carbon tetrachloride may be exposed to the chemical through environmental media. Terrestrial species populations living near industrial and commercial facilities using carbon tetrachloride may be exposed via multiple routes

such as ingestion of surface waters and inhalation of outdoor air. As described in Section 2.3.3 carbon tetrachloride is present and measurable through monitoring in a variety of environmental media including ambient air, surface water and ground water

### 2.3.5 Human Exposures

In this section, EPA presents occupational, consumer and general population exposures. Subpopulations, including PESS, within these exposed groups are also presented.

#### 2.3.5.1 Occupational Exposures

Exposure pathways and exposure routes are listed below for worker activities under the various conditions of use described in Section 2.2. In addition, exposures to occupational non-users (ONU), who do not directly handle the chemical but perform work in an area where the chemical is present, are listed. Engineering controls and/or personal protective equipment may impact the occupational exposure levels.

Workers and ONU may be exposed to carbon tetrachloride when performing activities associated with the conditions of use described in Section 2.2, including, but not limited to:

- Unloading and transferring carbon tetrachloride to and from storage containers to process vessels.
- Using carbon tetrachloride in process equipment.
- Cleaning and maintaining equipment.
- Sampling chemical, formulations or products containing carbon tetrachloride for quality control (QC).
- Repackaging chemical, formulations or products containing carbon tetrachloride.
- Handling, transporting and disposing waste containing carbon tetrachloride.
- Use of carbon tetrachloride in laboratories.
- Performing other work activities in or near areas where carbon tetrachloride is used.

Based on these activities, EPA will analyze inhalation exposure to vapor and mists. Dermal exposure, including skin contact with liquids and vapors for workers will also be analyzed. ONU would not intentionally handle liquids containing carbon tetrachloride, therefore, dermal exposure will not be analyzed further in the risk evaluation for ONU. The risk evaluation will not further analyze potential worker exposure through mists that deposit in the upper respiratory tract and are swallowed. Due to the high volatility of carbon tetrachloride which results in a high inhalation absorption of mists, swallowing of carbon tetrachloride mists is not considered a significant route of exposure.

***Key Data***

Key data that inform occupational exposure assessment and which EPA plans to evaluate include: the OSHA Chemical Exposure Health Data (CEHD) and National Institute of Occupational Safety and Health (NIOSH) Health Hazard Evaluation (HHE) program data. OSHA data are workplace monitoring data from OSHA inspections. The inspections can be random or targeted, or can be the result of a worker complaint. OSHA data can be obtained through the OSHA Integrated Management Information System (IMIS) at https://www.osha.gov/oshstats/index.html. Appendix C.2 provides a summary of carbon tetrachloride personal monitoring air samples obtained from OSHA inspections conducted between 2013 and 2015 and a summary of monitoring data from NIOSH HHEs conducted since 1990. NIOSH HHEs are conducted at the request of employees, union officials, or employers and help inform potential hazards at the workplace. HHEs can be downloaded at https://www.cdc.gov/niosh/hhe/. In public comment, EPA-HQ-OPPT-2016-0733-0064, Halogenated Solvents Industry Alliance characterized potential exposures groups during manufacturing and use of halogenated solvents such as

carbon tetrachloride and provided summaries of occupational monitoring data from three different companies. One of the data summaries includes 330 full-shift samples collected over 11 years. In addition, the Department of Defense has provided a compilation of carbon tetrachloride use scenarios with their respective exposure controls and workplace exposure assessment information for some of the use scenarios from the aerospace industry. During risk evaluation, EPA will review these data and evaluate the utility of these datasets in the risk evaluation.

***Inhalation***

EPA anticipates that inhalation to vapor is the most important exposure pathway of carbon tetrachloride for workers and ONU based on the high volatility of the chemical. ONU are not directly handling carbon tetrachloride; therefore, inhalation exposure to mists are not expected for ONU.

The United States has several regulatory and non-regulatory exposure limits for carbon tetrachloride: including an OSHA Permissible Exposure Limit (PEL) of 10 ppm time-weighted average (TWA) and 25 ppm ceiling and a NIOSH Recommended Exposure Limit (REL) of 2 ppm (12.6 mg/m$^3$) 60-minute Short-term Exposure Limit (STEL). Also, NIOSH indicates that carbon tetrachloride has an immediately dangerous to life and health (IDLH) value of 200 ppm based on acute inhalation toxicity data in humans, and provides a notation that carbon tetrachloride is considered a potential occupational carcinogen. The influence of these exposure limits on occupation exposures will be considered in the occupational exposure assessment.

During problem formulation, EPA has identified information on the thermal decomposition of carbon tetrachloride into phosgene, a highly toxic gas. However, thermal decomposition of carbon tetrachloride is more likely to occur in open environments and less likely in the type of closed systems used during the manufacturing and processing of carbon tetrachloride. Furthermore, TRI data shows that no single facility ever reported releases of both carbon tetrachloride and phosgene. EPA does not plan to evaluate exposure to phosgene during the manufacturing and processing of carbon tetrachloride.

#### 2.3.5.2 Consumer Exposures

Consumer products and/or commercial products containing chlorinated compounds made with carbon tetrachloride as a process agent are available for public purchase at common retailers [EPA-HQ-OPPT-2016-0733-0003, sections 3 and 4, (U.S. EPA, 2017d)]. However, these products are not expected to contain measurable amounts of carbon tetrachloride because carbon tetrachloride is not used in the manufacturing of the actual products. Trace levels of carbon tetrachloride in the chlorinated substances used to manufacture the products are expected to volatilize during the product manufacturing process. Therefore, EPA does not plan to evaluate consumer exposures to carbon tetrachloride due to the use of products containing chlorinated compounds made with carbon tetrachloride as a process agent (see Section 2.2.2.1).

#### 2.3.5.3 General Population Exposures

Wastewater/liquid wastes, solid wastes or air emissions of carbon tetrachloride could result in potential pathways for inhalation, oral or dermal exposure to the general population.

***Inhalation***

The volatility of carbon tetrachloride makes inhalation exposures a likely exposure pathway when it is released (via air or as a result of waste disposal) during industrial or commercial uses (see Figure 2-3) Inhalation of carbon tetrachloride, due to its volatilization, during household use of contaminated water (e.g., during bathing/showering, dishwashing) could be a source of exposure to the general population. According to a study from the New Jersey Department of Environmental Protection (NJ DEP), the

acceptable shower water criteria for carbon tetrachloride is 0.15 ug/L and the associated shower air concentration of carbon tetrachloride would be acceptable at 1.5 x $10^{-5}$ug/$m^3$ (NJDEP, 2002). Vapor intrusion is an additional source of exposure in indoor environments. VOCs such as carbon tetrachloride can evaporate rapidly and migrate into air. Therefore, there is a potential for carbon tetrachloride from TSCA conditions of use (see Table 2-7) to migrate from groundwater to indoor air via vapor intrusion.

***Oral***

Oral ingestion pathways may include exposure to contaminated drinking water or breast milk. However, breast milk is not expected to be significantly contaminated with carbon tetrachloride as the chemical does not bioaccumulate in tissues. EPA conducted a screening level estimate of carbon tetrachloride concentrations in drinking water using the PDM and the facility discharges in 2015 as reported in the NPDES Discharge Monitoring Reports. Ninety four percent of the modeled acute exposures were well below the EPA drinking water Minimum Contaminant Level of 5 ug/L.

Oral ingestion may include incidental ingestion of carbon tetrachloride residue on the hand/body. Based on the presence of carbon tetrachloride in water used for bathing or recreation, the oral ingestion of contaminated water could contribute, to a lesser degree, to oral exposures.

***Dermal***

Dermal exposure via water could occur through contact, such as washing and bathing with household water contaminated with carbon tetrachloride. The source of the contaminated water could either be contaminated surface or ground waters. As explained in Section 2.3.3, a first-tier analysis of the carbon tetrachloride monitored drinking water concentrations (i.e., SYR data) indicates that 94% of the reported facility discharge levels resulted in drinking water estimates below the EPA Minimum Contaminant Level of 5 ug/L.

#### 2.3.5.4 Potentially Exposed or Susceptible Subpopulations

TSCA requires that the determination of whether a chemical substance presents an unreasonable risk to "a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation" by EPA. TSCA § 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." General population is "the total of individuals inhabiting an area or making up a whole group" and refers here to the U.S. general population (U.S. EPA, 2011).

As part of the Problem Formulation, EPA identified potentially exposed and susceptible subpopulations (PESS) for further analysis during the development and refinement of the life cycle, conceptual models, exposure scenarios, and analysis plan. In this section, EPA addresses the PESS identified as relevant based on greater exposure. EPA will address the subpopulations identified as relevant based on greater susceptibility in the hazard section.

EPA identifies the following as PESS due to their greater exposure, that EPA expects to consider in the risk evaluation:

- Workers and ONU based on inhalation and dermal routes of exposure (See Figure 2-2).

In developing exposure scenarios, EPA will analyze available data to ascertain whether some human receptor groups may be exposed via exposure pathways that may be distinct to a particular

subpopulation or lifestage and whether some human receptor groups may have higher exposure via identified pathways of exposure due to unique characteristics (e.g., activities, duration or location of exposure) (U.S. EPA, 2006).

In summary, in the risk evaluation for carbon tetrachloride, EPA plans to analyze the following potentially exposed groups of human receptors: workers and ONU. EPA may also identify additional PESS that will be considered based on greater exposure.

## 2.4 Hazards (Effects)

For scoping, EPA conducted comprehensive searches for data on hazards of carbon tetrachloride, as described in the *Strategy for Conducting Literature Searches for Carbon Tetrachloride*: *Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0733). Based on initial screening, EPA plans to analyze the hazards of carbon tetrachloride identified in this problem formulation document. However, when conducting the risk evaluation, the relevance of each hazard within the context of a specific exposure scenario will be judged for appropriateness. For example, hazards that occur only as a result of chronic exposures may not be applicable for acute exposure scenarios. This means that it is unlikely that every identified hazard will be analyzed for every exposure scenario.

Further, as explained in Section 2.3, EPA's focus in the risk evaluation process is on conducting timely, relevant, high-quality, and scientifically credible risk evaluations 82 FR 33726, 33728 (July 20, 2017). Each risk evaluation will be "fit-for-purpose," meaning the Agency may be able to reach some conclusions without extensive or quantitative risk evaluations, and EPA expects to be able to reach conclusions about particular hazards without extensive evaluation.

### 2.4.1 Environmental Hazards

For the scope document, EPA consulted the following sources of environmental hazard data for carbon tetrachloride: ECHA (ECHA, 2017), OECD SIDS Initial Assessment Profile (SIAP) (OECD, 2011), and Australia's National Industrial Chemicals Notification and Assessment Scheme (NICNAS). These previous assessments included an evaluation of the environmental hazard data quality. Only the on-topic references listed in the Ecological Hazard Literature Search Results were considered as potentially relevant data/information sources for the risk evaluation. Inclusion criteria were used to screen the results of the ECOTOX literature search (as explained in the *Strategy for Conducting Literature Searches for Carbon Tetrachloride: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0733. Data from the screened literature are summarized below (Table 2-8) as ranges (min-max). EPA plans to review these data/information sources during risk evaluation using the data quality review evaluation metrics and the rating criteria described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018).

***Toxicity to Sediment and Terrestrial Organisms***

During data screening, the limited number of environmental toxicity studies for carbon tetrachloride on sediment and terrestrial organisms were determined to contain data or information not relevant (off-topic) for the risk evaluation. The studies were considered *off-topic* references during the data screening process (see Section 1.3). No relevant (on-topic) toxicity data were available for carbon tetrachloride to birds. Hazard studies for sediment and terrestrial organisms are not likely to be conducted because exposure to carbon tetrachloride by these organisms is not expected due to the fate and transport properties of the chemical.

***Toxicity to Aquatic Organisms***

During problem formulation, EPA identified aquatic (aqueous-only) data reported in literature to assess the aquatic hazard of carbon tetrachloride. For the aquatic environment, the acute hazard endpoint for fish (96-h $LC_{50}$) exposed to carbon tetrachloride ranges from 7.6 - 125 mg/L (Japanese Ministry of Environment, 2015; Dawson, 1977). The acute hazard endpoint for aquatic invertebrates (48-h $EC_{50}$) exposed to carbon tetrachloride ranges from 8.1 - 35 mg/L (Japanese Ministry of Environment, 2015; Leblanc, 1980). The acute hazard endpoint for aquatic plants (72-hr $EC_{50}$) exposed to carbon tetrachloride ranges from 0.246 – 23.590 mg/L (Tsai, 2007; Brack, 1994). The chronic hazard endpoint for fish (23-day $LC_{50}$) exposed to carbon tetrachloride is 1.97 mg/L (Black, 1982). The chronic hazard endpoint for aquatic invertebrates (21-day NOEC) exposed to carbon tetrachloride ranges from 0.49 – 3.1 mg/L (Japanese Ministry of Environment, 2015; Thomson et al., 1997). For aquatic plants, the chronic hazard endpoint (72-hr $EC_{10}$/NOEC ) for carbon tetrachloride ranges from 0.0717 - 2.2 mg/L (Gancet, 2011; Brack, 1994). The acute toxicity of amphibian embryo-larval stages ranged from 0.9 to 22.420 mg/L (Black, 1982; Birge, 1980).

**Table 2-8. Ecological Hazard Characterization of Carbon Tetrachloride**

| Duration | Test organism | Endpoint | Hazard value* | Units | Effect Endpoint | References |
|---|---|---|---|---|---|---|
| Acute | Fish | $LC_{50}$ | 7.6 - 125 | mg/L | Mortality | (Japanese Ministry of Environment, 2015; Dawson, 1977) |
| | Aquatic invertebrates | $EC_{50}$ | 8.1 – 35 | mg/L | Immobilization | (Japanese Ministry of Environment, 2015; Leblanc, 1980) |
| | Algae | $EC_{50}$ | 0.246-23.590 | mg/L | Biomass/growth rate | (Tsai, 2007; Brack, 1994) |
| | Amphibians | $L/EC_{50}$ | 0.9-22.420 | mg/L | Mortality | (Black, 1982; Birge, 1980) |
| | Acute COC | 0.062 | | mg/L | | |
| Chronic | Fish | ChV | 1.97 | mg/L | Mortality | (Black, 1982) |
| | Aquatic invertebrates | NOEC | 0.49-3.1 | mg/L | Growth and reproduction | (Japanese Ministry of Environment, 2015; Thomson et al., 1997) |
| | Algae | $EC_{10}$/NOEC | 0.0717 - 2.2 | mg/L | Biomass/growth rate | (Gancet, 2011; Brack, 1994). |
| | Chronic COC | 0.007 | | mg/L | | |

* Values in the tables are presented as reported by the study authors

***Concentrations of Concern***

The screening-level acute and chronic COCs for carbon tetrachloride were derived based on the lowest or most toxic ecological toxicity values (e.g., $L/EC_{50}$). The information below describes how the acute and chronic COC's were calculated for environmental toxicity of carbon tetrachloride using assessment factors. The application of assessment factors is based on established EPA/OPPT methods (U.S. EPA, 2013, 2012b) and were used in this hazard assessment to calculate lower bound effect levels (referred to as the concentration of concern; COC) that would likely encompass more sensitive species not specifically represented by the available experimental data. Also, assessment factors are included in the

COC calculation to account for differences in inter- and intra-species variability, as well as laboratory-to-field variability. It should be noted that these assessment factors are dependent upon the availability of datasets that can be used to characterize relative sensitivities across multiple species within a given taxa or species group, but are often standardized in risk assessments conducted under TSCA, due to limited data availability.

The acute COC is derived by dividing the algal 72-hr $EC_{50}$ of 0.246 mg/L (the lowest acute value in the dataset) by an assessment factor (AF) of 4:

- Lowest value for the 72-hr fish $EC_{50}$ (0.246 mg/L) / AF of 4 = 0.062 mg/L or 62 µg/L.

The acute COC of 62 µg/L, derived from experimental algal endpoint, is used as a conservative hazard level in this problem formulation for carbon tetrachloride.

The chronic COC is derived by dividing the 72-hr algal $EC_{10}$ of 0.0717 mg/L (the lowest chronic value in the dataset) by an assessment factor of 10:

- Lowest value for the 72-hr algal chronic value (0.0717 mg/L) / AF of 10 = 0.007 mg/L or 7 µg/L.

The chronic COC of 7 µg/L, derived from experimental algal endpoint, is used as the lower bound hazard level in this problem formulation for carbon tetrachloride.

### 2.4.2 Human Health Hazards

Carbon tetrachloride has an existing EPA IRIS Assessment (U.S. EPA, 2010) and an ATSDR Toxicological Profile (ATSDR, 2005); hence, many of the hazards of carbon tetrachloride have been previously compiled. EPA expects to use these previous analyses as a starting point for identifying key and supporting studies to inform the human health hazard assessment, including dose-response analysis. The relevant studies will be evaluated using the data quality criteria in the *Application of Systematic Review in TSCA Risk Evaluations* document. EPA also expects to consider other studies (e.g., more recently published, peer-reviewed alternative test data) that have been published since these reviews, as identified in the literature search conducted by the Agency for carbon tetrachloride (*Carbon tetrachloride (CASRN 56-23-5) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0733). EPA expects to consider potential human health hazards associated with carbon tetrachloride. Based on reasonably available information, the following sections describe the potential hazards associated with carbon tetrachloride. In addition to these hazards, EPA plans to evaluate hazards (e.g., reproductive toxicity, developmental toxicity) that may be identified during the evaluation of the key studies from the IRIS Toxicological Review of Carbon Tetrachloride.

#### 2.4.2.1 Non-Cancer Hazards

***Acute Toxicity***

Following acute exposures, human case reports identify liver as a primary target organ of toxicity and the kidney as an additional primary target organ of toxicity (U.S. EPA, 2010). Neurotoxicity indicated as central nervous system (CNS) depression is another primary effect of carbon tetrachloride in humans following acute exposures, with examples of neurotoxic effects including drowsiness, headache, dizziness, weakness, coma and seizures (U.S. EPA, 2010). Gastrointestinal symptoms such as nausea and vomiting, diarrhea and abdominal pain are considered another initial acute effect.

***Liver Toxicity***
Liver toxicity has consistently been demonstrated following human and animal exposures to carbon tetrachloride (U.S. EPA, 2010). Suggestive evidence of an effect of occupational exposure on serum enzymes indicative of hepatic effects was reported in a cross-sectional epidemiology study. Similar to humans, data from acute, subchronic and chronic animal studies suggest that the liver is the major target organ for carbon tetrachloride toxicity (U.S. EPA, 2010).

***Kidney Toxicity***
Renal toxicity effects include oliguria, elevated blood urea nitrogen (BUN) and histopathological changes (e.g., nephrosis, degeneration and interstitial inflammation in fatal cases) were observed in humans following acute exposures. In animals, renal toxicity was observed in inhalation (but not oral) studies. In subchronic studies, renal toxicity generally occurred at higher concentrations than those producing liver damage, whereas changes in renal and liver endpoints were reported at the same concentration in chronic inhalation toxicity studies in rats and mice (U.S. EPA, 2010).

***Irritation/Sensitization***
Following dermal exposures, primary irritation was observed in rabbits and guinea pigs (ATSDR, 2005). Guinea pigs also exhibited degenerative change in epidermal cells and edema (ATSDR, 2005). In the murine local lymph node assay, carbon tetrachloride showed weak dermal sensitization potential (OECD, 2011).

#### 2.4.2.2 Genotoxicity and Cancer Hazards
The IRIS Assessment for carbon tetrachloride evaluated data for genotoxicity and cancer hazard. Carbon tetrachloride has been extensively studied for its genotoxic and mutagenic effects. Overall, results are largely negative. There is little direct evidence that carbon tetrachloride induces intragenic or point mutations in mammalian systems. The mutagenicity studies that have been performed using transgenic mice have yielded negative results, as have the vast majority of the mutagenicity studies that have been conducted in bacterial systems. The weight of evidence suggests that carbon tetrachloride is more likely an indirect mutagenic agent (i.e., lipid peroxidation, protein modifications) rather than a direct mutagen (deoxyribonucleic acid [DNA] modifications) (U.S. EPA, 2010).

In the IRIS carcinogenicity assessment, carbon tetrachloride is considered "likely to be carcinogenic to humans" by all routes of exposure based on inadequate evidence of carcinogenicity in humans, and sufficient evidence in animals by oral and inhalation exposure. The animal evidence shows that carbon tetrachloride is a liver carcinogen in rats, mice and hamsters following oral and inhalation exposure in eight bioassays. Carbon tetrachloride also induced pheochromocytomas in mice exposed by the oral and inhalation routes of exposure.

#### 2.4.2.3 Potentially Exposed or Susceptible Subpopulations
TSCA requires that the determination of whether a chemical substance presents an unreasonable risk include consideration of unreasonable risk to “a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation” by EPA. TSCA § 3(12) states that “the term ‘potentially exposed or susceptible subpopulation’ means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers or the elderly.” In developing the hazard assessment, EPA will analyze available data to ascertain whether some human receptor groups may have greater susceptibility than the general population to the chemical’s hazard(s).

EPA's IRIS assessment identified the following as factors that might influence susceptibility to carbon tetrachloride: age (e.g., childhood, senescence), gender, nutritional status, disease status and exposure to other chemicals (U.S. EPA, 2010, 2006). The IRIS assessment noted that because metabolism of carbon tetrachloride to reactive metabolites by cytochrome P450 (CYP450) enzymes is hypothesized to be a key event in the toxicity of this compound, variability in CYP450 levels due to age-related differences or other factors such as exposure to other chemicals that either induce or inhibit microsomal enzymes may impact an individual's response to carbon tetrachloride. In addition, variability in nutritional status, alcohol consumption and/or underlying diseases (e.g., diabetes) may alter metabolism or antioxidant protection systems and thereby also alter susceptibility to carbon tetrachloride (U.S. EPA, 2010). EPA expects to consider these factors, and others that may be identified from more current literature, in the risk evaluation for carbon tetrachloride.

## 2.5 Conceptual Models

EPA risk assessment guidance (U.S. EPA, 2014, 1998) defines Problem Formulation as the part of the risk assessment framework that identifies the factors to be considered in the assessment. It draws from the regulatory, decision-making and policy context of the assessment and informs the assessment's technical approach.

A conceptual model describes the actual or predicted relationships between the chemical substance and receptors, either human or environmental. These conceptual models are integrated depictions of the conditions of use, exposures (pathways and routes), hazards and receptors. The initial conceptual models describing the scope of the assessment for carbon tetrachloride, have been refined during problem formulation. The changes to the conceptual models in this problem formulation are described along with the rationales.

In this section EPA outlines those pathways that will be included and further analyzed in the risk evaluation; will be included but will not be further analyzed in risk evaluation; and will not be included in the TSCA risk evaluation; and the underlying rationale for these decisions.

EPA determined as part of problem formulation that it is not necessary to conduct further analysis on certain exposure pathways that were identified in the carbon tetrachloride scope document and that remain in the risk evaluation. Each risk evaluation will be "fit-for-purpose," meaning not all conditions of use will warrant the same level of evaluation and the Agency may be able to reach some conclusions without extensive or quantitative risk evaluations.  82 FR 33726, 33734, 33739 (July 20, 2017).

As part of this problem formulation, EPA also identified exposure pathways under regulatory programs of other environmental statutes, administered by EPA, which adequately assess and effectively manage exposures and for which long-standing regulatory and analytical processes already exist, i.e., the CAA, the SDWA, the Clean Water Act (CWA) and the RCRA. OPPT worked closely with the offices within EPA that administer and implement the regulatory programs under these statutes. In some cases, EPA has determined that chemicals present in various media pathways (i.e., air, water, land) fall under the jurisdiction of existing regulatory programs and associated analytical processes carried out under other EPA-administered statutes and have been assessed and effectively managed under those programs. EPA believes that the TSCA risk evaluation should generally focus on those exposure pathways associated with TSCA conditions of use that are not adequately assessed and effectively managed under the regulatory regimes discussed above because these pathways are likely to represent the greatest areas of

risk concern. As a result, EPA does not expect to include in the risk evaluation certain exposure pathways identified in the carbon tetrachloride scope document.

### 2.5.1 Conceptual Model for Industrial and Commercial Activities and Uses: Potential Exposures and Hazards

The revised conceptual model (Figure 2-2) describes the pathways of exposure from industrial and commercial activities and uses of carbon tetrachloride that EPA expects to include in the risk evaluation. EPA plans to evaluate exposures to workers and/or ONU via inhalation routes and to workers via dermal routes during manufacturing, processing, use and disposal of carbon tetrachloride for all the identified uses. In addition to the pathways illustrated in the figure, EPA will evaluate activities resulting in exposures associated with distribution in commerce (e.g., loading, unloading) throughout the various lifecycle stages and conditions of use (e.g., manufacturing, processing, industrial use, commercial use, disposal) rather than a single distribution scenario.

***Inhalation***

Based on the physical-chemical properties (e.g., high vapor pressure), inhalation is expected to be the main exposure pathway for carbon tetrachloride. Inhalation exposures for workers are regulated by OSHA's occupational safety and health standards for carbon tetrachloride which include a PEL of 10 ppm TWA, exposure monitoring, control measures and respiratory protection (29 CFR 1910.1000). EPA expects that for workers and ONU, exposure via inhalation will be the most significant route of exposure for most exposure scenarios. EPA plans to further analyze inhalation exposures to vapors for workers and ONU in the risk evaluation.

There are potential worker exposures through mists that deposit in the upper respiratory tract. EPA initially assumed that mists may be swallowed. However, based on physical chemical properties, mists of carbon tetrachloride will likely be rapidly absorbed in the respiratory tract or evaporate and contribute to the amount of carbon tetrachloride vapor in the air. Furthermore, if carbon tetrachloride vapors were ingested orally the available toxicological data do not suggest significantly different toxicity from considering vapors as an inhalation exposure. ONU are not directly handling carbon tetrachloride; therefore, exposure to mists is not expected for ONU. EPA plans no further analysis of this pathway (swallowing of carbon tetrachloride mists) for workers or ONU in the risk evaluation.

***Dermal***

There is the potential for dermal exposures to carbon tetrachloride in many worker scenarios. These dermal exposures would be concurrent with inhalation exposures and the overall contribution of dermal exposure to the total exposure is expected to be small; however, there may be exceptions for occluded scenarios. ONU are not directly handling carbon tetrachloride; therefore, skin contact with liquid carbon tetrachloride is not expected for ONU. EPA does not plan to further analyze this pathway in the risk evaluation. EPA plans to further analyze dermal exposures for skin contact with liquids and vapors in occluded situations for workers.

***Waste Handling, Treatment and Disposal***

Figure 2-2 shows that waste handling, treatment and disposal is expected to lead to the same pathways as other industrial and commercial activities and uses. The path leading from the "Waste Handling, Treatment and Disposal" box to the "Hazards Potentially Associated with Acute and/or Chronic Exposures See Section 2.4.2" box was re-routed to accurately reflect the expected exposure pathways, routes, and receptors associated with these conditions of use of carbon tetrachloride.

For each condition of use identified in Table 2-3, a determination was made as to whether or not each unique combination of exposure pathway, route, and receptor will be analyzed further in the risk evaluation. The results of that analysis along with the supporting rationale are presented in Appendix F.

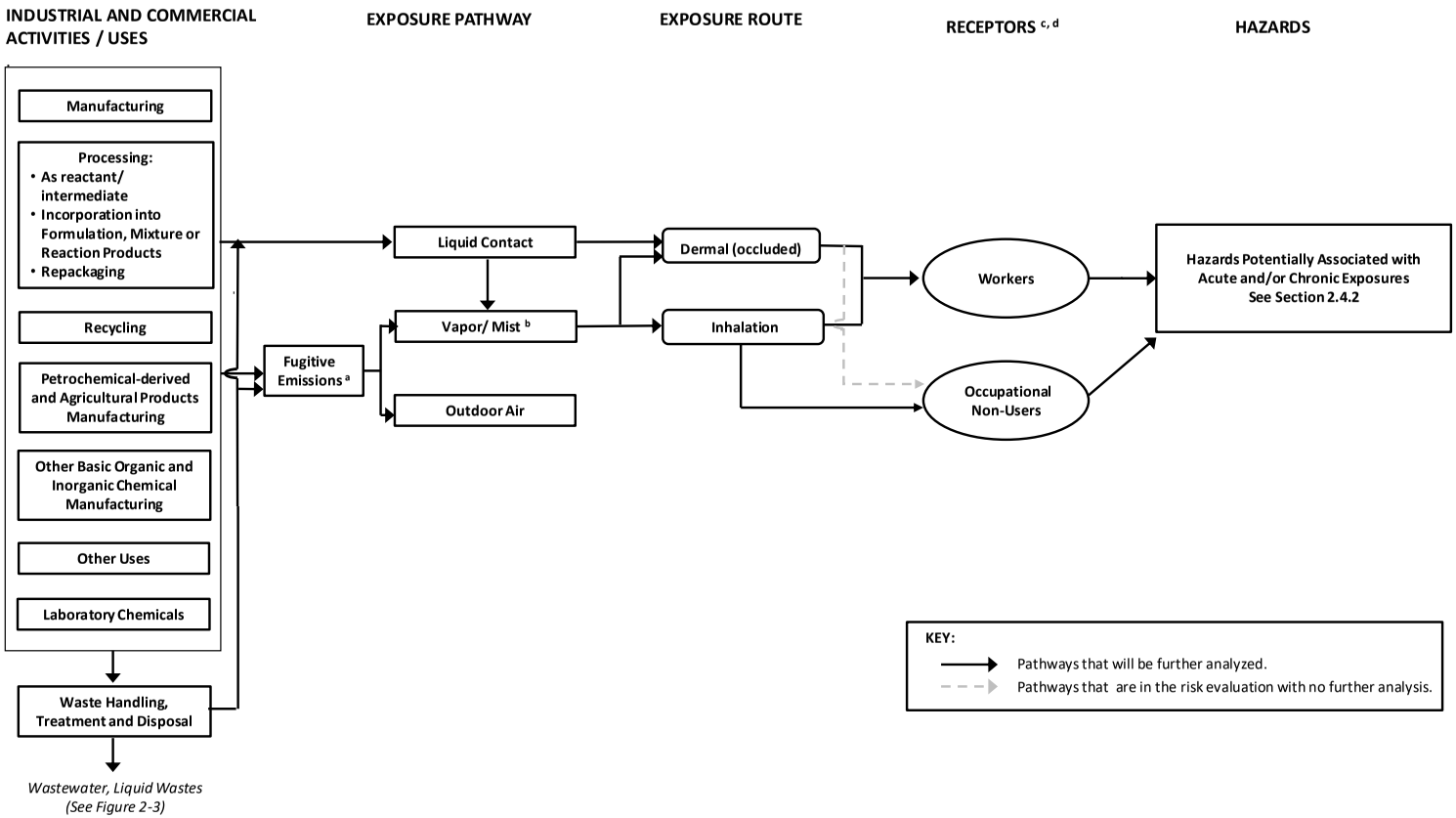


**Figure 2-2. Carbon Tetrachloride Conceptual Model for Industrial and Commercial Activities and Uses: Potential Exposures and Hazards**

The conceptual model presents the exposure pathways, exposure routes and hazards to human receptors from industrial and commercial activities and uses of carbon tetrachloride.

[a] Fugitive air emissions include fugitive equipment leaks from valves, pump seals, flanges, compressors, sampling connections, open-ended lines; evaporative losses from surface impoundment and spills; and releases from building ventilation systems.

[b] Includes possible vapor intrusion into industrial or commercial facility from carbon tetrachloride ground water; exposure to mists is not expected for ONU.

[c] Receptors include PESS (see Section 2.4.2.3).

[d] When data and information are available to support the analysis, EPA also considers the effect that engineering controls and/or personal protective equipment have on occupational exposure levels.

### 2.5.2 Conceptual Model for Consumer Activities and Uses: Potential Exposures and Hazards

As explained in Section 2.2.2.1, there are current regulatory actions that prevent the direct use of carbon tetrachloride in the formulation of commercially available products, besides the use of carbon tetrachloride as a laboratory chemical. The domestic and international use of carbon tetrachloride as a process agent is regulated under EPA's stratospheric ozone protection regulations at 40 CFR part 82. This process agent use is also addressed by the MP side agreement, Decision X/14: Process Agents, from the tenth meeting of the parties in November 1998 (UNEP/Ozone Secretariat, 1998). This MP decision lists a limited number of approved uses of carbon tetrachloride as a process agent (i.e., non-feedstock uses) in which carbon tetrachloride is not expected to be destroyed in the production process (see Appendix D). Based on the process agent uses, carbon tetrachloride is used to manufacture other chlorinated compounds (i.e., chlorinated paraffins) that may subsequently be added to commercially available products (i.e., adhesives). Given the high volatility of carbon tetrachloride and the extent of reaction and efficacy of the separation/purification process for purifying final products, EPA does not expect that carbon tetrachloride will be present in the commercially available products. Furthermore, the use of carbon tetrachloride in consumer products has been banned by the CPSC (16 CFR 1500.17) since 1970. EPA does not expect to evaluate consumer activities and uses for carbon tetrachloride, and has excluded these conditions of use from the scope of the risk evaluation (see Section 2.2.2.1). Therefore, there is no conceptual model provided for consumer activities and uses.

### 2.5.3 Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards

The revised conceptual model (Figure 2-3) illustrates the expected exposure pathways to human and ecological receptors from environmental releases and waste streams associated with industrial and commercial activities for carbon tetrachloride that EPA expects to include in the risk evaluation. The pathways that EPA expects to include but not further analyze in the risk evaluation are described in Section 2.5.3.1 and shown in the conceptual model, Figure 2-3. The pathways that EPA does not expect to include in the risk evaluation are described in Section 2.5.3.2. EPA does not expect to further analyze any exposure pathways to human or ecological receptors from environmental releases and waste streams associated with industrial and commercial activities for carbon tetrachloride.

#### 2.5.3.1 Pathways That EPA Expects to Include But Not Further Analyze

EPA does not expect to further analyze carbon tetrachloride exposures to aquatic species from sediments and suspended solids. Due to its log $K_{oc}$ (1.7 – 2.16) and high solubility of 793 mg/L at 25°C, sorption of carbon tetrachloride to sediments and suspended solids is unlikely.

EPA does not expect to further analyze risk to aquatic species exposed to carbon tetrachloride in surface water. Wastewater from industrial discharges as reported under TRI for 2015 shows only 468.2 pounds of carbon tetrachloride were released to surface water nationally and significant levels of carbon tetrachloride are not expected from disposal of consumer and commercial products.

EPA considered worst-case scenarios to estimate carbon tetrachloride concentrations in surface water resulting from industrial discharges. Using NPDES Discharge Monitoring Reporting data available for 2015, the largest releases of carbon tetrachloride were modeled for releases over 20 days and 250 days per year. In these conservative scenarios, surface water concentrations were below the acute COC for aquatic species (see Appendix E); hence there is not an acute aquatic concern. Although the chronic COC was exceeded by one facility by a factor of 3.5 (i.e., worst-case scenario) based on predicted conservative exposure concentrations in surface water, these carbon tetrachloride releases are not

continuously released over time (i.e., chronic exposure); hence there is not a chronic aquatic concern. Furthermore, carbon tetrachloride discharges to surface waters are expected to undergo volatilization and dilution in surface water, processes that were not considered for estimating the predicted conservative exposure concentrations in surface water. Due to its physical-chemical properties, carbon tetrachloride is not anticipated to bioaccumulate in fish (BCF 30-40) thus there is no bioconcentration or bioaccumulation concern. Thus, EPA does not expect to further analyze exposure pathways to ecological aquatic species in the risk evaluation.

#### 2.5.3.2 Pathways that EPA Does Not Expect to Include in the Risk Evaluation

Exposures to receptors (i.e. general population, terrestrial species) may occur from industrial and/or commercial uses; industrial releases to air, water or land; and other conditions of use. As described in Section 2.5, EPA does not expect to include in the risk evaluation pathways under programs of other environmental statutes, administered by EPA, which adequately assess and effectively manage exposures and for which long-standing regulatory and analytical processes already exist. These pathways are described below.

**Ambient Air Pathway**

The Clean Air Act (CAA) contains a list of HAP and provides EPA with the authority to add to that list pollutants that present, or may present, a threat of adverse human health effects or adverse environmental effects. For stationary source categories emitting HAP, the CAA requires issuance of technology-based standards and, if necessary, additions or revisions to address developments in practices, processes, and control technologies, and to ensure the standards adequately protect public health and the environment. The CAA thereby provides EPA with comprehensive authority to regulate emissions to ambient air of any HAP.

Carbon tetrachloride is a HAP. EPA has issued a number of technology-based standards for source categories that emit carbon tetrachloride to ambient air and, as appropriate, has reviewed or is in the process of reviewing remaining risks. Because stationary source releases of carbon tetrachloride to ambient air are adequately assessed and any risks effectively managed when under the jurisdiction of the CAA, EPA does not expect to include emission pathways to ambient air from commercial and industrial stationary sources or associated inhalation exposure of the general population or terrestrial species in this TSCA evaluation.

**Drinking Water Pathway**

EPA has regular analytical processes to identify and evaluate drinking water contaminants of potential regulatory concern for public water systems under the SDWA. Under SDWA, EPA must also review and revise "as appropriate" existing drinking water regulations every 6 years.

EPA has promulgated National Primary Drinking Water Regulations (NPDWRs) for carbon tetrachloride under the Safe Drinking Water Act. EPA has set an enforceable MCL as close as feasible to a health based, non-enforceable Maximum Contaminant Level Goal (MCLG). Feasibility refers to both the ability to treat water to meet the MCL and the ability to monitor water quality at the MCL, SDWA Section 1412(b)(4)(D), and public water systems are required to monitor for the regulated chemical based on a standardized monitoring schedule to ensure compliance with the MCL. The MCL and MCLG values for carbon tetrachloride are presented in Appendix A.1.

Hence, because the drinking water exposure pathway for carbon tetrachloride is currently addressed in the SDWA regulatory analytical process for public water systems, EPA does not expect to include this pathway in the risk evaluation for carbon tetrachloride under TSCA. EPA's OW and OPPT will continue

to work together providing understanding and analysis of the SDWA regulatory analytical processes and to exchange information related to toxicity and occurrence data on chemicals undergoing risk evaluation under TSCA.

**Ambient Water Pathways**

EPA develops recommended water quality criteria under section 304(a) of the CWA for pollutants in surface water that are protective of aquatic life or human health designated uses. EPA develops and publishes water quality criteria based on priorities of states and others that reflect the latest scientific knowledge. When states adopt criteria that EPA approves as part of states' regulatory water quality standards, exposure is considered when state permit writers determine if permit limits are needed and at what level for a specific discharger of a pollutant to ensure protection of the designated uses of the receiving water. This is the process used under the CWA to address risk to human health and aquatic life from exposure to a pollutant in ambient waters.

EPA has identified carbon tetrachloride as a priority pollutant and EPA has developed recommended water quality criteria for protection of human health for carbon tetrachloride which are available for adoption into state water quality standards for the protection of human health and are available for use by NPDES permitting authorities in deriving effluent limits to meet state narrative criteria. As such, EPA does not expect to include this pathway in the risk evaluation under TSCA. EPA's OW and OPPT will continue to work together providing understanding and analysis of the CWA water quality criteria development process and to exchange information related to toxicity of chemicals undergoing risk evaluation under TSCA. EPA may update its CWA section 304(a) water quality criteria for carbon tetrachloride in the future under the CWA.

EPA has not developed CWA section 304(a) recommended water quality criteria for the protection of aquatic life for carbon tetrachloride, so there are no national recommended criteria for this use available for adoption into state water quality standards and available for use in NPDES permits. As a result, this pathway will undergo aquatic life risk evaluation under TSCA but as described in Section 2.5.3.1 (i.e., conservative estimates of surface water concentrations) this pathway will not be further analyzed. EPA may publish CWA section 304(a) aquatic life criteria for carbon tetrachloride in the future if it is identified as a priority under the CWA.

**Biosolids Pathways**

CWA Section 405(d) requires EPA to 1) promulgate regulations that establish numeric criteria and management practices that are adequate to protect public health and the environment from any reasonably anticipated adverse effects of toxic pollutants during the use or disposal of sewage sludge, and 2) review such regulations at least every two years to identify additional toxic pollutants that occur in biosolids (i.e., "Biennial Reviews") and regulate those pollutants if sufficient scientific evidence shows they may be present in sewage sludge in concentrations which may adversely affect public health or the environment. EPA also periodically conducts surveys to determine what may be present in sewage sludge. EPA has conducted four sewage sludge surveys and identified compounds that occur in biosolids in seven Biennial Reviews. EPA has regulated 10 chemicals in biosolids under CWA 405(d).

EPA has identified carbon tetrachloride in biosolids biennial reviews. The purpose of such reviews is to identify additional toxic pollutants in biosolids. EPA can potentially regulate those pollutants under CWA 405(d), based on a subsequent assessment of risk. EPA's Office of Water is currently developing modeling tools in order to conduct risk assessments for chemicals in biosolids. Because the biosolids pathway for carbon tetrachloride is currently being addressed in the CWA regulatory analytical process, this pathway will not be further analyzed in the risk evaluation for carbon tetrachloride under TSCA.

EPA's OW and OPPT will continue to work together to discuss significant data gaps and exchange information related to exposure and toxicity of this chemical as OW conducts the risk assessment under the CWA.

**Disposal Pathways**

Carbon tetrachloride is included on the list of hazardous wastes to RCRA 3001 (40 CFR §§ 261.33) as a listed waste on the D, K, F and U lists. The general standard in RCRA section 3004(a) for the technical criteria that govern the management (treatment, storage, and disposal) of hazardous waste are those "necessary to protect human health and the environment," RCRA 3004(a). The regulatory criteria for identifying "characteristic" hazardous wastes and for "listing" a waste as hazardous also relate solely to the potential risks to human health or the environment. 40 C.F.R. §§ 261.11, 261.21-261.24. RCRA statutory criteria for identifying hazardous wastes require EPA to "tak[e] into account toxicity, persistence, and degradability in nature, potential for accumulation in tissue, and other related factors such as flammability, corrosiveness, and other hazardous characteristics." Subtitle C controls cover not only hazardous wastes that are landfilled, but also hazardous wastes that are incinerated (subject to joint control under RCRA Subtitle C and the CAA hazardous waste combustion MACT) or injected into UIC Class I hazardous waste wells (subject to joint control under Subtitle C and the SDWA).

EPA does not expect to include emissions to ambient air from municipal and industrial waste incineration and energy recovery units in the risk evaluation, as they are regulated under section 129 of the Clean Air Act. CAA section 129 also requires EPA to review and, if necessary, add provisions to ensure the standards adequately protect public health and the environment. Thus, combustion by-products from incineration treatment of carbon tetrachloride wastes (over 15 million lbs identified in Table 2-6) would be subject to the aforementioned regulations, as would carbon tetrachloride burned for energy recovery (5.6 million lbs).

EPA does not expect to include on-site releases to land that go to underground injection in its risk evaluation. TRI reporting in 2015 indicated 19,608 pounds released to underground injection to a Class I well and no releases to underground injection wells of Classes II-VI. Environmental disposal of carbon tetrachloride injected into Class I well types is managed and prevented from further environmental release by RCRA and SDWA regulations. Therefore, disposal of carbon tetrachloride via underground injection is not likely to result in environmental and general population exposures.

EPA does not expect to include on-site releases to land that go to RCRA Subtitle C hazardous waste landfills in its risk evaluation. Based on 2015 reporting to TRI, the majority of the chemical is disposed of in Subtitle C landfills (27,300 lbs on-site and 401 lbs other land disposal). Design standards for Subtitle C landfills require double liner, double leachate collection and removal systems, leak detection system, run on, runoff, and wind dispersal controls, and a construction quality assurance program. They are also subject to closure and post-closure care requirements including installing and maintaining a final cover, continuing operation of the leachate collection and removal system until leachate is no longer detected, maintaining and monitoring the leak detection and groundwater monitoring system. Bulk liquids may not be disposed in Subtitle C landfills. Subtitle C landfill operators are required to implement an analysis and testing program to ensure adequate knowledge of waste being managed, and to train personnel on routine and emergency operations at the facility. Hazardous waste being disposed in Subtitle C landfills must also meet RCRA waste treatment standards before disposal. Given these controls, general population and terrestrial organisms exposure to carbon tetrachloride in groundwater from Subtitle C landfill leachate is not expected to be a significant pathway.

EPA does not expect to include on-site releases to land from RCRA Subtitle C hazardous waste landfills or exposures of the general population (including susceptible subpopulations) or terrestrial species from such releases in the TSCA evaluation.

Based on 2015 reporting to TRI, 401 lb of carbon tetrachloride wastes were released as other land disposals (see Table 2-7). Upon evaluation of these reports of other land disposal releases, it was found that the reports consist of misreported disposal values. The incorrect code uses or waste identification were used in the reports. Therefore these 401 lbs of released waste do not consist of carbon tetrachloride waste released by other land disposal. EPA does not expect to include these misreported other land disposals for carbon tetrachloride in the TSCA evaluation.

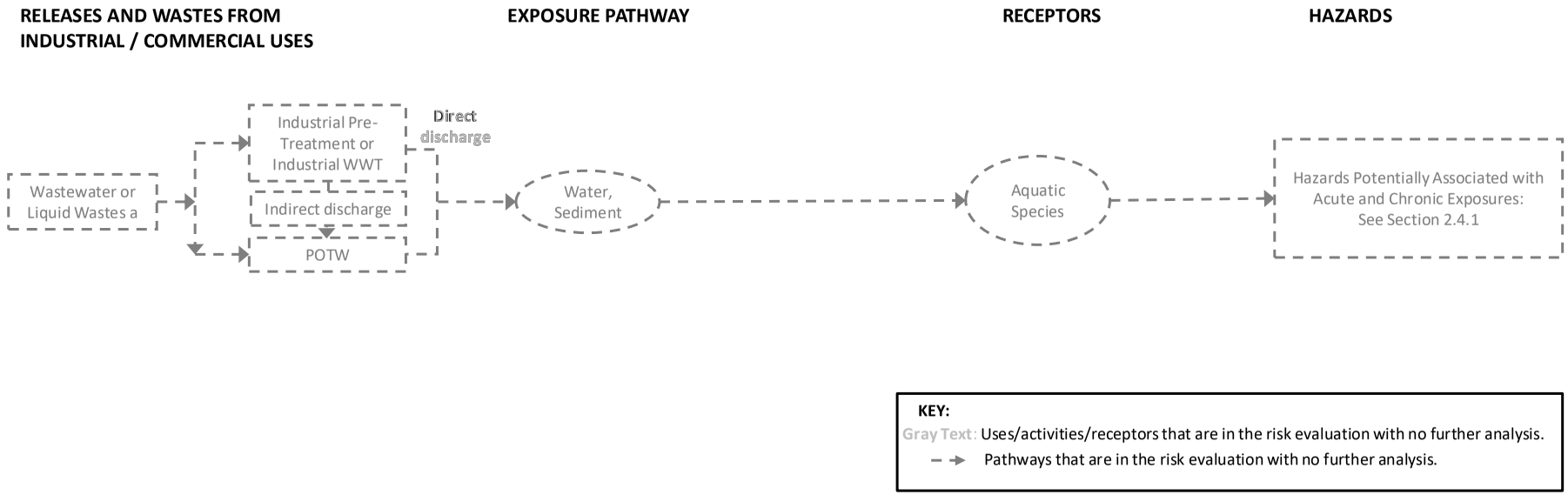


**Figure 2-3. Carbon Tetrachloride Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards**
The conceptual model presents the exposure pathways, exposure routes and hazards to environmental receptors from environmental water releases of carbon tetrachloride.

## 2.6 Analysis Plan

The analysis plan in the problem formulation elaborates on the initial analysis plan that was published in the *Scope of the Risk Evaluation for carbon tetrachloride* (U.S. EPA, 2017e).

The analysis plan outlined here is based on the conditions of use of carbon tetrachloride, as described in Section 2.2 of this problem formulation. EPA is implementing systematic review approaches and/or methods to identify, select, assess, integrate and summarize the findings of studies supporting the TSCA risk evaluation. The analytical approaches and considerations in the analysis plan are used to frame the scope of the systematic review activities for this assessment. The supplemental document, *Application of Systematic Review in TSCA Risk Evaluations*, provides additional information about the criteria, approaches and/or methods that have been and will be applied to the first ten chemical risk evaluations.

While EPA has conducted a search for readily available information from public sources as described in the Scope of the Risk Evaluation for Carbon Tetrachloride (U.S. EPA, 2017e), EPA encourages submission of additional existing data, such as full study reports or workplace monitoring from industry sources, that may be relevant for refining conditions of use, exposures, hazards and PESS. EPA will continue to consider new information submitted by the public.

During the risk evaluation, EPA will rely on the comprehensive literature results [*Carbon tetrachloride (CASRN 56-23-5) Bibliography: Supplemental File for the TSCA Scope Document*; (U.S. EPA, 2017a)] or perform supplemental literature searches to address specific questions. Further, EPA may consider any relevant CBI information in the risk evaluation in a manner that protects the confidentiality of the information from public disclosure. The analysis plan is based on EPA's knowledge of carbon tetrachloride to date which includes partial, but not complete review of identified literature. Should additional data or approaches become available, EPA may refine its analysis plan based on this information.

### 2.6.1 Exposure

Based on physical-chemical properties, expected sources, and transport and transformation within the outdoor and indoor environment chemical substances are more likely to be present in some media and less likely to be present in others. Media-specific concentrations will vary based on the chemical substance of interest. For most chemical substances, level(s) can be characterized through a combination of available monitoring data and modeling approaches.

#### 2.6.1.1 Environmental Releases, Fate and Exposures

EPA does not plan to further analyze environmental releases to environmental media based on information described in Section 2.5. For the purposes of developing estimates of occupational exposure, EPA may use release related data collected under selected data sources such as the Toxics Release Inventory (TRI) and National Emissions Inventory (NEI) programs. Analyses conducted using physical and chemical properties, fate information and TRI/DMR show that TSCA-related environmental releases for carbon tetrachloride do not result in significant exposure to aquatic species through water and sediment exposure pathways (see Section 2.5.3.1). For the pathways of exposures for the general population and terrestrial species, EPA has determined that the existing regulatory programs and associated analytical processes adequately assess and effectively manage the risks of carbon tetrachloride that may be present in other media pathways. EPA believes that the TSCA risk evaluation for carbon tetrachloride should focus not on those exposure pathways, but rather on exposure pathways

associated with TSCA conditions of use that are not subject to those regulatory processes, because the latter pathways are likely to represent the greatest areas of risk concern.

#### 2.6.1.2 Occupational Exposures

EPA expects to consider and analyze exposures to workers and ONU as follows:

1) Review reasonably available exposure monitoring data for specific condition(s) of use. Exposure data to be reviewed may include workplace monitoring data collected by government agencies such as OSHA and NIOSH, data submitted by Halogenated Solvents Industry Alliance and Department of Defense and monitoring data found in published literature. These workplace monitoring data include personal exposure monitoring data (direct exposures) and area monitoring data (indirect exposures). During risk evaluation, EPA will review these data and evaluate the utility of these datasets in the risk evaluation. Data, information, and studies will be evaluated using the evaluation strategies laid out in the *Application of Systematic Review in TSCA Risk Evaluations*.

   EPA has reviewed available monitoring collected by OSHA and NIOSH and matched them to applicable conditions of use. EPA has also identified data sources that may contain relevant monitoring data for the various conditions of use. EPA will review these sources. Data gaps will be identified where no data are found for particular conditions of use. EPA will attempt to address data gaps identified as described in steps 2 and 3 below. Where possible, job descriptions may be useful in distinguishing exposures to different subpopulations within a particular condition of use. EPA has also identified additional data sources that may contain relevant monitoring data for the various conditions of use. EPA will review these sources, identified in Table 2-9 and other relevant data sources, and will extract relevant data for consideration and analysis during risk evaluation.

**Table 2-9. Potential Sources of Occupational Exposure Data**

| |
|---|
| ATSDR Toxicological Profile for Carbon Tetrachloride |
| U.S. OSHA CEHD program data |
| U.S. NIOSH Health Hazard Evaluation (HHE) Program reports |
| Industry workplace exposure monitoring summary data submitted to EPA by Halogenated Solvents Industry Alliance |
| Industry workplace exposure information submitted to EPA by the Department of Defense |
| U.S. EPA Generic Scenarios |
| OECD Emission Scenario Documents (ESD) |
| Sector-specific Worker Exposure Descriptions (SWEDs) |

2) Review reasonably available exposure data for surrogate chemicals that have uses and chemical and physical properties similar to carbon tetrachloride. EPA will review literature sources identified and if surrogate data are found, these data will be matched to applicable conditions of use for potentially filling data gaps.

3) For conditions of use where data are limited or not available, review existing exposure models that may be applicable in estimating exposure levels. EPA has identified potentially relevant OECD ESDs and EPA GS corresponding to some conditions of use. EPA will need to critically review these generic scenarios and ESDs to determine their applicability to the conditions of use assessed. EPA is working in the identification of exposure scenarios corresponding to several conditions of use, including manufacture of carbon tetrachloride, use of carbon tetrachloride as an intermediate, and recycling of carbon tetrachloride. EPA will perform additional targeted research to understand those conditions of use, which may inform identification of exposure scenarios. EPA may also need to perform targeted research to identify applicable models that EPA may use to estimate exposures for certain conditions of use.

4) Review reasonably available data that may be used in developing, adapting, or applying exposure models to the particular risk evaluation. This step will be performed after Steps 2 and 3 above. Based on information developed from Step 2 and Step 3, EPA will evaluate relevant data to determine whether the data can be used to develop, adapt, or apply models for specific conditions of use (and corresponding exposure scenarios). EPA will consider the effect of evaporation when evaluating options for dermal exposure assessment. In addition, EPA will consider the impact of occluded exposure or repeated dermal contacts.

5) Consider and incorporate applicable engineering controls and/or personal protective equipment into exposure scenarios. EPA will review potentially relevant data sources on engineering controls and personal protective equipment as identified in Appendix F and to determine their applicability and incorporation into exposure scenarios during risk evaluation.

6) Evaluate the weight of the evidence of occupational exposure data. EPA will rely on the weight of the scientific evidence when evaluating and integrating occupational exposure data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

7) Map or group each condition of use to occupational exposure assessment scenario(s). EPA has identified exposure scenarios and mapped them to some conditions of use. EPA grouped similar conditions of use (based on factors including process equipment and handling, usage rates of carbon tetrachloride and formulations containing carbon tetrachloride, exposure/release sources) into scenario groupings but may further refine these groupings as additional information is identified during risk evaluation.

   EPA was not able to identify occupational exposure scenarios corresponding to several conditions of use due generally to a lack of understanding of those conditions of use. EPA will perform targeted research to understand those uses which may inform identification of occupational exposure scenarios.

8) Evaluate the weight of the evidence of occupational exposure data. EPA will rely on the weight of the scientific evidence when evaluating and integrating occupational exposure data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic

review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

#### 2.6.1.3 Consumer Exposures

EPA does not expect to consider and analyze consumer exposures in the risk evaluation for carbon tetrachloride. Based on domestic and international regulatory information; Use document, EPA-HQ-OPPT-2016-0733-0003; and submitted public comments; carbon tetrachloride is expected to be present in consumer products at trace levels resulting in de minimis exposures or otherwise insignificant risks.

#### 2.6.1.4 General Population

EPA does not expect to include general population exposures in the risk evaluation for carbon tetrachloride. EPA has determined that the existing regulatory programs and associated analytical processes adequately assess and effectively manage the risks of carbon tetrachloride that may be present in various media pathways (e.g., air, water, land) from TSCA conditions of use and subsequent partitioning and transport processes (i.e., vapor intrusion) for the general population. EPA believes that the TSCA risk evaluation should focus not on those exposure pathways, but rather on exposure pathways associated with TSCA conditions of use that are not subject to those regulatory processes, because the latter pathways are likely to represent the greatest areas of concern to EPA.

### 2.6.2 Hazards (Effects)

#### 2.6.2.1 Environmental Hazards

Environmental hazards will not be further analyzed because exposure analysis conducted using physical and chemical properties, fate information and TRI/DMR environmental releases for carbon tetrachloride show that aquatic species are not significantly exposed to TSCA-related environmental releases of this chemical. During data screening, the limited number of environmental toxicity studies for carbon tetrachloride on sediment and terrestrial organisms were determined to contain data or information not relevant (off-topic) for the risk evaluation. The studies were considered *off-topic* references during the data screening process (see Section 1.3). No relevant (on-topic) toxicity data were available for carbon tetrachloride to birds. Hazard studies for sediment and terrestrial organisms are not likely to be conducted because exposure to carbon tetrachloride by these organisms is not expected due to the fate and transport properties of the chemical. Furthermore, EPA does not expect to include exposures to sediment and terrestrial organisms in the risk evaluation because these are pathways under programs of other environmental statutes, administered by EPA, which adequately assess and effectively manage exposures and for which long-standing regulatory and analytical processes already exist (see Section 2.5.3.2).

#### 2.6.2.2 Human Health Hazards

EPA expects to consider and analyze human health hazards as follows:

1) Review reasonably available human health hazard data, including data from alternative test methods (e.g., computational toxicology and bioinformatics; high-throughput screening methods; data on categories and read-across; *in vitro* studies; systems biology).

   Human health studies will be evaluated using the evaluation strategies laid out in the *Application of Systematic Review in TSCA Risk Evaluations*. Human, animal, and mechanistic data will be identified and included as described in the inclusion and exclusion criteria in Appendix H. EPA plans to prioritize the evaluation of mechanistic evidence. Specifically, EPA does not plan to

evaluate mechanistic studies unless needed to clarify questions about associations between carbon tetrachloride and health effects and its relevance to humans. *Systematic Review Approaches and Methods Applied to TSCA Risk Evaluations* describes how studies will be evaluated using specific data evaluation criteria and a predetermined systematic approach. Study results will be extracted and presented in evidence tables by each hazard endpoint. EPA intends to review studies published after the IRIS assessment (see *Carbon tetrachloride (CASRN 56-23-5) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0733) using the approaches and/or methods described in the *Application of Systematic Review in TSCA Risk Evaluations* to ensure that EPA is considering information that has been made available since these assessments were conducted. EPA will also evaluate information in the IRIS assessment using OPPT's structured process described in the document, *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018, 2010). For irritation and sensitization (not addressed in the IRIS assessment), EPA will rely on the ATSDR Toxicological Profile and 2011 OECD SIDS Initial Assessment Profile as a starting point to understand data for this chemical (OECD, 2011; ATSDR, 2005). In addition, EPA intends to conduct a full review of the data collected (see *Carbon tetrachloride (CASRN 56-23-5) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0733) as described in *Application of Systematic Review in TSCA Risk Evaluations* to ensure that EPA is considering information that has been made available since these assessments were conducted.

2) In evaluating reasonably available data, determine whether particular human receptor groups may have greater susceptibility to the chemical's hazard(s) than the general population.

   Reasonably available human health hazard data will be evaluated to ascertain whether some human receptor groups may have greater susceptibility than the general population to carbon tetrachloride hazard(s). Susceptibility of particular human receptor groups to carbon tetrachloride will be determined by evaluating information on factors that influence susceptibility.

3) Conduct hazard identification (the qualitative process of identifying non-cancer and cancer endpoints) and dose-response assessment (the quantitative relationship between hazard and exposure) for identified human health hazard endpoints.

   Human health hazards from acute and chronic exposures will be identified by evaluating the human and animal data that meet the data quality criteria described in the *Application of Systematic Review in TSCA Risk Evaluations* document. Data quality evaluation will be performed on key studies identified from the IRIS assessment (U.S. EPA, 2010) and the ATSDR Toxicological Profile (ATSDR, 2005). Data quality evaluation will also be performed on studies published after 2009 that were identified in the comprehensive literature search and that met the inclusion criteria for full-text screening (see *Systematic Review Approaches and Methods Applied to TSCA Risk Evaluations* for more information). Hazards identified by studies meeting data quality criteria will be grouped by routes of exposure relevant to humans (oral, dermal, inhalation) and by cancer and noncancer endpoints.

   Dose-response assessment will be performed in accordance with methods from EPA technical documents (U.S. EPA, 2011, 2000a, 1994). Dose-response analyses performed for the EPA (2009) IRIS oral and inhalation reference dose determinations may be used if the data meet data quality criteria and if additional information on the identified hazard endpoints are not available or would not alter the analysis.

The cancer mode of action (MOA) determines how cancer risks can be quantitatively evaluated. EPA will evaluate information on genotoxicity and the mode of action for all cancer endpoints to determine the appropriate approach for quantitative cancer assessment in accordance with the U.S. EPA Guidelines for Carcinogen Risk Assessment (ATSDR, 2005).

4) Derive points of departure (PODs) where appropriate; conduct benchmark dose modeling depending on the available data. Adjust the PODs as appropriate to conform (e.g., adjust for duration of exposure) to the specific exposure scenarios evaluated.

   Hazard data will be evaluated to determine the type of dose-response modeling that is applicable. Where modeling is feasible, a set of dose-response models that are consistent with a variety of potentially underlying biological processes will be applied to empirically model the dose-response relationships in the range of the observed data consistent with the EPA *Benchmark Dose Technical Guidance Document*. Where dose-response modeling is not feasible, NOAELs or LOAELs will be identified.

   EPA will evaluate whether the available PBPK and empirical kinetic models are adequate for route-to-route and interspecies extrapolation of the POD, or for extrapolation of the POD to appropriate exposure durations for the risk evaluation.

5) Consider the route(s) of exposure (oral, inhalation, dermal), available route-to-route extrapolation approaches, available biomonitoring data and available approaches to correlate internal and external exposures to integrate exposure and hazard assessment.

   At this stage of review EPA believes there will be sufficient data to conduct dose-response analysis and benchmark dose modeling for both inhalation and oral routes of exposure. If sufficient dermal toxicity studies are not identified in the literature search to assess risks from dermal exposures, then a route-to-route extrapolation from the inhalation and oral toxicity studies would be needed to assess systemic risks from dermal exposures. Without an adequate PBPK model, the approaches described in the EPA guidance document *Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part E, Supplemental Guidance for Dermal Risk Assessment)* may be applied. These approaches may be able to further inform the relative importance of dermal exposures compared with other routes of exposure.

6) Evaluate the weight of the evidence of human health hazard data.

   EPA will rely on the weight of the scientific evidence when evaluating and integrating human health hazard data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

### 2.6.3 Risk Characterization

Risk characterization is an integral component of the risk assessment process for both ecological and human health risks. EPA will derive the risk characterization in accordance with EPA's *Risk Characterization Handbook* (U.S. EPA, 2000b). As defined in EPA's Risk Characterization Policy, "the risk characterization integrates information from the preceding components of the risk evaluation and synthesizes an overall conclusion about risk that is complete, informative and useful for decision makers." Risk characterization is considered to be a conscious and deliberate process to bring all

important considerations about risk, not only the likelihood of the risk but also the strengths and limitations of the assessment, and a description of how others have assessed the risk into an integrated picture.

Risk characterization at EPA assumes different levels of complexity depending on the nature of the risk assessment being characterized. The level of information contained in each risk characterization varies according to the type of assessment for which the characterization is written. Regardless of the level of complexity or information, the risk characterization for TSCA risk evaluations will be prepared in a manner that is transparent, clear, consistent and reasonable (TCCR) (U.S. EPA, 2000b). EPA will also present information in this section consistent with approaches described in the *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act* (82 FR 33726). EPA will also present information in this section consistent with approaches described in the Risk Evaluation Framework Rule. For instance, in the risk characterization summary, EPA will further carry out the obligations under TSCA section 26; for example, by identifying and assessing uncertainty and variability in each step of the risk evaluation, discussing considerations of data quality such as the reliability, relevance and whether the methods utilized were reasonable and consistent, explaining any assumptions used, and discussing information generated from independent peer review. EPA will also be guided by EPA's Information Quality Guidelines (U.S. EPA, 2002) as it provides guidance for presenting risk information. Consistent with those guidelines, in the risk characterization, EPA will also identify: (1) Each population addressed by an estimate of applicable risk effects; (2) the expected risk or central estimate of risk for the PESS affected; (3) each appropriate upper-bound or lower-bound estimate of risk; (4) each significant uncertainty identified in the process of the assessment of risk effects and the studies that would assist in resolving the uncertainty; and (5) peer reviewed studies known to the Agency that support, are directly relevant to, or fail to support any estimate of risk effects and the methodology used to reconcile inconsistencies in the scientific information.

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# APPENDICES

## Appendix A REGULATORY HISTORY

### A.1 Federal Laws and Regulations

**Table_Apx A-1. Federal Laws and Regulations**

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| **EPA Regulations** | | |
| TSCA - Section 6(b) | EPA is directed to identify and begin risk evaluations on 10 chemical substances drawn from the 2014 update of the TSCA Work Plan for Chemical Assessments. | Carbon tetrachloride is on the initial list of chemicals to be evaluated for unreasonable risk under TSCA (81 FR 91927, December 19, 2016). |
| TSCA - Section 8(a) | The TSCA section 8(a) CDR Rule requires manufacturers (including importers) to give EPA basic exposure-related information on the types, quantities and uses of chemical substances produced domestically and imported into the United States. | Carbon tetrachloride manufacturing (including importing), processing and use information is reported under the CDR Rule (76 FR 50816, August 16, 2011). |
| TSCA - Section 8(b) | EPA must compile, keep current and publish a list (the TSCA Inventory) of each chemical substance manufactured, processed, or imported in the United States. | Carbon tetrachloride was on the initial TSCA Inventory and therefore was not subject to EPA's new chemicals review process under TSCA section 5 (60 FR 16309, March 29, 1995). |
| TSCA - Section 8(d) | Provides EPA with authority to issue rules requiring producers, importers and (if specified) processors of a chemical substance or mixture to submit lists and/or copies of health and safety studies. | Two submissions received (1947-1994) (U.S. EPA, ChemView. Accessed April 13, 2017). |
| TSCA - Section 8(e) | Manufacturers (including imports), processors and distributors must immediately notify EPA if they obtain information that supports the conclusion that a chemical substance or mixture presents a substantial risk of injury to health or the environment. | Three submissions received (1992-2010) (U.S. EPA, ChemView. Accessed April 13, 2017). |
| TSCA - Section 4 | Provides EPA with authority to issue rules and orders requiring manufacturers (including importers) and processors to test chemical substances and mixtures. | Seven section 4 notifications received for carbon tetrachloride: two acute aquatic toxicity studies, one bioaccumulation report and four monitoring reports (1978-1980) |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | | (U.S. EPA, ChemView. Accessed April 13, 2017). |
| EPCRA - Section 313 | Requires annual reporting from facilities in specific industry sectors that employ 10 or more full time equivalent employees and that manufacture, process, or otherwise use a TRI-listed chemical in quantities above threshold levels. | Carbon tetrachloride is a listed substance subject to reporting requirements under 40 CFR 372.65 effective as of January 1, 1987. |
| Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) - Sections 3 and 6 | FIFRA governs the sale, distribution and use of pesticides. Section 3 of FIFRA generally requires that pesticide products be registered by EPA prior to distribution or sale. Pesticides may only be registered if, among other things, they do not cause "unreasonable adverse effects on the environment." Section 6 of FIFRA provides EPA with the authority to cancel pesticide registrations if either (1) the pesticide, labeling, or other material does not comply with FIFRA; or (2) when used in accordance with widespread and commonly recognized practice, the pesticide generally causes unreasonable adverse effects on the environment. | Use of carbon tetrachloride as a grain fumigant was banned under FIFRA in 1986 (51 FR 41004, November 12, 1986). |
| Federal Food, Drug, and Cosmetic Act (FFDCA) - Section 408 | FFDCA governs the allowable residues of pesticides in food. Section 408 of the FFDCA provides EPA with the authority to set tolerances (rules that establish maximum allowable residue limits), or exemptions from the requirement of a tolerance, for all residues of a pesticide (including both active and inert ingredients) that are in or on food. Prior to issuing a tolerance or exemption from tolerance, EPA must determine that the tolerance or exemption is "safe." Sections 408(b) and (c) of the FFDCA define "safe" to mean the Agency has a reasonable certainty that no harm will result from aggregate exposures to the pesticide residue, including all dietary exposure and all other exposure (e.g., non-occupational exposures) for which | EPA removed carbon tetrachloride from its list of pesticide product inert ingredients used in pesticide products in 1998 (63 FR 34384, June 24, 1998). |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | there is reliable information. Pesticide tolerances or exemptions from tolerance that do not meet the FFDCA safety standard are subject to revocation. In the absence of a tolerance or an exemption from tolerance, a food containing a pesticide residue is considered adulterated and may not be distributed in interstate commerce. | |
| CAA - Section 112(b) | This section lists 189 HAPs that must be addressed by EPA and includes authority for EPA to add or delete pollutants. EPA may, by rule, add pollutants that present, or may present, a threat of adverse human health effects or adverse environmental effects. | Lists carbon tetrachloride as a HAP (70 FR 75047, December 19, 2005). |
| CAA - Section 112(d) | Directs EPA to establish, by rule, National Emission Standards (NESHAPs) for each category or subcategory of major sources and area sources of HAPs. The standards must require the maximum degree of emission reduction that EPA determines is achievable by each particular source category. This is generally referred to as maximum achievable control technology (MACT). | There are a number of source-specific NESHAPs for carbon tetrachloride, including:<br>Rubber tire manufacturing (67 FR 45588, July 9, 2002)<br>Chemical Manufacturing Area Sources (74 FR 56008, October 29, 2009)<br>Organic HAP from the Synthetic Organic Chemical Manufacturing and Other Processes (59 FR 19402, April 22,1994),<br>Halogenated solvent cleaning operations (59 FR 61801, December 2, 1994)<br>Wood Furniture Manufacturing Operations (60 FR 62930, December 7,1995)<br>Group 1 Polymers and Resins (61 FR 46906, September 5, 1996)<br>Plywood and Composite Wood Products (69 FR 45944, July 30, 2004) |
| CAA – Sections 112(d) and 112(f) | Risk and technology review (RTR) of section 112(d) MACT standards. Section 112(f)(2) requires EPA to conduct risk assessments for each source category subject to section 112(d) MACT standards, and to determine if additional | EPA has promulgated a number of RTR NESHAP (e.g., the RTR NESHAP for Group 1 Polymers and Resins (76 FR 22566; April 21, 2011)) and will do so, as required, |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | standards are needed to reduce remaining risks. Section 112(d)(6) requires EPA to review and revise the MACT standards, as necessary, taking into account developments in practices, processes and control technologies. | for the remaining source categories with NESHAP. |
| CAA - Section 604 | Establishes a mandatory phase-out of ozone depleting substances. | The production and import of carbon tetrachloride for non-feedstock domestic uses was phased out in 1996 (58 FR 65018, December 10, 1993). However, this restriction does not apply to production and import of amounts that are transformed or destroyed. 40 CFR 82.4. "Transform" is defined as "to use and entirely consume (except for trace quantities) a controlled substance in the manufacture of other chemicals for commercial purposes." 40 CFR 82.3. |
| CWA - Section 304(a)(1) | Requires EPA to develop and publish ambient water quality criteria (AWQC) reflecting the latest scientific knowledge on the effects on human health that may be expected from the presence of pollutants in any body of water. | In 2015, EPA published updated AWQC for carbon tetrachloride, including recommendations for "water + organism" and "organism only" human health criteria for states and authorized tribes to consider when adopting criteria into their water quality standards. |
| CWA – Sections 301(b), 304(b), 306, and 307(b) | Requires establishment of Effluent Limitations Guidelines and Standards for conventional, toxic, and non-conventional pollutants. For toxic and non-conventional pollutants, EPA identifies the best available technology that is economically achievable for that industry after considering statutorily prescribed factors and sets regulatory requirements based on the performance of that technology. | |
| CWA - Section 307(a) | Establishes a list of toxic pollutants or combination of pollutants under the CWA. The statute specifies a list of families of toxic pollutants also listed in the Code of Federal Regulations at 40 | Carbon tetrachloride is designated as a toxic pollutant under section 307(a)(1) of the CWA and as such is subject to effluent limitations. |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | CFR 401.15. The "priority pollutants" specified by those families are listed in 40 CFR part 423, Appendix A. These are pollutants for which best available technology effluent limitations must be established on either a national basis through rules, see section 301(b), 304(b), 307(b), 306, or on a case-by-case best professional judgment basis in NPDES permits. CWA 402(a)(1)(B). | |
| SDWA - Section 1412 | Requires EPA to publish a non-enforceable maximum contaminant level goals (MCLGs) for contaminants which 1. may have an adverse effect on the health of persons; 2. are known to occur or there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern; and 3. in the sole judgment of the Administrator, regulation of the contaminant presents a meaningful opportunity for health risk reductions for persons served by public water systems. When EPA publishes an MCLG, EPA must also promulgate a National Primary Drinking Water Regulation (NPDWR) which includes either an enforceable maximum contaminant level (MCL), or a required treatment technique. Public water systems are required to comply with NPDWRs. | Carbon tetrachloride is subject to National Primary Drinking Water Regulations (NPDWR) under SDWA and EPA has set a MCLG of zero and an enforceable MCL of 0.005 mg/L (56 FR 3526 January 30, 1991). |
| Comprehensive Environmental Response, Compensation and Liability Act (CERCLA) - Sections 102(a) and 103 | Authorizes EPA to promulgate regulations designating as hazardous substances those substances which, when released into the environment, may present substantial danger to the public health or welfare or the environment. EPA must also promulgate regulations establishing the quantity of any hazardous substance the release of which must be reported under Section 103. Section 103 requires persons in charge of vessels or facilities to report to the National Response Center if they have | Carbon tetrachloride is a hazardous substance under CERCLA. Releases of carbon tetrachloride in excess of 10 pounds must be reported (40 CFR 302.4). |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | knowledge of a release of a hazardous substance above the reportable quantity threshold. | |
| RCRA - Section 3001 | Directs EPA to develop and promulgate criteria for identifying the characteristics of hazardous waste, and for listing hazardous waste, taking into account toxicity, persistence, and degradability in nature, potential for accumulation in tissue, and other related factors such as flammability, corrosiveness, and other hazardous characteristics. | Carbon tetrachloride is included on the list of hazardous wastes pursuant to RCRA 3001. Two categories of carbon tetrachloride wastes are considered hazardous: discarded commercial chemicals (U211) (40 CFR 261.31(a)), and spent degreasing solvent (F001) (40 CFR 261.33(f)) (45 FR 33084 May 19, 1980).<br><br>RCRA solid waste that leaches 0.5 mg/L or more carbon tetrachloride when tested using the TCLP leach test is RCRA hazardous (D019) under 40 CFR 261.24 (55 FR 11798 March 29, 1990).<br><br>In 2013, EPA modified its hazardous waste management regulations to conditionally exclude solvent-contaminated wipes that have been cleaned and reused from the definition of solid waste under RCRA (40 CFR 261.4(a)(26)) (78 FR 46447, July 31, 2013). |
| **Other Federal Regulations** | | |
| Federal Hazardous Substance Act (FHSA) | Requires precautionary labeling on the immediate container of hazardous household products and allows the Consumer Product Safety Commission (CPSC) to ban certain products that are so dangerous or the nature of the hazard is such that required labeling is not adequate to protect consumers. | Use of carbon tetrachloride in consumer products was banned in 1970 by the CPSC (16 CFR 1500.17). |
| FFDCA | Provides the U.S. Food and Drug Administration (FDA) with authority to oversee the safety of food, drugs and cosmetics. | The FDA regulates carbon tetrachloride in bottled water. The maximum permissible level of carbon tetrachloride in bottled water is 0.005 mg/L (21 CFR 165.110). |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | | All medical devices containing or manufactured with carbon tetrachloride must contain a warning statement that the compound may destroy ozone in the atmosphere (21 CFR 801.433).<br>Carbon tetrachloride is also listed as an "Inactive Ingredient for approved Drug Products" by FDA (FDA Inactive Ingredient Database. Accessed April 13, 2017). |
| OSHA | Requires employers to provide their workers with a place of employment free from recognized hazards to safety and health, such as exposure to toxic chemicals, excessive noise levels, mechanical dangers, heat or cold stress, or unsanitary conditions.<br><br>Under the Act, OSHA can issue occupational safety and health standards including such provisions as permissible exposure limits (PELs), exposure monitoring, engineering and administrative control measures, and respiratory protection. | In 1970, OSHA issued occupational safety and health standards for carbon tetrachloride that included a PEL of 10 ppm TWA, exposure monitoring, control measures and respiratory protection (29 CFR 1910.1000).<br><br>OSHA prohibits all workplaces from using portable fire extinguishers containing carbon tetrachloride (29 CFR 1910.157(c)(3)). |
| Atomic Energy Act | The Atomic Energy Act authorizes the Department of Energy to regulate the health and safety of its contractor employees. | 10 CFR 851.23, Worker Safety and Health Program, requires the use of the 2005 ACGIH TLVs if they are more protective than the OSHA PEL. The 2005 TLV for carbon tetrachloride is 5 ppm (8hr Time Weighted Average) and 10 ppm Short Term Exposure Limit (STEL). |

## A.2 State Laws and Regulations

**Table_Apx A-2. State Laws and Regulations**

| State Actions | Description of Action |
|---|---|
| **State agencies of interest** | |
| State permissible exposure limits | California PEL: 12.6 mg/L (Cal Code Regs. Title 8, section 5155), Hawaii PEL: 2 ppm (Hawaii Administrative Rules section 12-60-50). |

| State Actions | Description of Action |
|---|---|
| **State agencies of interest** | |
| State Right-to-Know Acts | Massachusetts (454 Code Mass. Regs. section 21.00), New Jersey (8:59 N.J. Admin. Code section 9.1), Pennsylvania (34 Pa. Code section 323). |
| State air regulations | Allowable Ambient Levels (AAL): Rhode Island (12 R.I. Code R. 031-022), New Hampshire (RSA 125-I:6, ENV-A Chap. 1400). |
| State drinking water standards and guidelines | Arizona (14 Ariz. Admin. Register 2978, August 1, 2008), California (Cal Code Regs. Title 26, section 22-64444), Delaware (Del. Admin. Code Title 16, section 4462), Connecticut (Conn. Agencies Regs. section 19-13-B102), Florida (Fla. Admin. Code R. Chap. 62-550), Maine (10 144 Me. Code R. Chap. 231), Massachusetts (310 Code Mass. Regs. section 22.00), Minnesota (Minn R. Chap. 4720), New Jersey (7:10 N.J Admin. Code section 5.2), Pennsylvania (25 Pa. Code section 109.202), Rhode Island (14 R.I. Code R. section 180-003), Texas (30 Tex. Admin. Code section 290.104). |
| Other | In California, carbon tetrachloride was added to the Proposition 65 list in 1987 (Cal. Code Regs. Title 27, section 27001).<br>Carbon tetrachloride is on the MA Toxic Use Reduction Act (TURA) list of 1989 (301 Code Mass. Regs. section 41.03). |

## A.3 International Laws and Regulations

**Table_Apx A-3. Regulatory Actions by Other Governments and Tribes**

| Country/Organization | Requirements and Restrictions |
|---|---|
| **Regulatory Actions by other Governments and Tribes** | |
| Montreal Protocol | Carbon tetrachloride is considered an ozone depleting substance (ODS) and its production and use are controlled under the 1987 Montreal Protocol on Substances That Deplete the Ozone Layer and its amendments (Montreal Protocol Annex B – Group II). |
| Canada | Carbon tetrachloride is on the Canadian List of Toxic Substances (CEPA 1999 Schedule 1). Other regulations include:<br>Federal Halocarbon Regulations, 2003 (SOR/2003-289).<br>ODS Regulations, 1998 (SOR/99-7). |
| European Union (EU) | Carbon tetrachloride was evaluated under the 2012 Community rolling action plan (CoRAP) under regulation (European Commission [EC]) No |

| Country/Organization | Requirements and Restrictions |
|---|---|
| | 1907/2006 - REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) ECHA database. Accessed April 18, 2017).<br><br>Carbon tetrachloride is restricted by regulation (EC) No 2037/2000 on substances that deplete the ozone layer. |
| Australia | Carbon tetrachloride was assessed under Environment Tier II of the Inventory Multi-Tiered Assessment and Prioritisation (IMAP), and there have been no reported imports of the chemical as a feedstock in the last 10 years (National Industrial Chemicals Notification and Assessment Scheme, NICNAS, 2017, *Environment Tier II Assessment for Methane, Tetrachloro-*. Accessed April, 18 2017). |
| Japan | Carbon tetrachloride is regulated in Japan under the following legislation:<br>• Industrial Safety and Health Act (ISHA)<br>• Act on the Evaluation of Chemical Substances and Regulation of Their Manufacture, etc. (Chemical Substances Control Law (CSCL))<br>• Act on Confirmation, etc. of Release Amounts of Specific Chemical Substances in the Environment and Promotion of Improvements to the Management Thereof<br>• Poisonous and Deleterious Substances Control Act<br>• Act on the Protection of the Ozone Layer through the Control of Specified Substances and Other Measures<br>• Air Pollution Control Law<br>• Water Pollution Control Law<br>• Soil Contamination Countermeasures Act<br><br>(National Institute of Technology and Evaluation (NITE) Chemical Risk Information Platform (CHIRP). Accessed April 13, 2017). |
| Australia, Austria, Belgium, Canada, Denmark, EU, Finland, France, Germany, Ireland, Israel, Japan, Latvia, New Zealand, People's Republic of China, Poland, Singapore, South Korea, Spain, Sweden, Switzerland, United Kingdom | Occupational exposure limits (OELs) for carbon tetrachloride. (GESTIS International limit values for chemical agents (Occupational exposure limits, OELs) database. Accessed April 18, 2017). |
| Basel Convention | Halogenated organic solvents (Y41) are listed as a category of waste under the Basel Convention-Annex I. Although the United States is not currently a party to the Basel Convention, this treaty still affects U.S. importers and exporter. |

| Country/Organization | Requirements and Restrictions |
|---|---|
| OECD Control of Transboundary Movements of Wastes Destined for Recovery Operations | Halogenated organic solvents (A3150) are listed as a category of waste subject to The Amber Control Procedure under Council Decision C (2001) 107/Final. |

# Appendix B SECOND SCREENING OF PEER-REVIEWED LITERATURE ON CARBON TETRACHLORIDE

This appendix describes the process used to re-screen the references identified as "on topic" in the first screening round, including prioritizing the literature for screening and the re-categorization criteria applied during the re-screening and tagging.

## B.1 Scope of the Literature Re-screening

The aim of the first literature screening phase was to include all potentially relevant references that met the screening criteria. A more detailed review of the "on topic" references revealed a large number of animal studies that were likely to be of limited use for the following reasons:

- The aim of the study was to induce a disease state in an animal (e.g., cirrhosis, fibrosis, organ damage: liver, kidney, testes and others) rather than evaluate the effects of carbon tetrachloride exposure in animals
- Exposure was often via injection

In order to refine the search results for full-text screening, the inclusion/exclusion criteria were revised to remove these studies from the "on topic" pool.

### B.1.1 Identifying Studies for Title/Abstract Re-screening

References (a total of 2,244) that were tagged to one or more of the categories below were identified for re-screening. These were studies where carbon tetrachloride-treated animals were used as a model for disease (e.g., cirrhosis, liver fibrosis) and/or in which the therapeutic or ameliorative properties of different compounds were evaluated in carbon tetrachloride-treated animals:

- Animal Hazard ID
- Health Effects (in addition to Animal Hazard ID)
  - Hepatic non-cancer
  - Renal non-cancer
  - Neurological non-cancer
  - Reproductive/Developmental non-cancer
  - Immunological non-cancer
  - Cardiovascular non-cancer
  - Gastrointestinal non-cancer
  - Irritation

  - Respiratory non-cancer
  - Carcinogenicity
  - Other non-cancer health effect
- ADME
- Susceptibility
- MOA
- Unable to Determine

References tagged to "human hazard ID" were not included for re-screening, since they met the screening criteria as "on topic". References tagged to "foreign language" were not considered a priority for re-screening and so were not included for re-screening. Similarly, references included in the IRIS assessment on carbon tetrachloride were not included in the re-screening since those studies conducted on carbon tetrachloride were "on topic", as explained in the Literature Search Strategy documents.

## B.2 Prioritizing References for Re-Screening

### B.2.1 First Round of Prioritization for Re-screening

A keyword search and topic extraction (i.e., a form of unsupervised machine learning) were used to identify a priority batch of 690 studies from the 2,244 studies eligible for re-screening (see Section B.1.1Identifying Studies for Title/Abstract Re-screening). Topic extraction was conducted in ICF's Document Classification and Topic Extraction Resource or DoCTER which includes functions for supervised and unsupervised machine learning.

#### B.2.1.1 Keyword Search Method

A set of keywords was derived from the titles and abstracts of the *on-topic* references to be tagged to *off-topic* during the second screening. The following references are examples of the types of studies that EPA identified as *off-topic*:

- HERO ID 3482047; Preethi, KCK, R. (2009). Hepato and reno protective action of *Calendula officinalis* L. flower extract. Indian journal of experimental biology 47: 163-168.

- HERO ID 3481928; Ozturk, FG, M. Ates, B. Ozturk, I. C. Cetin, A. Vardi, N. Otlu, A. Yilmaz, I. (2009). Protective effect of apricot (*Prunus armeniaca* L.) on hepatic steatosis and damage induced by carbon tetrachloride in Wistar rats. The British journal of nutrition 102: 1767-1775.

- HERO ID 3481815; Murugesan, GSS, M. Jayabalan, R. Binupriya, A. R. Swaminathan, K. Yun, S. E. (2009). Hepatoprotective and curative properties of Kombucha tea against carbon tetrachloride-induced toxicity. Journal of microbiology and biotechnology 19: 397-402.

- HERO ID 894818; Quan, JP, L. Wang, X. Li, T. Yin, X. (2009). *Rossicaside B* protects against carbon tetrachloride-induced hepatotoxicity in mice. Basic & Clinical Pharmacology & Toxicology Online Pharmacology Online 105: 380-386.

- HERO ID 1454032; Gao, JS, C. R. Yang, J. H. Shi, J. M. Du, Y. G. Zhang, Y. Y. Li, J. H. Wan, H. T. (2011). Evaluation of the hepatoprotective and antioxidant activities of *Rubus parvifolius* L. Journal of Zhejiang University Science B 12: 135-142.

The keyword search, conducted in EndNote on the 2,244 studies eligible for re-screening (see F-1.1. Identifying Studies for Title/Abstract Re-screening) returned 587 studies using the following search strategy:

(hepatoprotective OR hepato protective OR hepatoprotection OR renoprotective OR reno protective OR renoprotection)

#### B.2.1.2 DoCTER Method

To identify a priority set of studies for re-screening, we also used DoCTER's topic extraction function. Unsupervised machine learning or topic extraction does not require a training dataset or seed studies. DoCTER clusters or groups a list of titles and abstracts using automated text analysis on titles and abstracts into a user-specified number of clusters. Studies in the same cluster are expected to be more similar to one another based on automated text analysis of the titles and abstracts. DoCTER also produces a set of keywords for each cluster that serves as a *topic signature* and provides insight into the studies contained within.

Topic extraction was used to cluster all 2,749 *on topic* studies into 10 topic clusters using the k-means algorithm and a word grouping length of one word. The terms copyright, publication, and abstract were added as stop words and not included in the DoCTER analysis. Clusters 3 and 5 were prioritized for re-screening and were combined with the results of the keyword search described above (Table_Apx B-1). The 690 studies identified from the keyword search and topic extraction clusters 3 and 5 were re-screened.

**Table_Apx B-1. Topic Extraction Results for 2,749 On-topic Studies using 10 Clusters and k-means Algorithm**

| Cluster | Number of Results | Keywords |
|---|---|---|
| 1 | 157 | factor \| nf \| fibrosis \| expression \| inflammatory \| il \| tnf \| hepatic \| anti \| rats \| levels \| ccl \| kg \| oxidative \| effects \| treatment \| serum \| significantly \| aminotransferase \| injury |
| 2 | 98 | stem \| marrow \| bone \| cells \| mscs \| transplantation \| mesenchymal \| derived \| fibrosis \| human \| cell \| mice \| strong \| transplanted \| bm \| msc \| br \| injured \| differentiation \| cirrhosis |
| 3 | 200 | antioxidant \| **hepatoprotective** \| glutathione \| activities \| sod \| activity \| gsh \| ast \| superoxide \| alt \| mda \| ccl \| aminotransferase \| oxidative \| dismutase \| serum \| extract \| injury \| levels \| mice |
| 4 | 96 | mir \| fibrosis \| expression \| tgf \| hscs \| hsc \| activation \| hepatic \| cells \| stellate \| role \| factor \| cell \| mirnas \| proliferation \| growth \| fibrotic \| signaling \| microrna \| fibrogenesis |
| 5 | 266 | **hepatoprotective** \| extract \| activity \| antioxidant \| rats \| strong \| extracts \| br \| damage \| kg \| hepatotoxicity \| leaves \| effect \| mg \| silymarin \| serum \| significant \| total \| activities \| scavenging |

| Cluster | Number of Results | Keywords |
|---|---|---|
| 6 | 370 | fibrosis \| mice \| cells \| hepatic \| stellate \| expression \| hscs \| activation \| strong \| injury \| cell \| br \| chronic \| hsc \| type \| activated \| role \| collagen \| inflammation \| wild |
| 7 | 317 | kg \| rats \| ccl \| group \| mg \| oxidative \| antioxidant \| groups \| glutathione \| ml \| protective \| effect \| damage \| treated \| activities \| serum \| treatment \| dose \| lipid \| control |
| 8 | 110 | cirrhosis \| cirrhotic \| portal \| hypertension \| rats \| br \| strong \| pressure \| bacterial \| intestinal \| resistance \| arterial \| hepatic \| vascular \| fibrosis \| translocation \| increased \| expression \| gut \| ascites |
| 9 | 867 | rats \| injury \| mice \| exposure \| hepatotoxicity \| acute \| effect \| rat \| effects \| fibrosis \| hepatic \| metabolism \| toxicity \| damage \| cell \| role \| lipid \| response \| dna \| hepatocytes |
| 10 | 268 | strong \| br \| group \| fibrosis \| lt \| model \| rats \| groups \| expression \| control \| hepatic \| 05 \| significantly \| weeks \| methods \| normal \| levels \| 01 \| results \| tgf |

#### B.2.1.3 List of Prioritized References for Re-Screening

References identified using both the keyword search and DoCTER's topic extraction were combined and duplicate references removed to identify a priority batch of 690 studies from the 2,244 studies eligible for re-screening (see Section B.1.1). Note the batch of studies eligible for re-screening excludes studies cited in the IRIS assessment or tagged to human hazard identification or foreign-language.

### B.2.2 Second Round of Prioritization for Re-screening

#### B.2.2.1 Keyword Search Method

A second keyword search was conducted in EndNote on the 1,566 remaining studies eligible for re-screening. The 1,566 studies (2,244 studies eligible for screening (see Section B.1.1) minus 678 studies screened in the first round of prioritization; note 12 studies, primarily foreign-language, were screened in the batch of 690 from the first round of screening and were not included in the 2,244 studies eligible for re-screening.) The following search strategy returned 602 studies:

(((carbon tetrachloride-induced OR ccl4-induced) AND (cirrhosis OR fibrosis OR liver damage OR steatosis)) OR (oxidative stress OR oxidative damage OR antioxidant*))

#### B.2.2.2 DoCTER Method

For the second round of prioritization we used supervised clustering with an ensemble approach. With supervised clustering, DoCTER clusters or groups a list of titles and abstracts plus seed studies using automated text analysis on titles and abstracts into a user-specified number of clusters exactly as described above in Section B.2.1. Seed studies may be positive or negative. Positive seeds or known relevant studies are used to provide a quantitative signal as to which clusters to prioritize. Negative seeds or known *off-topic* studies are optional and are used to predict precision for each cluster.

Supervised clustering using an ensemble approach refers to running topic extraction with seeds using multiple models. A model refers to an algorithm–cluster size combination (e.g., using k-means algorithm to group into 10 clusters or KM-10 as a model). The results from each model run are compiled and each reference is given a score based on how many models predicted it to be relevant. Scores for each reference range from 0 (i.e., study not predicted relevant by any model) to n where n is the number of models used and is the maximum score a study can receive.

We ran the 1,566 eligible studies through six models using the k-means and NMF algorithms and 10, 20, and 30 clusters (i.e., KM-10, KM-20, KM-30, NMF-10, NMF-20, NMF-30) with 50 positive seeds. Seeds (references) were randomly selected from results of the first round of re-screening i.e., references that met the exclusion criteria (see Section B.2). A positive seed is a study used to find similar studies and in this context positive seeds are studies that were excluded or re-tagged as not on topic in the first round of re-screening. Supervised clustering was used here to identify additional studies that may be excluded from the on topic pool of carbon tetrachloride studies.

Recall was set to 0.90 in DoCTER, such that for each model clusters were included until at least 90 percent of seeds were captured. Using all six models 98 percent of seeds were actually captured and 493 studies were identified as a priority for re-screening by one or more models (see Table below).

**Table_Apx B-2. Supervised Clustering Results for 1,566 On-topic Studies Using Ensemble Approach (k-means and NMF Algorithms x 10, 20, and 30 clusters), 50 Seeds, and 0.9 Recall**

| Group | Cluster Score | Number of Studies | Running Total |
|---|---|---|---|
| A | 6 | 7 | 7 |
| B | 5 | 24 | 31 |
| C | 4 | 44 | 75 |
| D | 3 | 80 | 155 |
| E | 2 | 106 | 261 |
| F | 1 | 232 | 493 |
| **Total** | | **493** | |
| **Notes:**<br>Studies with a cluster score of 6 were predicted relevant by all six models | | | |

### B.2.2.3 List of Prioritized References for Re-Screening

References identified using both the second keyword search (602) and supervised clustering in DoCTER (493) were combined and duplicate references removed to identify 782 studies from the 1,566 studies eligible for re-screening (see Section B.1.1). These references were screened in two batches; 493 from DoCTER and 289 from the key word search method (duplicates removed). Note the batch of studies eligible for re-screening excludes studies cited in the IRIS assessment or tagged to human hazard identification or foreign-language.

Following the second round of prioritization, 784 studies remained. These were rescreened against the criteria below.

## B.3 Re-screening Criteria and Process

This section describes the criteria applied during the second screening of the literature, the new criteria applied and the process used to conduct the screening.

### B.3.1 Re-screening Process

All references were re-screened in Distiller. The same screeners involved in the first round of screening were involved in re-screening the literature. The screening process proceeded as follows:

- Batches of prioritized literature were imported into Distiller without the original tags from the first screening round.
- An experienced screener trialed the screening instructions and amended them as needed, prior to conducting the full screening exercise.
- Screeners were briefed on how to conduct the screening and given a set of instructions prior to commencing the screening.
- An experienced screener was available to answer any questions and provide feedback to screeners.
- Each study was screened independently by two reviewers. Two other invididuals not involved in the screening resolved the conflicts.

### B.3.2 Re-screening Criteria

Studies were considered *off-topic* if:

Carbon tetrachloride was used to induce a non-cancer effect (e.g., Liver effects: hepatotoxicity, hepatic steatosis, cirrhosis, liver injury, liver fibrosis; renal/kidney effects, repro/developmental effects: testicular injury and others) to evaluate the protective or therapeutic effects of another compound (e.g., plant extracts, drugs, antioxidants, or medicinal herbs).

Carbon tetrachloride was used as a model to induce a particular disease state in an animal. Often includes studies where carbon tetrachloride was given to animals via injection to induce cirrhosis, liver fibrosis or oxidative damage in the testes or brain. Often the study then evaluates either the MOA or ameliorative effects of a therapeutic compound.

Carbon tetrachloride was used to induce toxicity or organ damage by measuring levels of e.g., serum liver enzymes, markers of oxidative stress or damage in a particular organ (liver, kidney, testes, brain), or histological changes, prior to, or after administering another (therapeutic) compound.

Carbon tetrachloride was used to induce fibrosis or cirrhosis and treatment was given after as a way to treat that effect.

Studies that do not meet the exclusion criteria above were also considered *off-topic* if:

- Carbon tetrachloride was not specifically mentioned in the title or abstract
- Incorrectly tagged as *on-topic* during first round screening

## Table_Apx B-3. Overview of Complete (Revised) Tagging Structure for Carbon Tetrachloride

| Tag Category | Inclusion/Exclusion Criteria | Example Keywords |
|---|---|---|
| **ON TOPIC, GENERAL HUMAN HEALTH TAGS** | | |
| Animal Hazard ID | **INCLUDE:**<br>• Studies evaluating animal health effects resulting from controlled exposure to the chemical in mammals such as primates, rodents, dog, rabbit, and mink.<br>• **Also choose applicable health effect tags in next section "Carbon Tetrachloride Health Effect Tags"<br>**EXCLUDE:**<br>• Studies where carbon tetrachloride was used to induce a particular disease state or noncancer effect in an animal to (e.g., **Liver effects:** hepatotoxicity, hepatic steatosis, cirrhosis, liver injury, liver fibrosis; **renal/kidney effects**; **repro/developmental effects:** testicular injury, and others) to:<br>o evaluate the protective or therapeutic effects of another compound (e.g., plant extracts, drugs, antioxidants, or medicinal herbs) or,<br>• Studies where carbon tetrachloride was used in addition to other treatments (e.g., 2-AAf, LPS, or partial hepatectomy) in order to cause a specific effect or response in the liver<br>• Studies that evaluated carbon tetrachloride-induced toxicity or organ damage by measuring levels of e.g., serum liver enzymes, markers of oxidative stress or damage in a particular organ (liver, kidney, testes, brain), or histological changes, prior to, or after administering another (therapeutic) compound. | chronic; developmental; incidence; NOEL/LOEL; NOAEL/LOAEL; dose; response |
| MOA | **INCLUDE:**<br>• Studies evaluating the mode of action (MOA) of a chemical (i.e., molecular events occurring after exposure that may contribute to the development of adverse health effects) in animals and humans<br>• Studies in knockout mice<br>• Assessment of hormone levels or gland function, immune system parameters<br>**Also choose applicable MOA tags in section below under "Carbon Tetrachloride MOA Tags"<br>**EXCLUDE:**<br>• Studies that evaluated carbon tetrachloride-induced toxicity or organ damage by measuring levels of e.g., serum liver enzymes, markers of oxidative stress or damage in a particular organ (liver, kidney, testes, brain), or histological changes, prior to, or after administering another (therapeutic) compound. | *in vitro* models, genomics, proteomics, genotoxicity, indirect genotoxicity, changes in gene expression or mRNA levels |
| **ON TOPIC, CARBON TETRACHLORIDE (CCL4) HEALTH EFFECT TAGS** | | |
| Hepatic non-cancer | **INCLUDE**:<br>• Studies evaluating hepatic effects in the liver, biliary tract, gall bladder | fatty degeneration, cirrhosis, fibrosis, necrosis, hypertrophy, hyperplasia, proliferation, increased/decreased liver enzymes, bile acids, cholesterol and triglycerides in serum/blood, increased/decreased liver weight, jaundice, vacuolization |
| Renal non-cancer | **INCLUDE:**<br>• Studies evaluating renal effects in the kidney, bladder, ureter and related | nephropathy, oliguria, increased/decreased blood urea nitrogen, nephritis, nephrosis, hyaline droplet formation, necrosis and regeneration of proximal tubules, markers of kidney damage e.g. excretion of proteins/blood in urine, alpha |

| Tag Category | Inclusion/Exclusion Criteria | Example Keywords |
|---|---|---|
| | | 2U globulin |
| Neurological non-cancer | **INCLUDE:**<br>• Studies evaluating effects in the central nervous system (CNS) or peripheral nervous system, brain, nerves, behavior, neurochemical alterations, sensory effects, neurodevelopmental effects in exposed infants and children | changes in brain pathology, CNS depression (dizziness, drowsiness, sleepiness, loss of consciousness/ anesthesia, hypo activity, ataxia, lethargy, impaired coordination or balance, narcosis), nerve/neuronal injury and/or degeneration, neuropsychological outcomes (e.g. mood/personality changes), changes in neurobehavioral tests (cognitive, motor function) and neurophysiological effects (visual and auditory function), memory |
| Reproductive/Developmental non-cancer | **INCLUDE:**<br>• Studies examining reproductive outcomes, offspring and/or studies examining developmental effects<br>**Notes:**<br>Developmental neurotoxicity effects are categorized in the Reproductive/Developmental non-cancer tag and Neurological non-cancer tag | reduced fertility, effects on reproductive organs, sperm, estrous cycle, increased resorption and post implantation loss, viability, fetal death, birth weight, growth, maturation, teratogenicity, birth defects, visceral and/or skeletal malformations, follicle counts |
| Immunological non-cancer | **INCLUDE**:<br>• Studies examining susceptibility or resistance to infection or disease, function of innate or adaptive immunity | hypersensitization, increased/decreased white blood cells, effects on the spleen |
| Cardiovascular non-cancer | **INCLUDE:**<br>• Studies examining cardiovascular effects in the heart and vasculature | stroke, hypertension, tachycardia, cardiac arrhythmias |
| Gastrointestinal non-cancer | **INCLUDE:**<br>• Studies examining gastrointestinal effects on the mouth, on dentition, salivary glands, esophagus, stomach, intestines, rectum | nausea, vomiting, abdominal pain, anorexia |
| Irritation | **INCLUDE:**<br>• Studies examining irritation (primary or secondary) of the skin, eyes, gastrointestinal tract or respiratory tract | erythema, itching, blisters, swelling, edema (skin); pain swelling, lacrimation, photophobia (eyes); nausea, vomiting, and abdominal pain (gastrointestinal tract), rhinitis, prickling or burning sensation in the nose and throat, dry, scratchy throat (respiratory tract) |
| Respiratory non-cancer | **INCLUDE:**<br>• Studies examining non-cancer respiratory effects in the lungs | chemical pneumonitis, inflammation, bronchopneumonia, alveolar epithelial proliferation, edema, lung disease, bronchitis, pulmonary function tests, FEF, FEV1, bronchitis, COPD, cough, chest discomfort, PEFR, respiratory symptoms, respiratory infection, dyspnea, wheeze, lung function, effects on the nasal cavity (nasal |

| Tag Category | Inclusion/Exclusion Criteria | Example Keywords |
|---|---|---|
| | | respiratory and olfactory epithelium), bronchial or tracheal epithelium |
| Carcinogenicity | **INCLUDE:**<br>• Studies that evaluate any cancer effect | particular cancers include: breast, liver, kidney, blood, lymph, adrenal gland |
| Other non-cancer health effect | **INCLUDE:**<br>• Studies in which other non-cancer health effects, not defined by the categories above, were examined | NA |
| **ON TOPIC, CARBON TETRACHLORIDE ($CCl_4$) MOA TAGS** | | |
| **NOT ON TOPIC** | | |
| Not on topic | **INCLUDE:**<br>• Reference is not on topic in the context of any of the outlined categories (or tags) | NA |

## B.4 Results

Out of the 2,244 studies eligible for re-screening, 678 studies were identified in the first batch of prioritized references and screened independently by two individuals. These references were moved to off-topic since they met the re-screening exclusion criteria. Of the remaining 1,566 studies, the re-screening resulted in 45 references that met the inclusion criteria and were retained as *on-topic* references. The remaining studies, or 1,521, met the criteria for exclusion and were moved to *off-topic*.

# Appendix C PROCESS, RELEASE AND OCCUPATIONAL EXPOSURE INFORMATION

This appendix provides information and data found in preliminary data gathering for carbon tetrachloride.

## C.1 Process Information

Process-related information potentially relevant to the risk evaluation may include process diagrams, descriptions and equipment. Such information may inform potential release sources and worker exposure activities for consideration.

### C.1.1 Manufacture (Including Import)

#### C.1.1.1 Domestic Manufacture

Carbon tetrachloride was previously produced solely through the chlorination of carbon disulfide ($CS_2$); however, in the 1950s chlorination of hydrocarbons became popular (Holbrook, 2000). Currently, most Carbon tetrachloride is manufactured using one of three methods: chlorination of hydrocarbons or chlorinated hydrocarbons; oxychlorination of hydrocarbons; or $CS_2$ chlorination (Holbrook, 2000).

- ***Chlorination of hydrocarbons or chlorinated hydrocarbons*** - The chlorination of hydrocarbons involves a simultaneous breakdown of the organics and chlorination of the molecular fragments at pyrolytic temperatures and is often referred to as chlorinolysis (Holbrook, 2000). A variety of hydrocarbons and chlorinated hydrocarbon waste streams can be used as feedstocks; however, methane is the most common (Holbrook, 2000). PCE is formed as a major byproduct of this

process with small volumes of hexachloroethane, hexachlorobutadiene and hexachlorobenzene also produced (Holbrook, 2000).

- ***Oxychlorination of hydrocarbons*** - The oxychlorination of hydrocarbons involves the reaction of either chlorine or hydrochloric acid (HCl) and oxygen with a hydrocarbon feedstock in the presence of a catalyst (Marshall and Pottenger, 2016; Holbrook, 2000). This process can be utilized to convert HCl produced as a byproduct during the manufacture of chlorinated hydrocarbons into useful products (Marshall and Pottenger, 2016).
- ***$CS_2$ Chlorination*** - The chlorination of $CS_2$ involves the continuous reaction of $CS_2$ with chlorine in an annular reaction (Holbrook, 2000). The carbon tetrachloride produced is distilled to have a $CS_2$ content of 0 to 5 ppm. This process produces disulfur dichloride as a byproduct that is reduced with hydrogen without a catalyst or with a ferric chloride catalyst (Holbrook, 2000).

Based on EPA's knowledge of the chemical industry, worker activities at manufacturing facilities may involve manually adding raw materials or connecting/disconnecting transfer lines used to unload containers into storage or reaction vessels, rinsing/cleaning containers and/or process equipment, collecting and analyzing QC samples, manually loading carbon tetrachloride product or connecting/disconnecting transfer lines used to load carbon tetrachloride product into containers.

#### C.1.1.2 Import

EPA has identified activities related to the import of carbon tetrachloride through comments submitted in public docket EPA-HQ-OPPT-2016-0733. Based on EPA's knowledge of the chemical industry, imported chemicals are often stored in warehouses prior to distribution for further processing and use. In some cases, the chemicals may be repackaged into differently sized containers, depending on customer demand, and QC samples may be taken for analyses.

### C.1.2 Processing and Distribution

#### C.1.2.1 Reactant or Intermediate

Processing as a reactant or intermediate is the use of carbon tetrachloride as a feedstock in the production of another chemical product via a chemical reaction in which carbon tetrachloride is consumed to form the product. In the past, carbon tetrachloride was mainly used as feedstock for the manufacture chlorofluorocarbons (CFCs) (Marshall and Pottenger, 2016). However, due to the discovery that CFCs contribute to stratospheric ozone depletion, the use of CFCs was phased-out by the year 2000 to comply with the Montreal Protocol (Holbrook, 2000).

Currently, carbon tetrachloride is used as a feedstock to produce a variety of products including HCFCs, HFCs, HFOs, vinyl chloride, ethylene dichloride (EDC), PCE, chloroform, hafnium tetrachloride, thiophosgene and methylene chloride (EPA-HQ-OPPT-2016-0733-0003(U.S. EPA, 2017d; Marshall and Pottenger, 2016; Weil et al., 2006; Holbrook, 2003a, b)) . The specifics of the reaction process (e.g., use and types of catalysts, temperature conditions, etc.) will vary depending on the product being produced; however, a typical reaction process would involve unloading carbon tetrachloride from containers and feeding into the reaction vessel(s), where carbon tetrachloride would either fully or partially react with other raw materials to form the final product. Following the reaction, the product may or may not be purified to remove unreacted carbon tetrachloride (if any exists). Reacted carbon tetrachloride is assumed to be destroyed and thus not expected to be released or cause potential worker exposure.

Carbon tetrachloride is used in reactive ion etching (RIE). RIE involves ion bombardment to achieve directional etching and a reactive gas, such as carbon tetrachloride, to selectively maintain etched layers [EPA-HQ-OPPT-2016-0733-0003 (U.S. EPA, 2017d)].

EPA has not identified specific worker activities related to the processing of carbon tetrachloride as a reactant or intermediate at this time. However, based on EPA's knowledge of the chemical industry, worker activities are expected to be similar to that at manufacturing facilities including unloading and loading activities, rinsing/cleaning activities and collecting and analyzing QC samples.

#### C.1.2.2 Incorporation into a Formulation, Mixture or Reaction Products

Incorporation into a formulation, mixture or reaction product refers to the process of mixing or blending of several raw materials to obtain a single product or preparation. Process descriptions for use of carbon tetrachloride use as a process agent were not identified at this time. However, the processes are expected to be similar to those described above and typically involve unloading formulation components from transport containers, either directly into the mixing equipment or into an intermediate storage vessel, mixing of components either a batch or continuous system, QC sampling and final packaging of the formulation in to containers. Depending on the product, formulation products may be filtered prior to packaging. Transfer from transport containers into storage or mixing vessels may be manual or automated, through the use of a pumping system. If automated, an automated dispenser may be used to feed the components into the mixing vessel to ensure that precise amounts are added at the proper time during the mixing process. Final packaging occurs either through manual dispensing from transfer lines or through utilization of an automatic system.

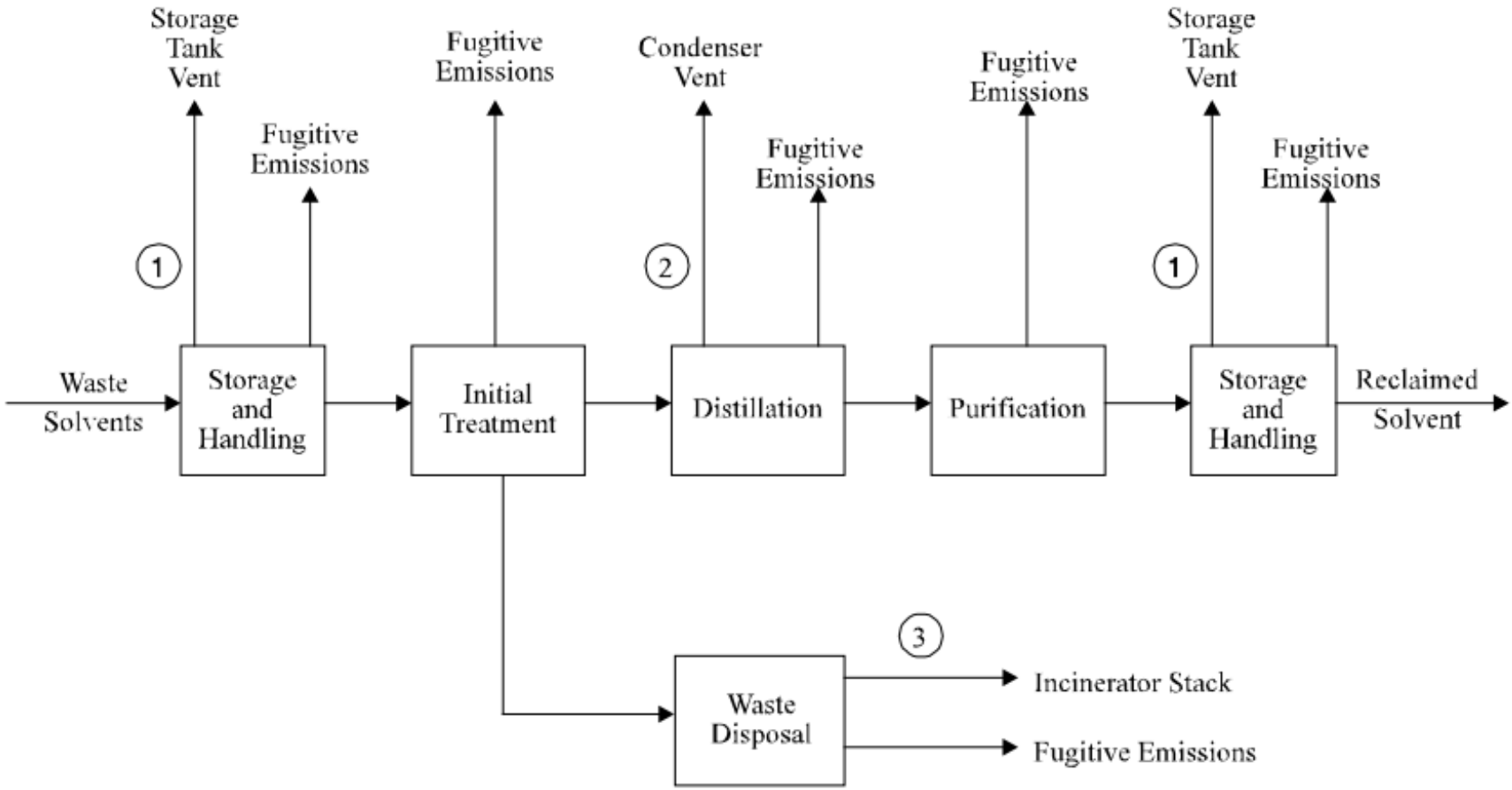
There is significant overlap in worker activities across the various formulation processes. The activities are expected to be similar to manufacturing activities and include unloading and loading activities, rinsing/cleaning activities and collecting and analyzing QC samples (OECD, 2009a, b).

#### C.1.2.3 Repackaging

Typically, repackaging sites receive the chemical in bulk containers and transfer the chemical from the bulk container into another smaller container in preparation for distribution in commerce. Based on EPA's knowledge of the chemical industry, worker activities at repackaging sites may involve manually unloading carbon tetrachloride from bulk containers into the smaller containers for distribution or connecting/disconnecting transfer lines used to transfer carbon tetrachloride product between containers and analyzing QC samples. EPA will further investigate the potential use of carbon tetrachloride in this type of process during the risk evaluation.

#### C.1.2.4 Recycling

TRI data from 2015 indicate that some sites ship carbon tetrachloride for off-site recycling. A general description of waste solvent recovery processes was identified. Waste solvents are generated when it becomes contaminated with suspended and dissolved solids, organics, water or other substance (U.S. EPA, 1980). Waste solvents can be restored to a condition that permits reuse via solvent reclamation/recycling (U.S. EPA, 1980). The recovery process involves an initial vapor recovery (e.g., condensation, adsorption and absorption) or mechanical separation (e.g., decanting, filtering, draining, setline and centrifuging) step followed by distillation, purification and final packaging (U.S. EPA, 1980). Worker activities are expected to be unloading of waste solvents and loading of reclaimed solvents. Figure_Apx C-1 illustrates a typical solvent recovery process flow diagram (U.S. EPA, 1980).




**Figure_Apx C-1. General Process Flow Diagram for Solvent Recovery Processes**

Source: (U.S. EPA, 1980)

### C.1.3 Uses

In this document, EPA has grouped uses based on CDR categories and identified examples within these categories as subcategories of use. Note that some subcategories may be grouped under multiple CDR categories. The differences between these uses will be further investigated and defined during risk evaluation.

#### C.1.3.1 Petrochemicals-derived Products Manufacturing

EPA has identified uses of carbon tetrachloride as a process agent (i.e., processing aid such as catalyst regeneration or as an additive) at manufacturing facilities of petrochemicals-derived products [EPA-HQ-OPPT-2016-0733-0003; (U.S. EPA, 2017d); (UNEP/Ozone Secretariat, 1998)]. EPA has also identified a patent which indicates a potential use of carbon tetrachloride as a fuel additive.

#### C.1.3.2 Agricultural Products Manufacturing

EPA has identified uses of carbon tetrachloride as a process agent in the manufacturing of fertilizers and other agricultural products [EPA-HQ-OPPT-2016-0733-0003; (U.S. EPA, 2017d); (UNEP/Ozone Secretariat, 1998).

#### C.1.3.3 Other Basic Organic and Inorganic Chemical Manufacturing

EPA has identified uses of carbon tetrachloride as a process agent in the manufacturing of inorganic compounds (i.e., chlorine), pharmaceuticals (i.e., ibuprofen) and chlorinated compounds that are used in the formulation of solvents for cleaning and degreasing, adhesive and sealants, paints and coatings and asphalt [EPA-HQ-OPPT-2016-0733-0003; (U.S. EPA, 2017d)]. Therefore, EPA expects carbon tetrachloride is only present in cleaning, degreasing, paints, coatings, and asphalt formulations as an impurity rather than serving a specific function. Appendix D presents a list of domestic and internationally approved uses of carbon tetrachloride as a process agent in MP side agreement: Decision X/14: Process Agents (UNEP/Ozone Secretariat, 1998).

#### C.1.3.4 Laboratory Chemicals

Carbon tetrachloride is used in laboratories as a chemical reagent, extraction solvent and a reference material or solvent in analytical procedures, such as spectroscopic measurements [EPA-HQ-OPPT-2016-0733-0003; (U.S. EPA, 2017d)].

#### C.1.3.5 Other Uses

Carbon tetrachloride may also be used in metal recovery and other specialty uses identified by the aerospace industry, such as the manufacture, operations and maintenance of aerospace products and for specific cleaning operations (EPA-HQ-OPPT-2016-0733-0063).

#### C.1.3.6 Disposal

Table 2-6 and Table 2-7 present the production-related waste managed data for carbon tetrachloride reported to the TRI program for 2015. Waste containing carbon tetrachloride is classified as hazardous waste (see Table_Apx A-1). Facilities generating waste containing carbon tetrachloride must comply with EPA regulations for treatment, storage, and disposal.

## C.2 Occupational Exposure Data

EPA presents below an example of occupational exposure-related information from the preliminary data gathering. EPA will consider this information and data in combination with other data and methods for

use in the risk evaluation. Table_Apx C-1. summarizes OSHA CEHD data by NAICS (North American Industrial Classification System) code (see Section 2.3.5.1) and Table_Apx C-2. summarizes NIOSH HHE data.

**Table_Apx C-1. Summary of Carbon Tetrachloride Personal Monitoring Air Samples Obtained from OSHA Inspections Conducted Between 2013 and 2015**

| Release/Exposure Scenario | NAICS | NAICS Description | 8-hr TWA Concentration (ppm)[a] | | | | | STEL, Peak, or Ceiling Concentration (ppm) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Number of Data Points | Minimum | Maximum | Average | Number of Zero Values[b] | Number of Data Points | Minimum | Maximum | Average | Number of Zero Values[b] |
| Unknown – job title and company information did not indicate how carbon tetrachloride may be used | 322121 | Paper (except Newsprint) Mills | 4 | 0 | 0 | 0 | 4 | 4 | 0 | 0 | 0 | 4 |
| Vapor degreasing or cold cleaning | 331512 | Steel Investment Foundries | 3 | 0.026 | 0.027 | 0.026 | 0 | No Data Available | | | | |
| Vapor degreasing or cold cleaning | 332439 | Other Metal Container Manufacturing | 2 | 0.026 | 0.026 | 0.026 | 0 | No Data Available | | | | |
| Vapor degreasing or cold cleaning | 336111 | Automobile Manufacturing | 2 | 0 | 0 | 0 | 2 | 2 | 0 | 0 | 0 | 2 |
| Unknown – this seems to be for OSHA inspectors which could have been collected during site inspections | 926150 | Regulation, Licensing, and Inspection of Miscellaneous Commercial Sectors | 1 | 0 | | 1 | 1 | 0 | | | | 1 |

[a] Assumes all TWA data are 8-hr TWA.
[b] For facilities where all samples are measured as zero, it is unclear if carbon tetrachloride is present at the facility.

**Table_Apx C-2. Summary of Monitoring Data from NIOSH Health Hazard Evaluations Conducted since 1990**

| Data Source | Report Number | Exposure/Release Scenario | Facility Description | Number of Exposure Samples | Minimum of Exposure Values (ppm) | Maximum of Exposure Values (ppm) | Comments |
|---|---|---|---|---|---|---|---|
| NIOSH 1992a | HETA-1990-223-2211 | Vapor degreasing | Cathode ray tube manufacturing | 0 | No exposure data for carbon tetrachloride provided. | | |
| NIOSH, 1992b | HETA-1991-188-2205 | General population exposures | Elementary school | 6 | ND | 0.03 | 1 to 2-hr area measurements. |
| NIOSH, 2005 | HETA-2004-169-2982 | Manufacture of carbon tetrachloride | Magnesium manufacturer | 11 | PBZ: ND Area: ND | PBZ: 0.03 Area: ND | 8-hr TWA values |

# Appendix D PROCESS AGENT USES FOR CARBON TETRACHLORIDE

**Table_Apx D-1. List of Uses of Carbon Tetrachloride as Process Agent in MP side agreement: Decision X/14: Process Agents**

| | | | |
|---|---|---|---|
| 1 | Elimination of nitrogen trichloride in the production of chlorine and caustic | 10 | Manufacture of chlorinated paraffin |
| 2 | Recovery of chlorine in tail gas from production of chlorine | 11 | Production of pharmaceuticals - ketotifen, anticol and disulfiram |
| 3 | Manufacture of chlorinated rubber | 12 | Production of tralomethrine (insecticide) |
| 4 | Manufacture of endosulphan (insecticide) | 13 | Bromohexine hydrochloride |
| 5 | Manufacture of isobutyl acetophenone (ibuprofen - analgesic) | 14 | Diclofenac sodium |
| 6 | Manufacture of 1-1, Bis (4-chlorophenyl) 2,2,2- trichloroethanol (dicofol insecticide) | 15 | Cloxacilin |
| 7 | Manufacture of chlorosulphonated polyolefin (CSM) | 16 | Phenyl glycine |
| 8 | Manufacture of poly-phenylene-terephtal-amide | 17 | Isosorbid mononitrate |
| 9 | Manufacture of styrene butadiene rubber | 18 | Omeprazol |

# Appendix E SURFACE WATER ANALYSIS FOR CARBON TETRACHLORIDE RELEASES

During problem formulation, EPA modeled industrial discharges to surface water to estimate surface water concentration using EPA NPDES permit Discharge Monitoring Report (DMR) data on the top 10 highest carbon tetrachloride releasing facilities. DMR data are submitted by facilities in order to comply with NPDES permit requirements, including limits to pollutants discharged to receiving waters. EPA used the Probabilistic Dilution Model (PDM) within E-FAST to estimate annual discharges for the facilities. In order to estimate a range of conservative surface water concentrations, the 2015 NPDES DMR data reporting carbon tetrachloride discharges were used in a first-tier analysis, which estimates conservative carbon tetrachloride surface water concentrations (i.e., conservative exposure scenarios). The surface water concentrations were estimated using a range of high-end number of release days (i.e., 20 and 250 days/year) instead of the default 365 days/year. Other conservative assumptions in the first-tier analysis include the use of zero percent removal of carbon tetrachloride by the wastewater treatment facility and low hydrological flow.

DMR data confirmed that facility discharges used in this first-tier analysis were discharging at least 20 days per year. EPA did not include a single day release scenario since this was not a likely scenario that would be allowed under current NPDES permit requirements. The other input parameter important for determining surface water concentrations is wastewater removal efficiency since the NPDES permits require industrial wastewater treatment removal. Table_Apx E-1 presents the first-tier estimate of surface water concentrations. Public owned treatment works (POTW with SIC 4952) are municipal facilities that receive industrial discharges containing carbon tetrachloride and reported these concentrations in the facility DMRs. Since these facilities discharge 365 days per year, the 20-day discharge scenario is not considered and the 250 day/year discharge is the only modeled scenario. Using these conservative scenarios, carbon tetrachloride surface water concentrations were mostly below the COCs for aquatic species (62 µg/L and 7 µg/L for acute and chronic, respectively). The PDM calculates the probability of the COC being exceeded using 7Q10 (i.e., 7 consecutive days of 10th percentile low flow) low flow statistics. Thus, surface water concentrations that slightly exceed the chronic COC are not considered statistically significant as to present a concern for aquatic organisms.

**Table_Apx E-1. Modeled Carbon Tetrachloride Surface Water Concentrations**

| SIC Code | Total Pounds (lbs/yr) - 2015 DMR Data | PDM Inputs | | Surface Water Concentrations | | Acute COC (ug/L) | Chronic COC (ug/L) |
|---|---|---|---|---|---|---|---|
| | | 20 days (kg/day) | 250 days (kg/day) | 20 days (ug/L) | 250 days (ug/L) | | |
| 4952 | 134 | N/A[a] | 0.24 | N/A[a] | 24.77[b] | 62 | 7 |
| 2819 | 110 | 2.49 | 0.20 | 0.13 | 0.011 | 62 | 7 |
| 2819 | 23.7 | 0.54 | 0.04 | 0.002 | 0.0002 | 62 | 7 |
| 2869 | 325 | 7.37 | 0.59 | 0.030 | 0.002 | 62 | 7 |
| 2869 | 20.9 | 0.12 | 0.04 | 28.37 | 8.98 | 62 | 7 |
| 2812 | 13.9 | 0.31 | 0.02 | 0.037 | 0.003 | 62 | 7 |
| 7996 | 13.8 | 0.31 | 0.03 | 0.74 | 0.06 | 62 | 7 |
| 2869 | 12.9 | 0.29 | 0.02 | 20.14 | 1.6 | 62 | 7 |

| SIC Code | Total Pounds (lbs/yr) - 2015 DMR Data | PDM Inputs | | Surface Water Concentrations | | Acute COC (ug/L) | Chronic COC (ug/L) |
|---|---|---|---|---|---|---|---|
| | | 20 days (kg/day) | 250 days (kg/day) | 20 days (ug/L) | 250 days (ug/L) | | |
| 2819 | 9.85 | 0.22 | 0.02 | 0.0009 | 0.0001 | 62 | 7 |
| 4953 | 8.94 | 0.20 | 0.02 | 13.05 | 1.04 | 62 | 7 |

[a] Not applicable; the 20-day discharge scenario is not considered because this facility only discharges 365 days per year.
[B] This surface water concentration value above the Chronic COC is based on highly conservative assumptions, including 0% removal of carbon tetrachloride by the waste water treatment facility. As explained in Section 2.3.1, the EPI Suite™ STP module estimates that about 90% of carbon tetrachloride in wastewater will be removed by volatilization and 2% by adsorption.

# Appendix F SUPPORTING TABLE FOR INDUSTRIAL AND COMMERCIAL ACTIVITIES AND USES CONCEPTUAL MODEL

During problem formulation, EPA reviewed preliminary data and mapped conditions of use into corresponding exposure scenarios. Table_Apx F-1 summarizes the scenario mapping. The table also provides rationale on whether EPA will further assess each scenario during risk evaluation.

**Table_Apx F-1. Industrial and Commercial Activities and Uses Conceptual Model Supporting Table**
(Note that rows shaded in gray are not proposed for further analysis)

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Manufacture | Domestic Manufacture | Domestic Manufacture | Manufacture of carbon tetrachloride via chlorination of hydrocarbons, oxychlorination of hydrocarbons, chlorination of carbon disulfide, and as a byproduct | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization. However, the number of workers exposed may be high per CDR (3 submissions reporting 100-500 workers per submission). |
| | | | | Vapor | Inhalation | Workers | Yes | Due to high volatility (VP = 115 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU[a] | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| | | | | Vapor | Inhalation | ONU | Yes | Due to high volatility (VP = 115 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during manufacturing. |
| Manufacture | Import | Import | Repackaging of import containers | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization. The number of import sites is limited (<6 sites) per CDR. Exposure will only occur in the event the imported material is repackaged. |
| | | | | Vapor | Inhalation | Workers | Yes | Exposure expected only in the event the imported material is repackaged into different sized containers. Exposure frequency may be low. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Exposure expected only in the event the imported material is repackaged into different sized containers. Exposure frequency may be low. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during import. |
| Processing | Processing as a reactant | Intermediate in industrial gas and semiconductor manufacturing; | Manufacture of HCFCs, HFCs, HFOs, and PCE; Reactive ion etching | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization. However, the number of workers may be high per CDR (2 submissions reporting <10 workers, 1 submission reporting 10-25 workers, 1 submission reporting 25-50 workers, and 2 submissions reporting 100-500 workers). |
| | | | | Vapor | Inhalation | Workers | Yes | Due to high volatility (VP = 115 mmHg) at room temperature, inhalation pathway should be further analyzed. However, potential for exposure may be low in scenarios where carbon tetrachloride is consumed as a chemical intermediate. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| | | | | Vapor | Inhalation | ONU | Yes | Due to high volatility (VP = 115 mmHg) at room temperature, inhalation pathway should be further analyzed. However, potential for exposure may be low in scenarios where carbon tetrachloride is consumed as a chemical intermediate. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during processing as an intermediate. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Processing | Incorporated into formulation, mixture or reaction product | Petrochemical-derived and agricultural products manufacturing; Other basic organic and inorganic chemical manufacturing; Other uses | Manufacturing of organic and inorganic chlorinated chemicals, pharmaceutical manufacturing, use in specialty operations by aerospace industry | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization. |
| | | | | Vapor | Inhalation | Workers | Yes | Exposure frequency may be low. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Exposure frequency may be low. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected. |
| Processing | Repackaging | Laboratory Chemicals | Repackaging into large and small containers | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization. |
| | | | | Vapor | Inhalation | Workers | Yes | Exposure frequency may be low. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Exposure frequency may be low. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during repackaging. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Processing | Recycling | Recycling | Recycling of process solvents containing carbon tetrachloride | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected at recycling sites. Due to high volatility (VP = 115 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected at recycling sites. Due to high volatility (VP = 115 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during recycling. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Distribution in commerce | Distribution | Distribution | Distribution of bulk shipment of carbon tetrachloride; and distribution of formulated products | Liquid Contact, Vapor | Dermal/ Inhalation | Workers, ONU | Yes | EPA will further analyze activities resulting in exposures associated with distribution in commerce (e.g. loading, unloading) throughout the various lifecycle stages and conditions of use (e.g. manufacturing, processing, industrial use) rather than as a single distribution scenario. |
| Industrial / commercial use | Petrochemical-derived and agricultural products manufacturing | Petrochemical-derived and agricultural products manufacturing | Inert solvent, processing agent, processing aid, and additive | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization. However, EPA will need additional information to fully understand the use of carbon tetrachloride in this scenario to determine potential for dermal exposure. |
| | | | | Vapor | Inhalation | Workers | Yes | Due to high volatility (VP = 115 mmHg) at room temperature, inhalation pathway should be further analyzed. However, EPA will need additional information to fully understand the use of carbon tetrachloride in this scenario to determine potential for inhalation exposure. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Due to high volatility (VP = 115 mmHg) at room temperature, inhalation pathway should be further analyzed. However, EPA will need additional information to fully understand the use of carbon tetrachloride in this scenario to determine potential for inhalation exposure. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during use of industrial processing agent. |
| Industrial / commercial use | Other basic organic and inorganic chemical manufacturing | Manufacturing of chlorinated compounds used in solvents for cleaning and degreasing, adhesives and sealants, paints and coatings, and asphalts; | Inert solvent, processing agent, processing aid, and additive | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization. However, EPA will need additional information to fully understand the use of carbon tetrachloride in this scenario to determine potential for dermal exposure. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| | | Manufacturing of inorganic compounds | | Vapor | Inhalation | Workers | Yes | Due to high volatility (VP = 115 mmHg) at room temperature, inhalation pathway should be further analyzed. However, EPA will need additional information to fully understand the use of carbon tetrachloride in this scenario to determine potential for inhalation exposure. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Due to high volatility (VP = 115 mmHg) at room temperature, inhalation pathway should be further analyzed. However, EPA will need additional information to fully understand the use of carbon tetrachloride in this scenario to determine potential for inhalation exposure. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during use of industrial processing agent. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Industrial / commercial | Other uses | Metal recovery; specialty uses by aerospace industry | Metal recovery; and uses in aerospace industry | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization. |
| | | | | Vapor | Inhalation | Workers | Yes | Due to high volatility (VP = 115 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Due to high volatility (VP = 115 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | EPA will further evaluate to determine if mist generation is applicable to specific conditions of use in this scenario. |
| Industrial / commercial use | Laboratory chemical | Laboratory chemical | Use as reagent in laboratories | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization. Number of exposed workers may be low per CDR (1 submission reports 10-25 workers). |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected from laboratory uses. Due to high volatility (VP = 115 mmHg) at room temperature, inhalation pathway should be further analyzed. However, number of exposed workers may be low per CDR (1 submission reports 10-25 workers). |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected from laboratory uses. Due to high volatility (VP = 115 mmHg) at room temperature, inhalation pathway should be further analyzed. However, number of exposed workers may be low per CDR (1 submission reports 10-25 workers). |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during laboratory uses. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Disposal | Waste Handling, Treatment and Disposal | Disposal of carbon tetrachloride wastes | Worker handling of wastes | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <2 min due to rapid volatilization. Frequency of exposure and the potential for dermal immersion needs to be further analyzed. |
| | | | | Vapor | Inhalation | Workers | Yes | Due to high volatility (VP = 115 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Due to high volatility (VP = 115 mmHg) at room temperature, inhalation pathway should be further analyzed. |

[a] ONU = occupational non-users

# Appendix G SUPPORTING TABLE FOR ENVIRONMENTAL RELEASES AND WASTES CONCEPTUAL MODEL

As part of the Problem Formulation, EPA considered if each unique combination of exposure pathway, route, and receptor in the lifecycle of carbon tetrachloride would be further evaluated. All possible exposure scenarios for each condition of use were identified according to the conditions of use identified in Table 2-3. EPA used readily available fate, engineering, exposure and/or toxicity information to determine whether to conduct further analysis on each exposure scenario based on available information. EPA identified exposure scenarios and mapped them to relevant conditions of use in Table_Apx G-1.

**Table_Apx G-1. Environmental Releases and Wastes Conceptual Model Supporting Table**

| Life Cycle Stage | Use Category | Category | Release | Exposure Pathway | Receptor | Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|
| Disposal | Disposal | Wastewater or Liquid Wastes | Industrial WWT operations | Water | Aquatic Species | No | Conservative high-end screening indicates that aquatic species exposures to carbon tetrachloride in water are orders of magnitude below hazardous concentrations. |
| | | | | Sediment | Aquatic Species | No | Based on the physical and chemical properties of carbon tetrachloride (log Koc of 1.7-2.16, high water solubility and volatility) sorption of carbon tetrachloride to sediments is unlikely. |

| Life Cycle Stage | Use Category | Category | Release | Exposure Pathway | Receptor | Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|
| | | | Industrial wastewater pre treatment operations, then transfer to POTW | Water | Aquatic Species | No | Conservative high-end screening indicates that aquatic species exposures to carbon tetrachloride in water are orders of magnitude below hazardous concentrations. |
| | | | | Sediment | Aquatic Species | No | Based on the physical and chemical properties of carbon tetrachloride (log Koc of 1.7-2.16, high water solubility and volatility) sorption of carbon tetrachloride to sediments is unlikely. |
| | | | Publicly owned treatment works (POTW) | Water | Aquatic Species | No | Conservative high-end screening indicates that aquatic species exposures to carbon tetrachloride in water are orders of magnitude below hazardous concentrations. |
| | | | | Sediment | Aquatic Species | No | Based on the physical and chemical properties of carbon tetrachloride (log Koc of 1.7-2.16, high water solubility and volatility) sorption of carbon tetrachloride to sediments is unlikely. |

# Appendix H INCLUSION AND EXCLUSION CRITERIA FOR FULL TEXT SCREENING

This appendix contains the eligibility criteria for various data streams informing the TSCA risk evaluation: environmental fate; engineering and occupational exposure; exposure to the general population and consumers; and human health hazard. The criteria are applied to the *on-topic* references that were identified following title and abstract screening of the comprehensive search results published on June 22, 2017.

Systematic reviews typically describe the study eligibility criteria in the form of PECO statements or a modified framework. PECO stands for Population, Exposure, Comparator and Outcome and the approach is used to formulate explicit and detailed criteria about those characteristics in the publication that should be present in order to be eligible for inclusion in the review. EPA/OPPT adopted the PECO approach to guide the inclusion/exclusion decisions during full text screening.

Inclusion and exclusion criteria were also used during the title and abstract screening, and documentation about the criteria can be found in the *Strategy for Conducting Literature Searches* document published in June 2017 along with each of the TSCA Scope documents. The list of *on-topic* references resulting from the title and abstract screening is undergoing full text screening using the criteria in the PECO statements. The overall objective of the screening process is to select the most relevant evidence for the TSCA risk evaluation. As a general rule, EPA is excluding non-English data/information sources and will translate on a case by case basis.

The inclusion and exclusion criteria for ecotoxicological data have been documented in the ECOTOX SOPs. The criteria can be found at https://cfpub.epa.gov/ecotox/help.cfm?helptabs=tab4) and in the *Strategy for Conducting Literature Searches* document published along with each of the TSCA Scope documents.

Since full text screening commenced right after the publication of the TSCA Scope document, the criteria were set to be broad to capture relevant information that would support the initial scope. Thus, the inclusion and exclusion criteria for full text screening do not reflect the refinements to the conceptual model and analysis plan resulting from problem formulation. As part of the iterative process, EPA is in the process of refining the results of the full text screening to incorporate the changes in information/data needs to support the revised scope.

These refinements will include changes to the inclusion and exclusion criteria discussed in this appendix to better reflect the revised scope of the risk evaluation and will likely reduce the number of data/information sources that will undergo evaluation.

## H.1 Inclusion Criteria for Data Sources Reporting Engineering and Occupational Exposure Data

EPA/OPPT developed a generic RESO statement to guide the full text screening of engineering and occupational exposure literature (Table_Apx H-1). RESO stands for Receptors, Exposure, Setting or Scenario, and Outcomes. Subsequent versions of the RESO statement may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the inclusion criteria specified in the RESO statement will be eligible for inclusion,

considered for evaluation, and possibly included in the environmental release and occupational exposure assessments, while those that do not meet these criteria will be excluded.

The RESO statement should be used along with the engineering and occupational exposure data needs table (Table_Apx H-2) when screening the literature.

Since full text screening commenced right after the publication of the TSCA Scope document, the criteria for engineering and occupational exposure data were set to be broad to capture relevant information that would support the initial scope. Thus, the inclusion and exclusion criteria for full text screening do not reflect the refinements to the conceptual model and analysis plan resulting from problem formulation. As part of the iterative process, EPA is in the process of refining the results of the full text screening to incorporate the changes in information/data needs to support the revised scope.

**Table_Apx H-1. Inclusion Criteria for Data Sources Reporting Engineering and Occupational Exposure Data**

| RESO Element | Evidence |
|---|---|
| **R**eceptors | • **Humans:**<br>Workers, including occupational non-users (ONU) |
| **E**xposure | • Worker exposure to and occupational environmental releases of the chemical substance of interest<br>  ○ Any exposure route (list included: dermal, inhalation, oral) as indicated in the conceptual model<br>  ○ Any media/pathway [list included: water, land, air, incineration, and other(s)] as indicated in the conceptual model<br><br>Please refer to the conceptual models for more information about the routes and media/pathways included in the TSCA risk evaluation. |
| **S**etting or **S**cenario | • Any occupational setting or scenario resulting in worker exposure and environmental releases (includes all manufacturing, processing, use, disposal indicated in Table A-3 below except (state none excluded or list excluded uses) |
| **O**utcomes | • Quantitative estimates* of worker exposures<br>• General information and data related and relevant to the occupational estimates* |

* Metrics (e.g., mg/kg/day or $mg/m^3$ for worker exposures, kg/site/day for releases) are determined by toxicologists for worker exposures and by exposure assessors for releases; also, the Engineering Data Needs (Table_Apx H-2) provides a list of related and relevant general information.

TSCA=Toxic Substances Control Act

**Table_Apx H-2. Engineering, Environmental Release and Occupational Data Necessary to Develop the Environmental Release and Occupational Exposure Assessments**

| Objective Determined during Scoping | Type of Data |
|---|---|
| General Engineering Assessment (may apply for either or both Occupational Exposures and / or Environmental Releases) | 1. Description of the life cycle of the chemical(s) of interest, from manufacture to end-of-life (e.g., each manufacturing, processing, or use step), and material flow between the industrial and commercial life cycle stages. [Tags: Life cycle description, Life cycle diagram][a]<br>2. The total annual U.S. volume (lb/yr or kg/yr) of the chemical(s) of interest manufactured, imported, processed, and used; and the share of total annual manufacturing and import volume that is processed or used in each life cycle step. [Tags: Production volume, Import volume, Use volume, Percent PV] [a]<br>3. Description of processes, equipment, unit operations, and material flows and frequencies (lb/site-day or kg/site-day and days/yr; lb/site-batch and batches/yr) of the chemical(s) of interest during each industrial/ commercial life cycle step. Note: if available, include weight fractions of the chemicals (s) of interest and material flows of all associated primary chemicals (especially water). [Tags: Process description, Process material flow rate, Annual operating days, Annual batches, Weight fractions (for each of above, manufacture, import, processing, use)] [a]<br>4. Basic chemical properties relevant for assessing exposures and releases, e.g., molecular weight, normal boiling point, melting point, physical forms, and room temperature vapor pressure. [Tags: Molecular weight, Boiling point, Melting point, Physical form, Vapor pressure, Water solubility] [a]<br>5. Number of sites that manufacture, process, or use the chemical(s) of interest for each industrial/ commercial life cycle step and site locations. [Tags: Numbers of sites (manufacture, import, processing, use), Site locations] [a] |
| Occupational Exposures | 6. Description of worker activities with exposure potential during the manufacture, processing, or use of the chemical(s) of interest in each industrial/commercial life cycle stage. [Tags: Worker activities (manufacture, import, processing, use)] [a]<br>7. Potential routes of exposure (e.g., inhalation, dermal). [Tags: Routes of exposure (manufacture, import, processing, use)] [a]<br>8. Physical form of the chemical(s) of interest for each exposure route (e.g., liquid, vapor, mist) and activity. [Tags: Physical form during worker activities (manufacture, import, processing, use)] [a]<br>9. Breathing zone (personal sample) measurements of occupational exposures to the chemical(s) of interest, measured as time-weighted averages (TWAs), short-term exposures, or peak exposures in each occupational life cycle stage (or in a workplace scenario similar to an occupational life cycle stage). [Tags: PBZ measurements (manufacture, import, processing, use)] [a]<br>10. Area or stationary measurements of airborne concentrations of the chemical(s) of interest in each occupational setting and life cycle stage (or in a workplace scenario similar to the life cycle stage of interest). [Tags: Area measurements (manufacture, import, processing, use)] [a]<br>11. For solids, bulk and dust particle size characterization data. [Tags: PSD measurements (manufacture, import, processing, use)] [a]<br>12. Dermal exposure data. [Tags: Dermal measurements (manufacture, import, processing, use)]<br>13. Data needs associated with mathematical modeling (will be determined on a case-by-case basis). [Tags: Worker exposure modeling data needs (manufacture, import, processing, use)] [a]<br>14. Exposure duration (hr/day). [Tags: Worker exposure durations (manufacture, import, processing, use)] [a]<br>15. Exposure frequency (days/yr). [Tags: Worker exposure frequencies (manufacture, import, processing, use)] [a]<br>16. Number of workers who potentially handle or have exposure to the chemical(s) of interest in each occupational life cycle stage. [Tags: Numbers of workers exposed (manufacture, import, processing, use)] [a]<br>17. Personal protective equipment (PPE) types employed by the industries within scope. [Tags: Worker PPE (manufacture, import, processing, use)] [a] |

| Objective Determined during Scoping | Type of Data |
|---|---|
| | 18. Engineering controls employed to reduce occupational exposures in each occupational life cycle stage (or in a workplace scenario similar to the life cycle stage of interest), and associated data or estimates of exposure reductions. [Tags: Engineering controls (manufacture, import, processing, use), Engineering control effectiveness data] [a] |
| Environmental Releases | 19. Description of sources of potential environmental releases, including cleaning of residues from process equipment and transport containers, involved during the manufacture, processing, or use of the chemical(s) of interest in each life cycle stage. [Tags: Release sources (manufacture, import, processing, use)] [a]<br>20. Estimated mass (lb or kg) of the chemical(s) of interest released from industrial and commercial sites to each environmental medium (air, water, land) and treatment and disposal methods (POTW, incineration, landfill), including releases per site and aggregated over all sites (annual release rates, daily release rates) [Tags: Release rates (manufacture, import, processing, use)] [a]<br>21. Release or emission factors. [Tags: Emission factors (manufacture, import, processing, use)] [a]<br>22. Number of release days per year. [Tags: Release frequencies (manufacture, import, processing, use)] [a]<br>23. Data needs associated with mathematical modeling (will be determined on a case-by-case basis). [Tags: Release modeling data needs (manufacture, import, processing, use)] [a]<br>24. Waste treatment methods and pollution control devices employed by the industries within scope and associated data on release/emission reductions. [Tags: Treatment/ emission controls (manufacture, import, processing, use), Treatment/ emission controls removal/ effectiveness data] [a] |

**Notes:**

[a] These are the tags included in the full text screening form. The screener makes a selection from these specific tags, which describe more specific types of data or information.

**Abbreviations:**

hr=Hour
kg=Kilogram(s)
lb=Pound(s)
yr=Year
PV=Particle volume
PBZ=
POTW=Publicly owned treatment works
PPE=Personal projection equipment
PSD=Particle size distribution
TWA=Time-weighted average

## H.2 Inclusion Criteria for Data Sources Reporting Human Health Hazards

EPA/OPPT developed a carbon tetrachloride-specific PECO statement to guide the full text screening of the human health hazard literature. Subsequent versions of the PECOs may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the criteria specified in the PECO statement will be eligible for inclusion, considered for evaluation, and possibly included in the human health hazard assessment, while those that do not meet these criteria will be excluded according to the exclusion criteria.

In general, the PECO statements were based on (1) information accompanying the TSCA Scope document, and (2) preliminary review of the health effects literature from authoritative sources cited in the TSCA Scope documents. When applicable, these authoritative sources (e.g., IRIS assessments, EPA/OPPT's Work Plan Problem Formulations or risk assessments) will serve as starting points to identify PECO-relevant studies.

**Table_Apx H-3. Inclusion and Exclusion Criteria for Data Sources Reporting Human Health Hazards Related to Carbon Tetrachloride Exposure [a]**

| PECO Element | Evidence Stream | Papers/Features Included | Papers/Features Excluded |
|---|---|---|---|
| **Population** | *Human* | • Any population<br>• All lifestages<br>• Study designs:<br>  ○ Controlled exposure, cohort, case-control, cross-sectional, case-crossover, case studies, and case series for all endpoints | |
| | *Animal* | • All non-human whole-organism mammalian species<br>• All lifestages | • Non-mammalian species |
| | *Mechanistic* | • All data that may inform mechanisms of genotoxicity and carcinogenicity [a] | • Data related to other mechanisms of toxicity [a] |
| *Exposure* | *Human* | • Exposure based on administered dose or concentration of carbon tetrachloride, biomonitoring data (e.g., urine, blood or other specimens), environmental or occupational-setting monitoring data (e.g., air, water levels), job title or residence<br>• Primary metabolites of interest as identified in biomonitoring studies<br>• Exposure identified as *or presumed to be* from oral, dermal, inhalation routes<br>• Any number of exposure groups<br>• Quantitative, semi-quantitative or qualitative estimates of exposure<br>• Exposures to multiple chemicals/mixtures only if carbon tetrachloride or related metabolites were independently measured and analyzed | • Route of exposure ***not*** by inhalation, oral or dermal type (e.g., intraperitoneal, injection)<br>• Multiple chemical/mixture exposures with no independent measurement of or exposure to carbon tetrachloride (or related metabolite) |
| | *Animal* | • A minimum of 2 quantitative dose or concentration levels of carbon tetrachloride plus a negative control group [a]<br>• Acute, subchronic, chronic exposure from oral, dermal, inhalation routes<br>• Exposure to carbon tetrachloride only (no chemical mixtures) | • Only 1 quantitative dose or concentration level in addition to the control [a]<br>• Route of exposure ***not*** by inhalation, oral or dermal type (e.g., intraperitoneal, injection)<br>• No duration of exposure stated<br>• Exposure to carbon tetrachloride in a chemical mixture |
| | *Mechanistic* | • Exposure based on concentrations of the neat material of carbon tetrachloride<br>• A minimum of 2 dose or concentration levels tested plus a control group [a] | • Exposure to carbon tetrachloride in a chemical mixture<br>• Only 1 quantitative dose or concentration level in addition to the control [a] |
| **Comparator** | *Human* | • A comparison population [not exposed, exposed to lower levels, exposed below detection] for all endpoints | • No comparison population for all endpoints |
| | *Animal* | • Negative controls that are vehicle-only treatment and/or no treatment | • Negative controls ***other than*** vehicle-only treatment or no treatment |

| PECO Element | Evidence Stream | Papers/Features Included | Papers/Features Excluded |
|---|---|---|---|
| | *Mechanistic* | • Exposed to vehicle-only treatment and/or no treatment<br>• ***For genotoxicity studies only***, studies using positive controls | • Negative controls ***other than*** vehicle-only treatment or no treatment<br>• ***For genotoxicity studies only***, a lack of positive controls |
| **Outcome** | *Human and Animal* | • Endpoints described in the carbon tetrachloride scope document [b]:<br>  ○ Cancer<br>  ○ Liver toxicity<br>  ○ Kidney toxicity<br>  ○ Neurotoxicity<br>  ○ Gastrointestinal toxicity<br>  ○ Irritation<br>  ○ Sensitization<br>• Other endpoints (e.g., reproductive toxicity) [b,c] | |
| | *Mechanistic* | • All data that may inform the mechanism(s) of cancer and genotoxicity [a] | • Data related to other mechanisms of toxicity [a] |
| **General Considerations** | | **Papers/Features Included** | **Papers/Features Excluded** |
| | | • Written in English [d]<br>• Reports a primary source or meta-analysis [a]<br>• Full-text available<br>• Reports both carbon tetrachloride exposure ***and*** a health outcome (or mechanism of action) | • Not written in English<br>• Reports a secondary source (e.g., review papers) [a]<br>• No full-text available (e.g., only a study description/abstract, out-of-print text)<br>• Reports a carbon tetrachloride-related exposure ***or*** a health outcome, but not both (e.g. incidence, prevalence report) |

[a] Some of the studies that are excluded based on the PECO statement may be considered later during the systematic review process. For carbon tetrachloride, EPA will evaluate studies related to susceptibility and may evaluate toxicokinetics and physiologically based pharmacokinetic models after other data (e.g., human and animal data identifying adverse health outcomes) are reviewed. EPA may need to evaluate mechanistic data in addition to data on mechanisms of genotoxicity and carcinogenicity depending on the review of health effects data. Finally, EPA may also review other data as needed (e.g., animal studies using one concentration, review papers).

[b] EPA will review key and supporting studies in the IRIS assessment that were considered in the dose-response assessment for non-cancer and cancer endpoints as well as studies published after the IRIS assessment.

[c] EPA may screen for hazard effects other than those listed in the scope document if identified in the updated literature search for carbon tetrachloride that accompanied the scope document.

[d] EPA may translate studies as needed.

# Appendix I LIST OF RETRACTED PAPERS

The following on-topic articles were retracted by the journal ad are considered off-topic.


Cha, JY; Ahn, HY; Moon, HI; Jeong, YK; Cho, YS. (2012). Effect of fermented Angelicae gigantis Radix on carbon tetrachloride-induced hepatotoxicity and oxidative stress in rats. Immunopharmacol Immunotoxicol 34: 265-274. http://dx.doi.org/10.3109/08923973.2011.600765

El-Sayed, YS; Lebda, MA; Hassinin, M; Neoman, SA. (2015). Chicory (Cichorium intybus L.) root extract regulates the oxidative status and antioxidant gene transcripts in CCl4-induced hepatotoxicity. PLoS ONE 10: e0121549. http://dx.doi.org/10.1371/journal.pone.0121549

Li, C; Jiang, W; Zhu, H; Hou, J. (2012). Antifibrotic effects of protocatechuic aldehyde on experimental liver fibrosis. Pharmaceutical Biology 50: 413-419. http://dx.doi.org/10.3109/13880209.2011.608193

Ping, J; Gao, AM; Qin, HQ; Wei, XN; Bai, J; Liu, L; Li, XH; Li, RW; Ao, Y; Wang, H. (2011). Indole-3-carbinol enhances the resolution of rat liver fibrosis and stimulates hepatic stellate cell apoptosis by blocking the inhibitor of κB kinase α/inhibitor of κB-α/nuclear factor-κB pathway. J Pharmacol Exp Ther 339: 694-703. http://dx.doi.org/10.1124/jpet.111.179820

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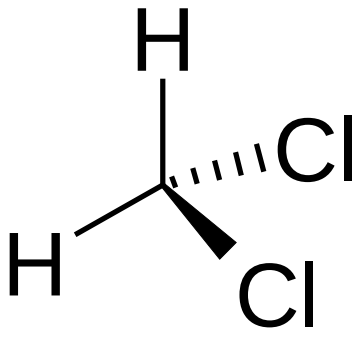
Office of Chemical Safety and
Pollution Prevention

United States
Environmental Protection Agency

# Problem Formulation of the Risk Evaluation for Methylene Chloride (Dichloromethane, DCM)

## CASRN: 75-09-2




*May 2018*

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# ACKNOWLEDGEMENTS

This report was developed by the United States Environmental Protection Agency (U.S. EPA), Office of Chemical Safety and Pollution Prevention (OCSPP), Office of Pollution Prevention and Toxics (OPPT).

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**Docket**

Supporting information can be found in public docket: EPA-HQ-OPPT-2016-0742.

**Disclaimer**

Reference herein to any specific commercial products, process or service by trade name, trademark, manufacturer or otherwise does not constitute or imply its endorsement, recommendation or favoring by the United States Government.

# ABBREVIATIONS

| | |
|---|---|
| °C | Degrees Celsius |
| ACGIH | American Conference of Government Industrial Hygienists |
| AEGL | Acute Exposure Guideline Level |
| atm | Atmosphere(s) |
| ATSDR | Agency for Toxic Substances and Disease Registry |
| BAF | Bioaccumulation Factor |
| BCF | Bioconcentration Factor |
| CAA | Clean Air Act |
| CASRN | Chemical Abstracts Service Registry Number |
| CBI | Confidential Business Information |
| CDR | Chemical Data Reporting |
| CEHD | Chemical Exposure Health Data |
| CEPA | Canadian List of Toxic Substances |
| CERCLA | Comprehensive Environmental Response, Compensation and Liability Act |
| CFR | Code of Federal Regulations |
| CHIRP | Chemical Risk Information Platform |
| $cm^3$ | Cubic Centimeter(s) |
| CNS | Central Nervous System |
| COC | Concentration of Concern |
| CoCAP | Cooperative Chemicals Assessment Program |
| COHb | Carboxyhemoglobin |
| CPSA | Consumer Product Safety Act |
| CPSC | Consumer Product Safety Commission |
| CSCL | Chemical Substances Control Law |
| CSHO | Certified Safety and Health Official |
| CWA | Clean Water Act |
| DCM | Dichloromethane (Methylene Chloride) |
| DIY | Do it yourself |
| DMR | Discharge Monitoring Report |
| DOT | Department of Transportation |
| $EC_{50}$ | Effect concentration at which 50% of test organisms exhibit an effect |
| ECHA | European Chemicals Agency |
| EG | Effluent Guidelines |
| EHC | Environmental Health Criteria |
| EPA | Environmental Protection Agency |
| EPCRA | Emergency Planning and Community Right-to-Know Act |
| ESD | Emission Scenario Document |
| EU | European Union |
| FDA | Food and Drug Administration |
| FFDCA | Federal Food, Drug, and Cosmetic Act |
| FSHA | Federal Hazardous Substance Act |
| g | Gram(s) |
| HAP | Hazardous Air Pollutant |
| HFC | Hydrofluorocarbon |
| HHE | Health Hazard Evaluation |
| HMTA | Hazardous Materials Transportation Act |
| HPV | High Production Volume |
| Hr | Hour |

| | |
|---|---|
| IARC | International Agency for Research on Cancer |
| ICIS | Integrated Compliance Information System |
| IDLH | Immediately Dangerous to Life and Health |
| IMAP | Inventory Multi-Tiered Assessment and Prioritisation |
| IRIS | Integrated Risk Information System |
| ISHA | Industrial Safety and Health Act |
| $K_{oc}$ | Soil Organic Carbon-Water Partitioning Coefficient |
| $K_{ow}$ | Octanol/Water Partition Coefficient |
| kg | Kilogram(s) |
| L | Liter(s) |
| lb | Pound(s) |
| $LC_{50}$ | Lethal Concentration at which 50% of test organisms die |
| $LD_{50}$ | Lethal Dose at which 50% of test organisms die |
| LOD | Limit of detection |
| Log $K_{oc}$ | Logarithmic Organic Carbon:Water Partition Coefficient |
| Log $K_{ow}$ | Logarithmic Octanol: Water Partition Coefficient |
| $m^3$ | Cubic Meter(s) |
| MACT | Maximum Achievable Control Technology |
| MCL | Maximum Contaminant Level |
| MCLG | Maximum Contaminant Level Goal |
| mg | Milligram(s) |
| mmHg | Millimeter(s) of Mercury |
| MOA | Mode of Action |
| mPa·s | Millipascal(s)-Second |
| MSW | Municipal Solid Waste |
| NAC | National Advisory Committee |
| NAICS | North American Industry Classification System |
| NATA | National Scale Air-Toxics Assessment |
| NAWQA | National Water Quality Assessment Program |
| ND | Non-detect |
| NEI | National Emissions Inventory |
| NESHAP | National Emission Standards for Hazardous Air Pollutants |
| NHANES | National Health and Nutrition Examination Survey |
| NICNAS | National Industrial Chemicals Notification and Assessment Scheme |
| NIH | National Institutes of Health |
| NIOSH | National Institute of Occupational Safety and Health |
| NITE | National Institute of Technology and Evaluation |
| NOAA | National Oceanic and Atmospheric Administration |
| NPDES | National Pollutant Discharge Elimination System |
| NPDWR | National Primary Drinking Water Regulation |
| NRC | National Research Council |
| NTP | National Toxicology Program |
| NWIS | National Water Information System |
| OCSPP | Office of Chemical Safety and Pollution Prevention |
| OECD | Organisation for Economic Co-operation and Development |
| OEHHA | Office of Environmental Health Hazard Assessment |
| OEL | Occupational Exposure Limits |
| ONU | Occupational Non-User |
| OPPT | Office of Pollution Prevention and Toxics |

| | |
|---|---|
| OSHA | Occupational Safety and Health Administration |
| OTVD | Open-Top Vapor Degreaser |
| PBPK | Physiologically-Based Pharmacokinetic |
| PBZ | Personal Breathing Zone |
| PECO | Population, Exposure, Comparator, and Outcome |
| PEL | Permissible Exposure Limit |
| PESS | Potentially Exposed or Susceptible Subpopulations |
| POD | Point of Departure |
| POTW | Publicly Owned Treatment Works |
| ppb | Part(s) per Billion |
| PPE | Personal Protective Equipment |
| ppm | Part(s) per Million |
| PSD | Particle Size Distribution |
| PV | Production Volume |
| QC | Quality Control |
| RCRA | Resource Conservation and Recovery Act |
| REACH | Registration, Evaluation, Authorisation and Restriction of Chemicals |
| REL | Recommended Exposure Limit |
| RICE | Reciprocating Internal Combustion Engines |
| RTR | Risk and Technology Review |
| SDS | Safety Data Sheets |
| SDWA | Safe Drinking Water Act |
| SIDS | Screening Information Data Set |
| SMAC | Spacecraft Maximum Allowable Concentrations |
| SNAP | Significant New Alternatives Policy |
| SpERC | Specific Environmental Release Categories |
| STEL | Short-Term Exposure Limit |
| STORET | STOrage and RETrieval and Water Quality exchange |
| TCCR | Transparent, clear, consistent, and reasonable |
| TLV | Threshold Limit Value |
| TRI | Toxics Release Inventory |
| TSCA | Toxic Substances Control Act |
| TTO | Total Toxic Organics |
| TWA | Time-Weighted Average |
| U.S. | United States |
| USGS | United States Geological Survey |
| VOC | Volatile Organic Compound |
| VP | Vapor Pressure |
| WHO | World Health Organization |
| Yr | Year(s) |

# EXECUTIVE SUMMARY

TSCA § 6(b)(4) requires the U.S. Environmental Protection Agency (EPA) to establish a risk evaluation process. In performing risk evaluations for existing chemicals, EPA is directed to "determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of costs or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator under the conditions of use." In December of 2016, EPA published a list of 10 chemical substances that are the subject of the Agency's initial chemical risk evaluations (81 FR 91927), as required by TSCA § 6(b)(2)(A). Methylene chloride was one of these chemicals.

TSCA § 6(b)(4)(D) requires that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use and potentially exposed or susceptible subpopulations that the Administrator expects to consider. In June 2017, EPA published the Scope of the Risk Evaluation for methylene chloride. As explained in the scope document, because there was insufficient time for EPA to provide an opportunity for comment on a draft of the scope, as EPA intends to do for future scope documents, EPA is publishing and taking public comment on a problem formulation document to refine the current scope, as an additional interim step prior to publication of the draft risk evaluation for methylene chloride. Comments received on this problem formulation document will inform development of the draft risk evaluation.

This problem formulation document refines the conditions of use, exposures and hazards presented in the scope of the risk evaluation for methylene chloride and presents refined conceptual models and analysis plans that describe how EPA expects to evaluate the risk for methylene chloride.

Methylene chloride, also known as dichloromethane and DCM, is a volatile and high production volume (HPV) chemical that is used as a solvent in a wide range of industrial, commercial and consumer applications. Methylene chloride is subject to a number of federal and state regulations and reporting requirements. Methylene chloride has been a reportable Toxics Release Inventory (TRI) chemical under Section 313 of the Emergency Planning and Community Right-to-Know Act (EPCRA) since 1987. It is designated a Hazardous Air Pollutant (HAP) under the Clean Air Act (CAA), a hazardous waste under the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA), a drinking water contaminant subject to national primary drinking water regulations under the Safe Drinking Water Act (SDWA), and certain household products containing methylene chloride are hazardous substances required to be labeled under the Federal Hazardous Substances Act (FHSA) by the Consumer Product Safety Commission (CPSC) including a recent update to the labelling for paint removers (83 FR 12254, March 21, 2018 and 83 FR 18219, April 26, 2018).

Information on domestic manufacture, processing and use of methylene chloride is available to EPA through its Chemical Data Reporting (CDR) Rule, issued under TSCA. In 2015, more than 260 million lbs of methylene chloride was reported to be manufactured (including imported) in the U.S. According to the ICIS (2007) chemical profile in 2005, the primary uses for methylene chloride are paint stripping and removal (30%), adhesives (22%), pharmaceuticals (11%), metal cleaning (8%), aerosols (8%), chemical processing (8%), flexible polyurethane foam (5%) and miscellaneous (8%).

This document presents the potential exposures that may result from the conditions of use of methylene chloride. Exposures may occur to workers and occupational non-users (workers who do not directly handle the chemical but perform work in an area where the chemical is used), consumers and bystanders (non-product users that are incidentally exposed to the product) and the general population through inhalation, dermal and oral pathways. Workers and occupational non-users may be exposed to

methylene chloride during a variety of conditions of use, such as manufacturing, processing and industrial and commercial uses, including uses in paint removal, adhesives and degreasing. EPA expects that the highest exposures to methylene chloride generally involve workers in industrial and commercial settings. Methylene chloride can be found in numerous products and can, therefore, result in exposures to commercial and consumer users in indoor or outdoor environments. For methylene chloride, EPA considers workers, occupational non-users, consumers, bystanders, and certain other groups of individuals who may experience greater exposures than the general population due to proximity to conditions of use to be potentially exposed or susceptible subpopulations. Exposures to the general population may occur from industrial and/or commercial uses; industrial releases to air, water or land; and other conditions of use. EPA will evaluate whether groups of individuals within the general population may be exposed via pathways that are distinct from the general population due to unique characteristics (e.g., life stage, behaviors, activities, duration) that increase exposure and whether groups of individuals have heightened susceptibility, and should therefore be considered potentially exposed or susceptible subpopulations for purposes of the risk evaluation. EPA plans to further analyze inhalation exposures to vapors and mists for workers and occupational non-users (workers who do not directly handle the chemical but perform work in an area where the chemical is present) and dermal exposures for skin contact with liquids in occluded situations for workers in the risk evaluation. EPA plans to further analyze inhalation exposures to vapors and mists for consumers and bystanders and dermal exposures for skin contact with liquids in the risk evaluation. For environmental release pathways, EPA plans to further analyze surface water exposure to aquatic invertebrates and aquatic plants in the risk evaluation.

Methylene chloride has been the subject of numerous human health reviews including EPA's Integrated Risk Information System (IRIS) Toxicological Review and Agency for Toxic Substances and Disease Registry's (ATSDR's) Toxicological Profile. A number of targets of toxicity from exposures to methylene chloride have been identified in animal and human studies for both oral and inhalation exposures. EPA plans to evaluate all potential hazards for methylene chloride, using these previous analyses as a starting point for identifying key and supporting studies and including any found in recent literature. The relevant studies will be evaluated using the data quality criteria in the *Application of Systematic Review in TSCA Risk Evaluations* document (U.S. EPA, 2018). Hazard endpoints identified in previous assessments include: acute toxicity (via central nervous system [CNS] depression which can result in death), irritation, liver toxicity and neurotoxicity. Methylene chloride is also likely carcinogenic in humans. If additional hazard concerns are identified during the systematic review of the literature, these will also be considered. These hazards will be evaluated based on the specific exposure scenarios identified.

The revised conceptual models presented in this problem formulation identify conditions of use; exposure pathways (e.g., media); exposure routes (e.g., inhalation, dermal, oral); potentially exposed or susceptible subpopulations; and hazards EPA expects to consider in the risk evaluation. The initial conceptual models provided in the scope document were revised during problem formulation based on evaluation of reasonably available information for physical and chemical properties, fate, exposures, hazards, and conditions of use and based upon consideration of other statutory and regulatory authorities. In each problem formulation document for the first 10 chemical substances, EPA also refined the activities, hazards and exposure pathways that will be included in and excluded from the risk evaluation.

EPA's overall objectives in the risk evaluation process are to conduct timely, relevant, high-quality, and scientifically credible risk evaluations within the statutory deadlines, and to evaluate the conditions of use that raise greatest potential for risk 82 FR 33726, 33728 (July 20, 2017).

# 1 INTRODUCTION

This document presents for comment the problem formulation of the risk evaluation to be conducted for methylene chloride under the Frank R. Lautenberg Chemical Safety for the 21st Century Act. The Frank R. Lautenberg Chemical Safety for the 21st Century Act amended the Toxic Substances Control Act (TSCA), the Nation's primary chemicals management law, on June 22, 2016. The new law includes statutory requirements and deadlines for actions related to conducting risk evaluations of existing chemicals.

In December of 2016, EPA published a list of 10 chemical substances that are the subject of the Agency's initial chemical risk evaluations (81 FR 91927), as required by TSCA § 6(b)(2)(A). These 10 chemical substances were drawn from the 2014 update of EPA's TSCA Work Plan for Chemical Assessments, a list of chemicals that EPA identified in 2012 and updated in 2014 (currently totaling 90 chemicals) for further assessment under TSCA. EPA's designation of the first 10 chemical substances constituted the initiation of the risk evaluation process for each of these chemical substances, pursuant to the requirements of TSCA § 6(b)(4).

TSCA § 6(b)(4)(D) requires that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use and potentially exposed or susceptible subpopulations that the Administrator expects to consider, within 6 months after the initiation of a risk evaluation. The scope documents for all first 10 chemical substances were issued on June 22, 2017. The first 10 problem formulation documents are a refinement of what was presented in the first 10 scope documents. TSCA § 6(b)(4)(D) does not distinguish between scoping and problem formulation, and requires EPA to issue scope documents that include information about the chemical substance, including the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations that the Administrator expects to consider in the risk evaluation. In the future, EPA expects scoping and problem formulation to be completed prior to the issuance of scope documents and intends to issue scope documents that include problem formulation.

As explained in the scope document, because there was insufficient time for EPA to provide an opportunity for comment on a draft of the scope, as EPA intends to do for future scope documents, EPA is publishing and taking public comment on a problem formulation document to refine the current scope, as an additional interim step prior to publication of the draft risk evaluation for methylene chloride. Comments received on this problem formulation document will inform development of the draft risk evaluation.

The Agency defines problem formulation as the analytical phase of the risk assessment in which "the purpose for the assessment is articulated, the problem is defined and a plan for analyzing and characterizing risk is determined" (see Section 2.2 of the Framework for Human Health Risk Assessment to Inform Decision Making). The outcome of problem formulation is a conceptual model(s) and an analysis plan. The conceptual model describes the linkages between stressors and adverse human health effects, including the stressor(s), exposure pathway(s), exposed life stage(s) and population(s), and endpoint(s) that will be addressed in the risk evaluation (U.S. EPA, 2014a). The analysis plan follows the development of the conceptual model(s) and is intended to describe the approach for conducting the risk evaluation, including its design, methods and key inputs and intended outputs as described in the EPA Human Health Risk Assessment Framework (U.S. EPA, 2014a). The problem formulation documents refine the initial conceptual models and analysis plans that were provided in the scope documents.

First, EPA has removed from the risk evaluation any activities and exposure pathways that EPA has concluded do not warrant inclusion in the risk evaluation. For example, for some activities which were listed as "conditions of use" in the scope document, EPA has insufficient information following the further investigations during problem formulation to find they are circumstances under which the chemical is actually "intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of."

Second, EPA also identified certain exposure pathways that are under the jurisdiction of regulatory programs and associated analytical processes carried out under other EPA-administered environmental statutes – namely, the Clean Air Act (CAA), the Safe Drinking Water Act (SDWA), the Clean Water Act (CWA), and the Resource Conservation and Recovery Act (RCRA) – and which EPA does not expect to include in the risk evaluation.

As a general matter, EPA believes that certain programs under other Federal environmental laws adequately assess and effectively manage the risks for the covered exposure pathways. To use Agency resources efficiently under the TSCA program, to avoid duplicating efforts taken pursuant to other Agency programs, to maximize scientific and analytical efforts, and to meet the three-year statutory deadline, EPA is planning to exercise its discretion under TSCA 6(b)(4)(D) to focus its analytical efforts on exposures that are likely to present the greatest concern and consequently merit a risk evaluation under TSCA, by excluding, on a case-by-case basis, certain exposure pathways that fall under the jurisdiction of other EPA-administered statutes.[1] EPA does not expect to include any such excluded pathways as further explained below in the risk evaluation. The provisions of various EPA-administered environmental statutes and their implementing regulations represent the judgment of Congress and the Administrator, respectively, as to the degree of health and environmental risk reduction that is sufficient under the various environmental statutes.

Third, EPA identified any conditions of use, hazards, or exposure pathways which were included in the scope document and that EPA expects to include in the risk evaluation but which EPA does not expect to further analyze in the risk evaluation. EPA expects to be able to reach conclusions about particular conditions of use, hazards or exposure pathways without further analysis and therefore expects to conduct no further analysis on those conditions of use, hazards or exposure pathways in order to focus the Agency's resources on more extensive or quantitative analyses. Each risk evaluation will be "fit-for-purpose," meaning not all conditions of use will warrant the same level of evaluation and the Agency may be able to reach some conclusions without comprehensive or quantitative risk evaluations 82 FR 33726, 33734, 33739 (July 20, 2017).

EPA received comments on the published scope document for methylene chloride and has considered the comments specific to methylene chloride in this problem formulation document. EPA is soliciting public comment on this problem formulation document and when the draft risk evaluation is issued the Agency intends to respond to comments that are submitted. In its draft risk evaluation, EPA may revise the conclusions and approaches contained in this problem formulations, including the conditions of use and pathways covered and the conceptual models and analysis plans, based on comments received.

[1] As explained in the final rule for chemical risk evaluation procedures, "EPA may, on a case-by case basis, exclude certain activities that EPA has determined to be conditions of use in order to focus its analytical efforts on those exposures that are likely to present the greatest concern, and consequently merit an unreasonable risk determination." [82 FR 33726, 33729 (July 20, 2017)]

## 1.1 Regulatory History

EPA conducted a search of existing domestic and international laws, regulations and assessments pertaining to methylene chloride. EPA compiled this summary from data available from federal, state, international and other government sources, as cited in Appendix A. EPA evaluated and considered the impact of existing laws and regulations (e.g., regulations on landfill disposal, design, and operations) in the problem formulation step to determine what, if any future analysis might be necessary as part of the risk evaluation. Consideration of the nexus between these existing regulations and TSCA conditions of use may additionally be made as detailed/specific conditions of use and exposure scenarios are developed in conducting the analysis phase of the risk evaluation.

***Federal Laws and Regulations***

Methylene chloride is subject to federal statutes or regulations, other than TSCA, that are implemented by other offices within EPA and/or other federal agencies/departments. A summary of federal laws, regulations and implementing authorities is provided in Appendix A.1.

***State Laws and Regulations***

Methylene chloride is subject to state statutes or regulations implemented by state agencies or departments. A summary of state laws, regulations and implementing authorities is provided in Appendix A.2.

***Laws and Regulations in Other Countries and International Treaties or Agreements***

Methylene chloride is subject to statutes or regulations in countries other than the United States and/or international treaties and/or agreements. A summary of these laws, regulations, treaties and/or agreements is provided in Appendix A.3.

## 1.2 Assessment History

EPA has identified assessments conducted by other EPA Programs and other organizations (see Table 1-1). Depending on the source, these assessments may include information on conditions of use, hazards, exposures and potentially exposed or susceptible subpopulations. Table 1-1 shows the assessments that have been conducted. EPA found no additional assessments beyond those listed in the Scope document, but the WHO IPCS Environmental Health Criteria (EHC) document which was cited in the Scope document was added to the assessment history table.

In addition to using this information, EPA intends to conduct a full review of the relevant data and information collected in the initial comprehensive search [see *Methylene Chloride (CASRN 75-09-2) Bibliography: Supplemental File for the TSCA Scope Document* EPA-HQ-OPPT-2016-0742-0059 (U.S. EPA, 2017a)] using the literature search and screening strategies documented in the *Strategy for Conducting Literature Searches for Methylene Chloride: Supplemental File for the TSCA Scope Document* EPA-HQ-OPPT-2016-0742-0060 (U.S. EPA, 2017c). This will ensure that EPA considers data and information that has been made available since these assessments were conducted.

**Table 1-1. Assessment History of Methylene Chloride**

| Authoring Organization | Assessment |
|---|---|
| **EPA Assessments** | |
| U.S. EPA, Office of Pollution Prevention and Toxics (OPPT) | TSCA Work Plan Chemical Risk Assessment Methylene Chloride: Paint Stripping Use CASRN: 75-09-2 U.S. EPA (2014b) |

| Authoring Organization | Assessment |
|---|---|
| U.S. EPA, Integrated Risk Information System (IRIS) | Toxicological Review of Dichloromethane (Methylene Chloride) (CAS No. 75-09-2) U.S. EPA (2011b) |
| U.S. EPA, Office of Water (OW) | Ambient Water Quality Criteria for the Protection of Human Health U.S. EPA (2015) |
| **Other U.S.-Based Organizations** | |
| Agency for Toxic Substances and Disease Registry (ATSDR) | Toxicological Profile for Methylene Chloride ATSDR (2000) and ATSDR (2010)addendum |
| National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances (NAC/AEGL Committee) | Interim Acute Exposure Guideline Levels (AEGL) for Methylene Chloride NAC/AEGL (2008) |
| U.S. National Academies, National Research Council (NRC) | Spacecraft Maximum Allowable Concentrations (SMAC) for Selected Airborne Contaminants: Methylene chloride (Volume 2) NRC (1996a) |
| National Toxicology Program (NTP), National Institutes of Health (NIH) | Report on Carcinogens, Twelfth Edition, Dichloromethane NIH (2016) |
| Occupational Safety and Health Administration (OSHA) | Occupational Exposure to Methylene Chloride OSHA (1997) |
| California Environmental Protection Agency, Office of Environmental Health Hazard Assessment (OEHHA) | Acute Reference Exposure Level (REL) and Toxicity Summary for Methylene Chloride OEHHA (2008) |
| | Public Health Goal for Methylene Chloride in Drinking Water OEHHA (2000) |
| **International** | |
| Organisation for Economic Co-operation and Development (OECD), Cooperative Chemicals Assessment Program (CoCAP) | Dichloromethane: SIDS Initial Assessment Profile OECD (2011) |
| International Agency for Research on Cancer (IARC) | IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 110 IARC (2016) |
| World Health Organization (WHO) | Air Quality Guidelines for Europe WHO (2000) |
| WHO International Programme on Chemical Safety (IPCS) | Environmental Health Criteria 164 Methylene Chloride WHO (1996) |
| Government of Canada, Environment Canada, Health Canada | Dichloromethane. Priority substances list assessment report. Health and Environment Canada (1993) |

| Authoring Organization | Assessment |
|---|---|
| National Industrial Chemicals Notification and Assessment Scheme (NICNAS), Australian Government | Human Health Tier II Assessment for Methane, dichloro- CAS Number: 75-09-2 NICNAS (2016) |

## 1.3 Data and Information Collection

EPA/OPPT generally applies a systematic review process and workflow that includes: (1) data collection; (2) data evaluation; and (3) data integration of the scientific data used in risk evaluations developed under TSCA. Scientific analysis is often iterative in nature as new knowledge is obtained. Hence, EPA/OPPT expects that multiple refinements regarding data collection will occur during the process of risk evaluation. Additional information that may be considered and was not part of the initial comprehensive bibliographies will be documented in the Draft Risk Evaluation for methylene chloride.

***Data Collection: Data Search***

EPA/OPPT conducted chemical-specific searches for information on: physical and chemical properties; environmental fate and transport; conditions of use information; environmental and human exposures, including potentially exposed or susceptible subpopulations; ecological and human health hazard, including potentially exposed or susceptible subpopulations.

EPA/OPPT designed its initial data search to be broad enough to capture a comprehensive set of sources containing information potentially relevant to the risk evaluation. For most disciplines, the search was not limited by date and was conducted on a wide range of data sources, including but not limited to: peer-reviewed literature and gray literature (e.g., publicly-available industry reports, trade association resources, government reports). For human health hazard, EPA/OPPT relied on the search strategies from recent assessments, such as the 2011 EPA Integrated Risk Information System (IRIS) assessment to identify relevant information published after the end date of the previous search to capture more recent literature. The *Strategy for Conducting Literature Searches for Methylene Chloride: Supplemental File for the TSCA Scope Document* EPA-HQ-OPPT-2016-0742-0060 (U.S. EPA, 2017c) provides details about the data and information sources and search terms that were used in the literature search.

***Data Collection: Data Screening***

Following the data search, references were screened and categorized using selection criteria outlined in the *Strategy for Conducting Literature Searches for Methylene Chloride: Supplemental File for the TSCA Scope Document* EPA-HQ-OPPT-2016-0742-0060 (U.S. EPA, 2017c). Titles and abstracts were screened against the criteria as a first step with the goal of identifying a smaller subset of the relevant data to move into the subsequent data extraction and data evaluation steps. Prior to full-text review, EPA/OPPT anticipates refinements to the search and screening strategies, as informed by an evaluation of the performance of the initial title/abstract screening and categorization process.

The categorization scheme (or tagging structure) used for data screening varies by scientific discipline (i.e., physical and chemical properties; environmental fate and transport; chemical use/conditions of use information; human and environmental exposures, including potentially exposed or susceptible subpopulations identified by virtue of greater exposure; human health hazard, including potentially exposed or susceptible subpopulations identified by virtue of greater susceptibility; and ecological hazard). However, within each data set, there are two broad categories or data tags: (1) o*n-topic* references or (2) *off-topic* references. *On-topic* references are those that may contain data and/or

information relevant to the risk evaluation. O*ff-topic* references are those that do not appear to contain data or information relevant to the risk evaluation. The supplemental document, *Strategy for Conducting Literature Searches for Methylene Chloride: Supplemental File for the TSCA Scope Document* EPA-HQ-OPPT-2016-0742-0060 (U.S. EPA, 2017c), discusses the inclusion and exclusion criteria that EPA/OPPT used to categorize references as *on-topic* or *off-topic*.

Additional data screening using sub-categories (or sub-tags) was also performed to facilitate further sorting of data/information - for example, identifying references by source type (e.g., published peer-reviewed journal article, government report); data type (e.g., primary data, review article); human health hazard (e.g., liver toxicity, cancer, reproductive toxicity); or chemical-specific and use-specific data or information. These sub-categories are described in the supplemental document, *Strategy for Conducting Literature Searches for Methylene Chloride: Supplemental File for the TSCA Scope Document* EPA-HQ-OPPT-2016-0742-0060 (U.S. EPA, 2017c), and will be used to organize the different streams of data during the stages of data evaluation and data integration steps of systematic review.

Results of the initial search and categorization can be found in the *Methylene Chloride (CASRN 75-09-2) Bibliography: Supplemental File for the TSCA Scope Document* EPA-HQ-OPPT-2016-0742-0059 (U.S. EPA, 2017a). This document provides a comprehensive list (bibliography) of the sources of data identified by the initial search and the initial categorization for *on-topic* and *off-topic* references. Because systematic review is an iterative process, EPA/OPPT expects that some references may move from the *on-topic* to the *off-topic* categories, and vice versa. Moreover, targeted supplemental searches may also be conducted to address specific needs for the analysis phase (e.g., to locate specific data needed for modeling); hence, additional *on-topic* references not initially identified in the initial search may be identified as the systematic review process proceeds.

## 1.4 Data Screening During Problem Formulation

EPA/OPPT is in the process of completing the full text screening of the *on-topic* references identified in the *Methylene Chloride* (*CASRN 75-09-2) Bibliography: Supplemental File for the TSCA Scope Document* EPA-HQ-OPPT-2016-0742-0059 (U.S. EPA, 2017a). The screening process at the full-text level is described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018). Appendix F provides the inclusion and exclusion criteria applied at the full text screening. The eligibility criteria are guided by the analytical considerations in the revised conceptual models and analysis plan, as discussed in the problem formulation document. Thus, it is expected that the number of data/information sources entering evaluation is reduced to those that are relevant to address the technical approach and issues described in the analysis plan of this document.

Following the screening process, the quality of the included data/information sources will be assessed using the evaluation strategies that are described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018).

# 2 PROBLEM FORMULATION

As required by TSCA, the scope of the risk evaluation identifies the conditions of use, hazards, exposures and potentially exposed or susceptible subpopulations that the Administrator expects to consider. To communicate and visually convey the relationships between these components, EPA included in the scope document a life cycle diagram and conceptual models that describe the actual or potential relationships between methylene chloride and human and ecological receptors. During the problem formulation, EPA revised the conceptual models based on further data gathering and analysis, as presented in this problem formulation document. An updated analysis plan is also included which identifies, to the extent feasible, the approaches and methods that EPA may use to assess exposures, effects (hazards) and risks under the conditions of use for methylene chloride.

## 2.1 Physical and Chemical Properties

Physical-chemical properties influence the environmental behavior and the toxic properties of a chemical, thereby informing the potential conditions of use, exposure pathways and routes and hazards that EPA intends to consider. For scope development, EPA considered the measured or estimated physical-chemical properties set forth in Table 2-1; EPA found no additional information during problem formulation that would change these values.

**Table 2-1. Physical and Chemical Properties of Methylene Chloride**

| Property | Value [a] | References |
|---|---|---|
| **Molecular formula** | $CH_2Cl_2$ | |
| **Molecular weight** | 84.93 g/mol | |
| **Physical form** | Colorless liquid; sweet, pleasant odor resembling chloroform | U. S. Coast Guard (1984) |
| **Melting point** | -95°C | O'Neil (2013) |
| **Boiling point** | 39.7°C | O'Neil (2013) |
| **Density** | 1.33 g/cm$^3$ at 20°C | O'Neil (2013) |
| **Vapor pressure** | 435 mmHg at 25°C | Boublík et al. (1984) |
| **Vapor density** | 2.93 (relative to air) | Holbrook (2003) |
| **Water solubility** | 13 g/L at 25°C | Horvath (1982) |
| **Octanol/water partition coefficient (log $K_{ow}$)** | 1.25 | Hansch et al. (1995) |
| **Henry's Law constant** | 0.00325 atm-m$^3$/mole | Leighton and Calo (1981) |
| **Flash point** | Not readily available | |
| **Autoflammability** | Not readily available | |
| **Viscosity** | 0.437 mPa·s at 20°C | Rossberg et al. (2011) |
| **Refractive index** | 1.4244 at 20°C | O'Neil (2013) |
| **Dielectric constant** | 9.02 at 20°C | Laurence et al. (1994) |

[a] Measured unless otherwise noted.

## 2.2 Conditions of Use

TSCA § 3(4) defines the conditions of use as ‘‘the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of.’’

### 2.2.1 Data and Information Sources

In the scope documents, EPA identified, based on reasonably available information, the conditions of use for the subject chemicals. EPA searched a number of available data sources (e.g., *Use and Market Profile for Methylene Chloride*, EPA-HQ-OPPT-2016-0742). Based on this search, EPA published a preliminary list of information and sources related to chemical conditions of use (see *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: Methylene Chloride*, EPA-HQ-OPPT-2016-0742-0003) prior to a February 2017 public meeting on scoping efforts for risk evaluation convened to solicit comment and input from the public. EPA also convened meetings with companies, industry groups, chemical users and other stakeholders to aid in identifying conditions of use and verifying conditions of use identified by EPA. The information and input received from the public and stakeholder meetings was incorporated into this problem formulation document to the extent appropriate. Thus, EPA believes the manufacture, processing, distribution, use and disposal activities constitute the intended, known, and reasonably foreseeable activities associated with the subject chemical, based on reasonably available information.

### 2.2.2 Identification of Conditions of Use

To determine the current conditions of use of methylene chloride and inversely, activities that do not qualify as conditions of use, EPA conducted extensive research and outreach. This included EPA’s review of published literature and online databases including the most recent data available from EPA’s Chemical Data Reporting program (CDR) and Safety Data Sheets (SDSs). EPA also conducted online research by reviewing company websites of potential manufacturers, importers, distributors, retailers, or other users of methylene chloride and queried government and commercial trade databases. EPA also received comments on the *Scope of the Risk Evaluation for Methylene Chloride* (EPA-HQ-OPPT-2016-0742) that were used to determine the conditions of use. In addition, EPA convened meetings with companies, industry groups, chemical users, states, environmental groups, and other stakeholders to aid in identifying conditions of use and verifying conditions of use identified by EPA. Those meetings included a February 14, 2017 public meeting with such entities (EPA-HQ-OPPT-2016-0742).

EPA has removed from the risk evaluation any activities that EPA concluded do not constitute conditions of use – for example because EPA has insufficient information to find certain activities are circumstances under which the chemical is actually “intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used or disposed of.” EPA has also identified any conditions of use that EPA does not expect to include in the risk evaluation. As explained in the final rule for Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act, TSCA section 6(b)(4)(D) requires EPA to identify "the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations the Administrator expects to consider” in a risk evaluation, suggesting that EPA may exclude certain activities that EPA has determined to be conditions of use on a case-by-case basis. (82 FR 33726, 33729; July 20, 2017). For example, EPA may exclude conditions of use that the Agency has sufficient basis to conclude would present only de minimis exposures or otherwise insignificant risks (such as use in a closed system that effectively precludes exposure or use as an intermediate).

The activities that EPA no longer believes are conditions of use or were otherwise excluded during problem formulation are described in Section 2.2.2.1. The conditions of use included in the scope of the risk evaluation are summarized in Section 2.2.2.2.

#### 2.2.2.1 Categories and Subcategories Determined Not to be Conditions of Use or Otherwise Excluded During Problem Formulation

For methylene chloride, EPA has conducted public outreach and literature searches to collect information about methylene chloride's conditions of use and has reviewed reasonably available information obtained or possessed by EPA concerning activities associated with methylene chloride. Based on this research and outreach, other than the category and subcategory described in Section 2.2.2.1, EPA does not have reason to believe that any conditions of use identified in the methylene chloride scope should be excluded from risk evaluation. Therefore, all the conditions of use for methylene chloride will be included in the risk evaluation.

During problem formulation, EPA determined that methylene chloride-based extraction solvents for oils, waxes, fats, spices, and hops meet the definition of food additive in section 201 of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 321, and are therefore excluded from the definition of "chemical substance" in TSCA § 3(2)(B)(vi). Activities and releases associated with such extraction solvents are therefore not "conditions of use" (defined as circumstances associated with "a chemical substance," TSCA § 3(4)) and will not be evaluated during risk evaluation. In particular, the use of methylene chloride-based extraction solvent for oils, waxes, fats, spices, and hops in agricultural chemical manufacturing and food processing was identified as a condition of use in the methylene chloride scope document but is no longer considered a condition of use and will not be evaluated in the risk evaluation.

In its 2014 risk evaluation, EPA assessed the risk from methylene chloride in consumer and commercial paint removal (U.S. EPA, 2014b). The Agency determined that those risks were unreasonable and, on January 19, 2017, proposed restrictions under TSCA section 6 to address the risks from methylene chloride in paint and coating removal by consumers and most commercial users except for commercial furniture stripping (82 FR 7464, January 19, 2017). While paint and coating removal falls under the conditions of use for methylene chloride, based on the intention to finalize the rulemaking the scenarios already assessed in the 2014 risk assessment these uses will not be re-evaluated and EPA will rely on the 2014 risk evaluation (https://www.epa.gov/newsreleases/epa-announces-action-methylene-chloride).

**Table 2-2. Categories and Subcategories Determined Not to be Conditions of Use or Otherwise Excluded During Problem Formulation**

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| Industrial, commercial and consumer uses | Other Uses | Extraction solvent for oils, waxes, fats, spices and hops in agricultural chemical manufacturing and food processing | U.S. EPA (2016b) Market profile EPA-HQ-OPPT-2016-0742 |
| | Paints and coatings | Paints and coating removers except for commercial furniture stripping | proposed restrictions under TSCA section 6 (82 FR 7464, January 19, 2017). |

#### 2.2.2.2 Categories and Subcategories of Conditions of Use Included In the Scope of Risk Evaluation

Methylene chloride has known applications as a process solvent in paint removers and the manufacture of pharmaceuticals and film coatings. It is used as an agent in urethane foam blowing and in the manufacture of hydrofluorocarbon (HFC) refrigerants, such as HFC-32. It can also be found in aerosol propellants and in solvents for electronics manufacturing, metal cleaning and degreasing and furniture finishing.

According to the ICIS (2007) chemical profile, the use percentages of methylene chloride by sector were as follows: paint stripping and removal (30%), adhesives (22%), pharmaceuticals (11%), metal cleaning (8%), aerosols (8%), chemical processing (8%), flexible polyurethane foam (5%) and miscellaneous (8%).

Table 2-3 summarizes each life cycle stage and the corresponding categories and subcategories of conditions of use for methylene chloride that EPA expects to consider in the risk evaluation. Using the 2016 CDR (U.S. EPA, 2016b), EPA identified industrial processing or use activities, industrial function categories and commercial and consumer use product categories. EPA identified the subcategories by supplementing CDR data with other published literature and information obtained through stakeholder consultations. For risk evaluations, EPA intends to consider each life cycle stage (and corresponding use categories and subcategories) and assess certain relevant potential sources of release and human exposure associated with that life cycle stage.

Beyond the uses identified in the *Scope of the Risk Evaluation for Methylene Chloride*, EPA has received no additional information identifying additional current conditions of use for methylene chloride from public comment and stakeholder meetings.

**Table 2-3. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation**

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| Manufacturing | Domestic manufacturing | Manufacturing | U.S. EPA (2016b) |
| | Import | Import | U.S. EPA (2016b) |
| Processing | Processing as a reactant | Intermediate in industrial gas manufacturing (e.g., manufacture of fluorinated gases used as refrigerants) | U.S. EPA (2016b); U.S. EPA (2014b) Market profile EPA-HQ-OPPT-2016-0742 Public Comments EPA-HQ-OPPT-2016-0742-0016, EPA-HQ-OPPT-2016-0742-0017, EPA-HQ-OPPT-2016-0742-0019 |
| | | Intermediate for pesticide, fertilizer, and other agricultural chemical manufacturing | U.S. EPA (2016b) |
| | | CBI function for petrochemical manufacturing | U.S. EPA (2016b) |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| Processing | Processing as a reactant | Intermediate for other chemicals | Public Comment EPA-HQ-OPPT-2016-0742-0008 |
| | Incorporated into formulation, mixture, or reaction product | Solvents (for cleaning or degreasing), including manufacturing of:<br>• All other basic organic chemical<br>• Soap, cleaning compound and toilet preparation | U.S. EPA (2016b) |
| | Incorporated into formulation, mixture, or reaction product | Solvents (which become part of product formulation or mixture), including manufacturing of:<br>• All other chemical product and preparation<br>• Paints and coatings | U.S. EPA (2016b) |
| | | Propellants and blowing agents for all other chemical product and preparation manufacturing; | U.S. EPA (2016b) |
| | | Propellants and blowing agents for plastics product manufacturing | Use document EPA-HQ-OPPT-2016-0742-0003, Market profile EPA-HQ-OPPT-2016-0742 |
| | | Paint additives and coating additives not described by other codes for CBI industrial sector | U.S. EPA (2016b) |
| | | Laboratory chemicals for all other chemical product and preparation manufacturing | U.S. EPA (2016b), EPA-HQ-OPPT-2016-0742-0005, EPA-HQ-OPPT-2016-0742-0014 |
| | | Laboratory chemicals for CBI industrial sectors | U.S. EPA (2016b) |
| | | Processing aid, not otherwise listed for petrochemical manufacturing | U.S. EPA (2016b) |
| | | Adhesive and sealant chemicals in adhesive manufacturing | Use document EPA-HQ-OPPT-2016-0742-0003; U.S. EPA (2016b) |
| | | Unknown function for oil and gas drilling, extraction, and support activities | Use document EPA-HQ-OPPT-2016-0742-0003; U.S. EPA (2016b) |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| Processing | Repackaging | Solvents (which become part of product formulation or mixture) for all other chemical product and preparation manufacturing | Use document EPA-HQ-OPPT-2016-0742-0003; U.S. EPA (2016b) |
| | | CBI functions for all other chemical product and preparation manufacturing | Use document EPA-HQ-OPPT-2016-0742-0003; U.S. EPA (2016b) |
| | Recycling | Recycling | U.S. EPA (2017d) |
| Distribution in commerce | Distribution | Distribution | Use document EPA-HQ-OPPT-2016-0742-0003 U.S. EPA (2016b) |
| Industrial, commercial and consumer uses | Solvents (for cleaning or degreasing) [c] | Batch vapor degreaser (e.g., open-top, closed-loop) | Use document EPA-HQ-OPPT-2016-0742-0003; U.S. EPA (2016b); Public comment EPA-HQ-OPPT-2016-0742-0017 |
| | | In-line vapor degreaser (e.g., conveyorized, web cleaner) | Use document EPA-HQ-OPPT-2016-0742-0003; U.S. EPA (2016b); Public comment EPA-HQ-OPPT-2016-0742-0017 |
| | | Cold cleaner | Use document EPA-HQ-OPPT-2016-0742-0003; U.S. EPA (2016b, 2014b) |
| | | Aerosol spray degreaser/cleaner | U.S. EPA (2016b, 2014b) EPA-HQ-OPPT-2016-0742-0003; Market profile EPA-HQ-OPPT-2016-0742 |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| Industrial, commercial and consumer uses | Adhesives and sealants | Single component glues and adhesives and sealants and caulks | Use document EPA-HQ-OPPT-2016-0742-0003; U.S. EPA (2016b); Public comments EPA-HQ-OPPT-2016-0742-0005, EPA-HQ-OPPT-2016-0742-0013, EPA-HQ-OPPT-2016-0742-0014, EPA-HQ-OPPT-2016-0742-0017, EPA-HQ-OPPT-2016-0742-0021, EPA-HQ-OPPT-2016-0742-0033 |
| | Paints and coatings including paint and coating removers for commercial furniture stripping | Paints and coatings use and paints and coating removers for commercial furniture stripping | U.S. EPA (2016b, 2014b); Market profile EPA-HQ-OPPT-2016-0742 Public Comments EPA-HQ-OPPT-2016-0742-0005, EPA-HQ-OPPT-2016-0742-0009, EPA-HQ-OPPT-2016-0742-0014, EPA-HQ-OPPT-2016-0742-0017, EPA-HQ-OPPT-2016-0742-0021, EPA-HQ-OPPT-2016-0742-0025 |
| | | Adhesive/caulk removers | Use document EPA-HQ-OPPT-2016-0742-0003, Market profile EPA-HQ-OPPT-2016-0742 |
| | Metal products not covered elsewhere | Degreasers – aerosol and non-aerosol degreasers and cleaners e.g., coil cleaners | Market profile EPA-HQ-OPPT-2016-0742 U.S. EPA (2016b) |
| | Fabric, textile and leather products not covered elsewhere | Textile finishing and impregnating/ surface treatment products e.g. water repellant | Market profile EPA-HQ-OPPT-2016-0742 |
| | Automotive care products | Function fluids for air conditioners: refrigerant, treatment, leak sealer | Use document EPA-HQ-OPPT-2016-0742-0003; Market profile EPA-HQ-OPPT-2016-0742, U.S. EPA (2016b) |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| Industrial, commercial and consumer uses | Automotive care products | Interior car care – spot remover | Use document EPA-HQ-OPPT-2016-0742-0003 |
| | | Degreasers: gasket remover, transmission cleaners, carburetor cleaner, brake quieter/cleaner | Use document EPA-HQ-OPPT-2016-0742-0003, Market profile EPA-HQ-OPPT-2016-0742, U.S. EPA (2016b) |
| | Apparel and footwear care products | Post-market waxes and polishes applied to footwear e.g. shoe polish | Market profile EPA-HQ-OPPT-2016-0742 |
| | Laundry and dishwashing products | Spot remover for apparel and textiles | Use document EPA-HQ-OPPT-2016-0742-0003 |
| | Lubricants and greases | Liquid and spray lubricants and greases | U.S. EPA (2016b); EPA-HQ-OPPT-2016-0742-0003; Market profile EPA-HQ-OPPT-2016-0742; Public Comment EPA-HQ-OPPT-2016-0742-0021 |
| | | Degreasers – aerosol and non-aerosol degreasers and cleaners | U.S. EPA (2016b); EPA-HQ-OPPT-2016-0742-0003; Market profile EPA-HQ-OPPT-2016-0742; Public Comments EPA-HQ-OPPT-2016-0742-0005, EPA-HQ-OPPT-2016-0742-0014 |
| | Building/ construction materials not covered elsewhere | Cold pipe insulation | Use document EPA-HQ-OPPT-2016-0742-0003 |
| | Solvents (which become part of product formulation or mixture) | All other chemical product and preparation manufacturing | U.S. EPA (2016b) |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| Industrial, commercial and consumer uses | Processing aid not otherwise listed | In multiple manufacturing sectors[d] | Use document EPA-HQ-OPPT-2016-0742-0003; Market profile EPA-HQ-OPPT-2016-0742; U.S. EPA (2016b) |
| | Propellants and blowing agents | Flexible polyurethane foam manufacturing | Market profile EPA-HQ-OPPT-2016-0742 |
| | Arts, crafts and hobby materials | Crafting glue and cement/concrete | Use document EPA-HQ-OPPT-2016-0742-0003 |
| | Other Uses | Laboratory chemicals - all other chemical product and preparation manufacturing | Use document EPA-HQ-OPPT-2016-0742-0003; Market profile EPA-HQ-OPPT-2016-0742; Public Comment: EPA-HQ-OPPT-2016-0742-0066 |
| | | Electrical equipment, appliance, and component manufacturing | U.S. EPA (2016b), Public Comment EPA-HQ-OPPT-2016-0742-0017 |
| | | Plastic and rubber products | U.S. EPA (2016b) |
| | | Anti-adhesive agent - anti-spatter welding aerosol | Use document EPA-HQ-OPPT-2016-0742-0003; Market profile EPA-HQ-OPPT-2016-0742; Public Comment EPA-HQ-OPPT-2016-0742-0005 |
| | | Oil and gas drilling, extraction, and support activities | Use document EPA-HQ-OPPT-2016-0742-0003; U.S. EPA (2016b) |
| | | Functional fluids (closed systems) in pharmaceutical and medicine manufacturing | U.S. EPA (2016b) |
| | | Toys, playground, and sporting equipment - including novelty articles (toys, gifts, etc.) | Use document EPA-HQ-OPPT-2016-0742-0003; EPA-HQ-OPPT-2016-0742-0069; |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| Industrial, commercial and consumer uses | Other Uses | Carbon remover, lithographic printing cleaner, brush cleaner, use in taxidermy, and wood floor cleaner | Use document EPA-HQ-OPPT-2016-0742-0003; Market profile EPA-HQ-OPPT-2016-0742; U.S. EPA (2016b) |
| Disposal | Disposal | Industrial pre-treatment | U.S. EPA (2017d) |
| | | Industrial wastewater treatment | |
| | | Publicly owned treatment works (POTW) | |
| | | Underground injection | |
| | | Municipal landfill | |
| | | Hazardous landfill | |
| | | Other land disposal | |
| | | Municipal waste incinerator | |
| | | Hazardous waste incinerator | |
| | | Off-site waste transfer | |

[a] These categories of conditions of use appear in the initial life cycle diagram, reflect CDR codes and broadly represent conditions of use for methylene chloride in industrial and/or commercial settings.
[b] These subcategories reflect more specific uses of methylene chloride.
[c] Reported for the following sectors in the 2016 CDR for manufacturing of: plastic materials and resins, plastics products, miscellaneous, all other chemical product and preparation (U.S. EPA, 2016b).
[d] Reported for the following sectors in the 2016 CDR for manufacturing of: petrochemicals, plastic materials and resins, plastics products, miscellaneous, all other chemical product and CBI (U.S. EPA, 2016b) also including as a chemical processor for polycarbonate resins and cellulose triacetate (photographic film).

#### 2.2.2.3 Overview of Conditions of Use and Lifecycle Diagram

The life cycle diagram provided in Figure 2-1 depicts the conditions of use that are considered within the scope of the risk evaluation during various life cycle stages including manufacturing, processing, distribution, use (industrial, commercial, consumer; when distinguishable) and disposal. Additions or changes to conditions of use based on additional information gathered or analyzed during problem formulation were described in Section 2.2.2.1 and 2.2.2.2. The activities that EPA determined are out of scope during problem formulation are not included in the life cycle diagram. The information is grouped according to Chemical Data Reporting (CDR) processing codes and use categories (including functional use codes for industrial uses and product categories for commercial and consumer uses), in combination with other data sources (e.g., published literature and consultation with stakeholders), to provide an overview of conditions of use. EPA notes that some subcategories may be grouped under multiple CDR categories.

Use categories include the following: “industrial use” means use at a site at which one or more chemicals or mixtures are manufactured (including imported) or processed. “Commercial use” means the use of a chemical or a mixture containing a chemical (including as part of an article) in a commercial

enterprise providing saleable goods or services. “Consumer use” means the use of a chemical or a mixture containing a chemical (including as part of an article, such as furniture or clothing) when sold to or made available to consumers for their use (U.S. EPA, 2016b).

To understand conditions of use relative to one another and associated potential exposures under those conditions of use, the life cycle diagram includes the production volume associated with each stage of the life cycle, as reported in the 2016 CDR reporting (U.S. EPA, 2016b), when the volume was not claimed confidential business information (CBI).

The 2016 CDR reporting data for methylene chloride are provided in Table 2-4 from EPA’s CDR database. This information has not changed during problem formulation from that provided in the scope document.

**Table 2-4. Production Volume of Methylene Chloride in CDR Reporting Period (2012 to 2015) [a]**

| Reporting Year | 2012 | 2013 | 2014 | 2015 |
|---|---|---|---|---|
| Total Aggregate Production Volume (lbs) | 230,896,388 | 230,498,027 | 248,241,495 | 263,971,494 |

[a] The CDR data for the 2016 reporting period is available via ChemView (https://java.epa.gov/chemview) (U.S. EPA, 2016b). Because of an ongoing CBI substantiation process required by amended TSCA, the CDR data available in the scope document is more specific than currently in ChemView.

Descriptions of the industrial, commercial and consumer use categories identified from the 2016 CDR (U.S. EPA, 2016b) and included in the life cycle diagram (Figure 2-1) are summarized below. The descriptions provide a brief overview of the use category; Appendix B contains more detailed descriptions (e.g., process descriptions and worker activities) for each manufacturing, processing, use and disposal category. The descriptions provided below are primarily based on the corresponding industrial function category and/or commercial and consumer product category descriptions from the 2016 CDR and can be found in EPA’s Instructions for Reporting 2016 TSCA Chemical Data Reporting (U.S. EPA, 2016a).

The **“Solvents for Cleaning and Degreasing”** category encompasses chemical substances used to dissolve oils, greases and similar materials from a variety of substrates including metal surfaces, glassware and textiles. This category includes the use of methylene chloride in vapor degreasers and cold cleaners and in industrial, commercial and consumer aerosol degreasing products. Methylene chloride degreasers are often designed to clean electronic parts, electric motors and other water-sensitive parts in industrial and commercial settings. Methylene chloride is also found in products available to consumers such as brush cleaners or products designed to remove oil and grease from electronic or mechanical parts.

The **“Adhesives and Sealants”** category encompasses chemical substances contained in adhesive and sealant products used to fasten other materials together. The adhesives and sealants are found in both liquid and aerosol forms. Examples include adhesives for bonding laminate to particle board or other surfaces, foam to textiles, fiberglass to metal ductwork, carpet installation and cement for bonding acrylic.

The **“Paints and Coatings”** category encompasses chemical substances used in a variety of paints, varnishes, lacquers or other types of coatings used on a variety of substrates including wood and metal. This category also covers paints and coatings removal uses, which include uses addressed in a previous

risk assessment. Both of these categories have industrial, commercial and consumer uses with products used in liquid, aerosol and paste forms.

The **"Metal Products Not Covered Elsewhere"** category encompasses chemical substances contained in metal products not covered elsewhere that are intended for consumer or commercial use. Examples of metal products not covered elsewhere include metal products produced by forging, stamping, plating, turning, and other processes; hand tools; metal tubing/pipes/duct work; wire fencing; tableware; and small appliances and cookware.

The **"Fabric, Textile, and Leather Products Not Covered Elsewhere"** category encompasses chemical substances used to clean and treat a variety of textiles including upholstery and leather. This category is primarily industrial and commercial users and the products are generally in liquid formulations.

The "**Automotive Care Products**" category encompasses chemical substances contained in products used to seal leaks in car air conditioners or used in auto air conditioner refrigerants. These products are generally used in aerosol form and used in both commercial and consumer settings.

The **"Apparel and Footwear Care Products"** category encompasses chemical substances contained in apparel and footwear care products that are applied post-market. Examples of apparel and footwear care products include footwear polishes/waxes, garment waterproofing sprays, and stain repellents. These products are primarily consumer or commercial uses.

The **"Laundry and Dishwashing Products"** category encompasses chemical substances contained in laundry and dishwashing products and aids. Examples of laundry and dishwashing products include detergents, fabric softeners, pre-soaks and prewashes to remove soil and stains, dryer sheets, bleach, rinse aids, and film, lime and rust removers. These products are generally used as liquids, granular, powders, gels, cakes, and flakes and used in both consumer and commercial settings.

The **"Lubricants and Greases"** category encompasses chemical substances contained in products used in lubricants for cables, chains, metal parts, doors and dry film. These are primarily commercial or industrial uses with both liquid and aerosol formulations.

Other uses of methylene chloride include uses in building/construction materials not covered elsewhere; solvents (which become part of product formation or mixture); processing aids not otherwise listed; propellants and blowing agents; arts, crafts and hobby materials (e.g., crafting glue and cement); functional fluids (closed systems); laboratory chemicals; novelty items (e.g., Red Retro Happy Dippy Drinking Bird).

Figure 2-1 depicts the life cycle diagram of methylene chloride from manufacture to the point of disposal. Activities related to the distribution (e.g., loading, unloading) will be considered throughout the methylene chloride life cycle rather, than using a single distribution scenario.

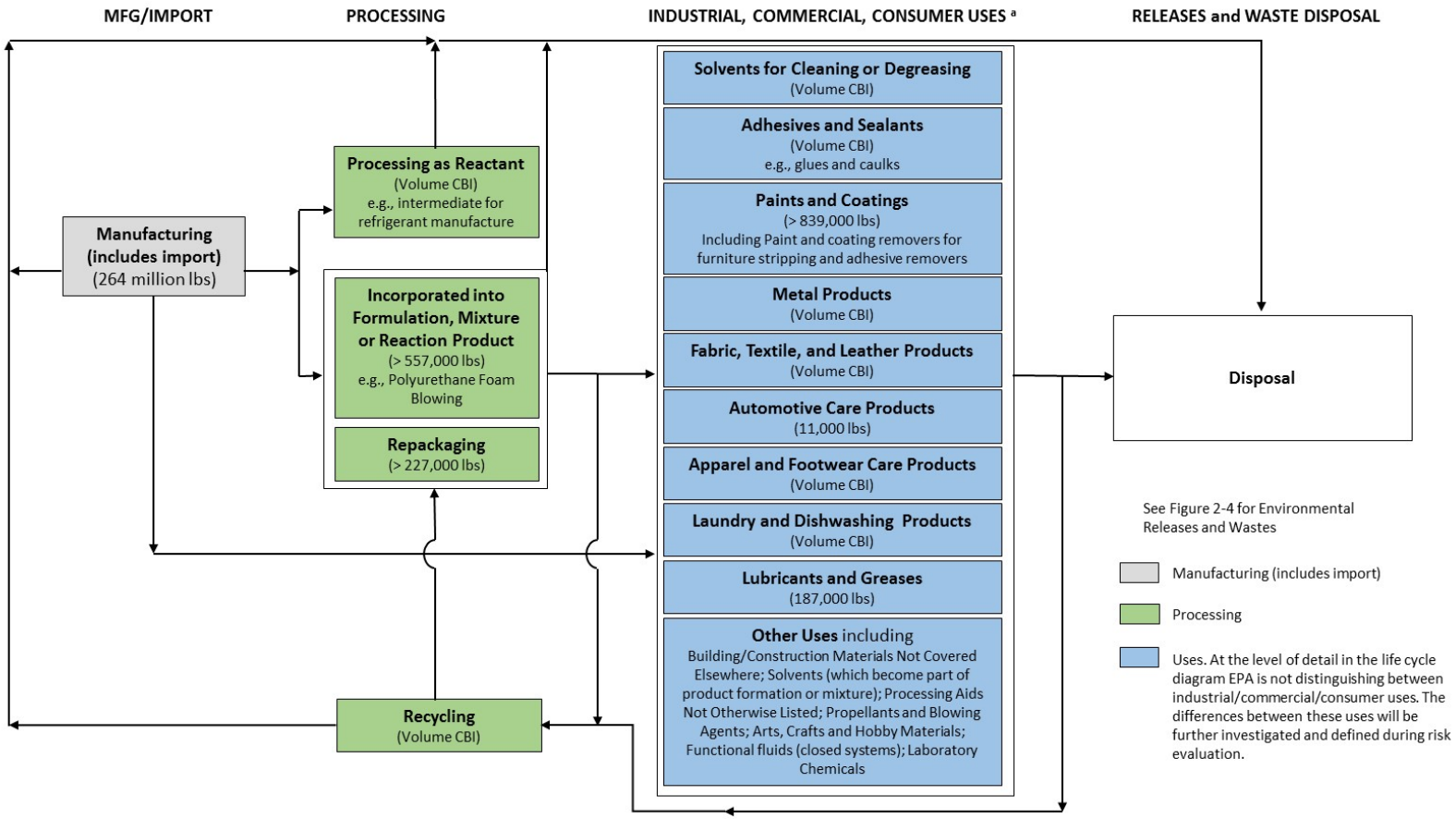


**Figure 2-1. Methylene Chloride Life Cycle Diagram**

The life cycle diagram depicts the conditions of use that are within the scope of the risk evaluation during various life cycle stages including manufacturing, processing, use (industrial, commercial, consumer), distribution and disposal. The production volumes shown are for reporting year 2015 from the 2016 CDR reporting period (U.S. EPA, 2016b). Activities related to distribution (e.g., loading and unloading) will be considered throughout the methylene chloride life cycle, rather than using a single distribution scenario.

[a] See Table 2-3 for additional uses not mentioned specifically in this diagram.

## 2.3 Exposures

For TSCA exposure assessments, EPA expects to evaluate exposures and releases to the environment resulting from the conditions of use applicable to methylene chloride. Post-release pathways and routes will be described to characterize the relationship or connection between the conditions of use for methylene chloride and the exposure to human receptors, including potentially exposed or susceptible subpopulations and ecological receptors. EPA will take into account, where relevant, the duration, intensity (concentration), frequency and number of exposures in characterizing exposures to methylene chloride.

### 2.3.1 Fate and Transport

Environmental fate includes both transport and transformation processes. Environmental transport is the movement of the chemical within and between environmental media. Transformation occurs through the degradation or reaction of the chemical with other species in the environment. Hence, knowledge of the environmental fate of the chemical informs the determination of the specific exposure pathways and potential human and environmental receptors EPA expects to consider in the risk evaluation. Table 2-5 provides environmental fate data that EPA identified and considered in developing the scope for methylene chloride. This information has not changed from that provided in the scope document.

Fate data including volatilization during wastewater treatment, volatilization from lakes and rivers, biodegradation rates, and organic carbon:water partition coefficient (log $K_{OC}$) were used when considering changes to the conceptual models. Model results and basic principles were used to support the fate data used in problem formulation while the literature review is currently underway through the systematic review process.

EPI Suite™ (U.S. EPA, 2012b) modules were used to estimate volatilization of methylene chloride from wastewater treatment plants, lakes, and rivers and to confirm the data showing slow biodegradation. The EPI Suite™ module that estimates chemical removal in sewage treatment plants ("STP" module) was run using default settings to evaluate the potential for methylene chloride to volatilize to air or adsorb to sludge during wastewater treatment. The STP module estimates that 56% of methylene chloride in wastewater will be removed by volatilization while < 1% of methylene chloride will be removed by adsorption.

The EPI Suite™ module that estimates volatilization from lakes and rivers ("Volatilization" module) was run using default settings to evaluate the volatilization half-life of methylene chloride in surface water. The parameters required for volatilization (evaporation) rate of an organic chemical from the water body are water depth, wind and current velocity of the river or lake. The volatilization module estimates that the half-life of methylene chloride in a model river will be 1.1 hours and the half-life in a model lake will be 3.7 days.

The EPI Suite™ module that predicts biodegradation rates ("BIOWIN" module) was run using default settings to estimate biodegradation rates of methylene chloride in soil and sediment. The aerobic biodegradation models (BIOWIN 1-6) estimate that methylene chloride is not readily biodegradable in aerobic environments, which supports the biodegradation data presented in the methylene chloride scoping document demonstrating slow biodegradation under aerobic conditions. The anaerobic biodegradation model (BIOWIN 7) predicts that methylene chloride will rapidly biodegrade under anaerobic conditions. Previous assessments of methylene chloride reported moderate aerobic biodegradation, particularly following an acclimation period, and evidence of anaerobic biodegradation (OECD, 2011; U.S. EPA, 2011b; ATSDR, 2010, 2000; Health and Environment Canada, 1993).

The organic carbon:water partition coefficient (log $K_{OC}$) reported in the methylene chloride scoping document was predicted using EPI Suite™. That value (1.4) is supported by the basic principles of environmental chemistry which states that the $K_{OC}$ is typically within one order of magnitude (one log unit) of the octanol:water partition coefficient ($K_{OW}$). Indeed, the log $K_{OW}$ reported for methylene chloride in the scoping document was 1.25, which is within the expected range. The log $K_{OC}$ reported in previous assessments of methylene chloride were in the range of 1.27 – 1.4 (ATSDR, 2000; Health and Environment Canada, 1993).

**Table 2-5. Environmental Fate Characteristics of Methylene Chloride**

| Property or Endpoint | Value [a] | References |
|---|---|---|
| Indirect photodegradation | 107 days (estimated) | OECD (2011) |
| Hydrolysis half-life | 18 months | OECD (2011) |
| Biodegradation | 13% in 28 days (not readily biodegradable) (aerobic sludge) | NITE (2002) |
| Bioconcentration factor (BCF) | 2.0 to 5.4 (carp)<br><6.4 to 40 (carp) | NITE (2002) |
| Bioaccumulation factor (BAF) | 2.6 (estimated) | U.S. EPA (2012b) |
| Organic carbon:water partition coefficient (log $K_{oc}$) | 1.4 (estimated) | U.S. EPA (2012b) |

[a] Measured unless otherwise noted. Data retrieved from the 2014 EPA risk assessment on methylene chloride (U.S. EPA, 2014b).

Releases of methylene chloride to the air and water are likely to evaporate to the atmosphere, or if released to soil, migrate to ground water. Methylene chloride is expected to undergo photooxidation in the atmosphere but considering its photodegradation half-life (107 days) it is moderately persistent and is expected to be subject to atmospheric transport.

Methylene chloride is not readily biodegradable but has been shown to biodegrade over a range of rates under aerobic and anaerobic conditions. Measured BCFs for methylene chloride considered in the 2014 EPA risk assessment on methylene chloride (U.S. EPA, 2014b) are 40 (log BCF 1.60) or below. The estimated bioaccumulation factor for methylene chloride is 2.6 (log BAF 0.4). Therefore, methylene chloride is not considered to be bioaccumulative.

### 2.3.2 Releases to the Environment

Releases to the environment from conditions of use (e.g., industrial and commercial processes, commercial or consumer uses resulting in down-the-drain releases) are one component of potential exposure and may be derived from reported data that are obtained through direct measurement, calculations based on empirical data and/or assumptions and models.

A source of information that EPA considered in evaluating exposure are data reported under the Toxics Release Inventory (TRI) program. Under the Emergency Planning and Community Right-to-Know Act (EPCRA) Section 313 rule, methylene chloride is a TRI-reportable substance effective January 1, 1987. During problem formulation EPA further analyzed the TRI data and examined the definitions of elements in the TRI data to determine the level of confidence that a release would result from certain

types of disposal to land (e.g. RCRA Subtitle C hazardous landfill and Class I underground Injection wells) and incineration. EPA also examined how methylene chloride is treated at industrial facilities.

Table 2-6 provides production-related waste managed data (also referred to as waste managed) for methylene chloride reported by industrial facilities to the TRI program for 2015. Table 2-7 provides more detailed information on the quantities released to air or water or disposed of on land.

**Table 2-6. Summary of Methylene Chloride TRI Production-Related Waste Managed in 2015 (lbs)**

| Number of Facilities | Recycling | Energy Recovery | Treatment | Releases [a, b, c] | Total Production Related Waste |
|---|---|---|---|---|---|
| 271 | 96,865,223 | 15,619,010 | 37,832,075 | 3,390,985 | 153,707,292 |

Data source: 2015 TRI Data (updated March 2017) (U.S. EPA, 2017d)
[a] Terminology used in these columns may not match the more detailed data element names used in the TRI public data and analysis access points.
[b] Does not include releases due to one-time event not associated with production such as remedial actions or earthquakes.
[c] Counts all releases including release quantities transferred and release quantities disposed of by a receiving facility reporting to TRI.

In 2015, 271 facilities reported a total of about 153.7 million pounds of methylene chloride waste managed. Of this total, about 96.9 million pounds were recycled, 15.6 million pounds were recovered for energy, 37.8 million pounds were treated, and 3.4 million pounds were released into the environment.

**Table 2-7. Summary of Methylene Chloride TRI Releases to the Environment in 2015 (lbs)**

| | Number of Facilities | Air Releases | | Water Releases | Land Disposal | | | Other Releases [a] | Total On- and Off-site Disposal or Other Releases [b, c] |
|---|---|---|---|---|---|---|---|---|---|
| | | Stack Air Releases | Fugitive Air Releases | | Class I Under-ground Injection | RCRA Subtitle C Landfills | All other Land Disposal [a] | | |
| **Subtotal** | | 1,279,661 | 1,262,485 | | 59,711 | 36,091 | 18,199 | | |
| **Totals** | 271 | 2,542,146 | | 2,366 | 114,001 | | | 713,241 | 3,371,754 |

Data source: 2015 TRI Data (updated March 2017) (U.S. EPA, 2017d)
[a] Terminology used in these columns may not match the more detailed data element names used in the TRI public data and analysis access points.
[b] These release quantities do include releases due to one-time events not associated with production such as remedial actions or earthquakes.
[c] Counts release quantities once at final disposition, accounting for transfers to other TRI reporting facilities that ultimately dispose of the chemical waste.

Of these releases, 75%, or 2.5 million pounds, were released to air (stack and fugitive air emissions), 2,366 pounds were released to water (surface water discharges), 114,000 pounds were released to land (of which Class I Underground Injection and Resource Conservation and Recovery Act (RCRA) Subtitle C landfills were the primary disposal methods) and 713,000 pounds were released in other forms such as to waste brokers. For stack releases, multiple types of facilities reported on incineration destruction, including hazardous waste facilities and facilities that perform other industrial activities and may be privately or publicly (i.e., federal, state or municipality) owned or operated. Off-site transfers for incineration (energy recovery, incineration/thermal treatment, incineration/insignificant fuel value)[2] of methylene chloride from TRI facilities nearly all go to RCRA Subtitle C facilities. Of the 14.9 million

[2] Quantities reported as managed on-site or off-site through incineration are within the energy recovery category and a portion of treatment category in Table 2-6.

lbs transferred for incineration, only 89,000 lbs were instead sent to facilities in Canada. The 713 thousand pounds released in other forms were transfers off-site for disposal. The majority were to waste brokers (662 thousand pounds), 39 thousand pounds were for disposal by other techniques, 8 thousand pounds were for off-site storage and 3 thousand pounds for unknown disposal.

Of the methylene chloride that went to on-site land disposal in 2015, most was disposed of in Class I underground injection wells (about 59,700 lbs) or RCRA Subtitle C Landfills (about 30,800 lbs). An additional 250 lbs were disposed of in landfills other than RCRA Subtitle C. No methylene chloride was reported to be disposed of in on-site Class II-V underground injection wells, on-site land treatment, or on-site surface impoundments. Of the off-site land disposal, about 5,300 lbs went to RCRA Subtitle C Landfills and about 8,200 lbs went to landfills other than RCRA Subtitle C. Almost negligible amounts were transferred off-site to land treatment, and Class I underground injection wells.

While production-related waste managed shown in Table 2-6 excludes any quantities reported as catastrophic or one-time releases (TRI section 8 data), release quantities shown in Table 2-7 include both production-related and non-routine quantities (TRI section 5 and 6 data). As a result, release quantities may differ slightly and may further reflect differences in TRI calculation methods for reported release range estimates (U.S. EPA, 2017d).

Other sources of information provide evidence of releases of methylene chloride, including EPA effluent guidelines (EGs) promulgated under the Clean Water Act (CWA), National Emission Standards for Hazardous Air Pollutants (NESHAPs) promulgated under the Clean Air Act (CAA), or other EPA standards and regulations that set legal limits on the amount of methylene chloride that can be emitted to a particular media. EPA is aware of additional agency resources for methylene chloride emissions data, including National Emissions Inventory (NEI) and the Discharge Monitoring Report (DMR) Pollutant Loading Tool, which provide additional release data specific to air and surface water, respectively. NEI provides comprehensive and detailed estimates of air emissions for criteria pollutants, criteria precursors and Hazardous Air Pollutants (HAPs) on a 3-year cycle. The DMR loading tool calculates pollutant loadings from permit and DMR data from EPA's Integrated Compliance Information System for the National Pollutant Discharge Elimination System (ICIS-NPDES). EPA expects to consider these data in conducting the exposure assessment component of the risk evaluation for methylene chloride.

### 2.3.3 Presence in the Environment and Biota

Monitoring studies or a collection of relevant and reliable monitoring studies provide(s) information that can be used in an exposure assessment. Monitoring studies that measure environmental concentrations or concentrations of chemical substances in biota provide evidence of exposure. Monitoring and biomonitoring data were identified in EPA's data search for methylene chloride.

Due to its variety of uses and subsequent release to the environment, methylene chloride is present and measurable through monitoring in a variety of environmental media including ambient and indoor air, surface water and ground water, including sources used for drinking water supplies, sediment, soil and food products.

Ambient air samples worldwide have shown measured levels of methylene chloride, with background levels usually around 50 parts per trillion (ATSDR, 2000). National Oceanic and Atmospheric Administration (NOAA) monitoring data between 1994 and 2016 show mid-latitude northern hemisphere atmospheric concentrations to decrease slightly from 1994 to the early 2000s, and then increase thereafter to present day, with monthly mean concentrations ranging from approximately 30-80 parts per trillion (Hossaini et al., 2015). Similarly, air concentrations in the continental U.S. between 2003 and 2014 showed either no trend or increasing levels of methylene chloride (U.S. EPA, 2016b).

The 2011 National Air Toxics Assessment (NATA) modeled concentrations for various air toxics nationwide at a census tract level. This screening level tool modeled a maximum total methylene chloride concentration of 5,000 parts per trillion (18 µg/$m^3$). Greater than 94% of all modeled tracts were less than 100 parts per trillion. While available indoor air measurements for methylene chloride are less prevalent, it may be present in this environment due to its variety of uses including consumer uses.

Methylene chloride has been detected in ground water and surface water, including finished drinking water, through varied national monitoring efforts and water quality databases such as U.S. EPA's STOrage and RETrieval and Water Quality exchange (STORET) and U.S. Geological Survey's National Water Quality Assessment Program (NAWQA) (U.S. EPA, 2009; ATSDR, 2000). As part of its 6-year review of drinking water regulations, U.S. EPA (U.S. EPA, 2009) compiled a nationwide dataset of over 372,000 samples of ground water and surface water used for drinking water. Methylene chloride was detected approximately 1% of the time, with median concentrations similar for ground water and surface water. Other monitoring efforts have shown that with volatilization being limited in a ground water environment and the ability of methylene chloride to readily transport to ground water, concentrations are often higher in ground water as compared to surface water. Data compiled between 1992 and 2001 from NAWQA showed methylene chloride to be found in 6% of all ground water and surface water samples, with occurrences more common in surface water (U.S. EPA, 2009). Methylene chloride was detected in 20% of sediment samples in the STORET database (ATSDR, 2000).

Methylene chloride and its metabolites have been measured in expired air, blood, urine and breast milk however methylene chloride measurements in human milk have not been quantified and there are no animal studies testing to what extent methylene chloride can pass into milk (ATSDR, 2000). Elimination of methylene chloride from the body is rapid and therefore, is only representative of recent exposures. Blood concentrations of methylene chloride were below the level of detection in 1,165 individuals who participated in the National Health and Nutrition Examination Survey (NHANES) 2003-2004 subsample of the U.S. population (CDC, 2009). The methylene chloride metabolite, carboxyhemoglobin (COHb), has also been measured in blood and used as a biomarker; however, COHb results from exposure to carbon monoxide (such as in tobacco smoke and automobile exhaust) is not specific to methylene chloride (ATSDR, 2000).

### 2.3.4 Environmental Exposures

The manufacturing, processing, distribution, use and disposal of methylene chloride can result in releases to the environment. In this section, EPA presents exposures to aquatic and terrestrial organisms.

***Aquatic Environmental Exposures***

Based on national-scale monitoring data from EPA's STORET and U.S.G.S.'s NAWQA, methylene chloride is detected in surface and ground water. In an evaluation of the STORET database containing nearly 9,000 samples, methylene chloride was detected 30% of the time at a median concentration of 0.1 ppb (ATSDR, 2000; Staples et al., 1985). In an evaluation of USGS NAWQA data from 1992-2001, methylene chloride was found above the reporting limit in both groundwater and surface water at 2.9% and 14.6% of all samples respectively and 5.6% overall. When calculated as a percentage of sampled sites, 3.2% of all groundwater sites, 31.9% of all surface water sites and 4.4% of all sites overall recorded a detectable result (U.S. EPA, 2009). Methylene chloride was detected in groundwater with a median value of 0.05 µg/L and ranged from 0.008 to 25.8 µg/L ($99^{th}$ percentile = 21.6 µg/L) and in surface water samples with a median of 0.035 µg/L and ranged from 0.0055 to 34 µg/L ($99^{th}$ percentile = 1.55 µg/L).

A recent review of the multi-agency Water Quality Portal which includes data from the National Water Information System (NWIS), STORET, and USDA STEWARDS databases also shows hundreds of

measures of methylene chloride in soil and sediment. In a literature review of various VOC concentrations found in landfill leachates, Klett et al. (2005) found methylene chloride ranged in concentration from 1.0 – 58,200 µg/L. Staples et al. (1985) reported that methylene chloride was found in 20% of sediment samples in the STORET database. Methylene chloride concentrations in soil and sediment pore water are expected to be similar to the concentrations in groundwater (in soil) or overlying water (in sediment) because methylene chloride does not partition to organic matter (estimated log $K_{OC}$ = 1.4) and biodegrades slowly (13% biodegradation in 28 days; (NITE, 2002)). Thus, the methylene chloride detected in soil and sediments is likely from the pore water and not methylene chloride that was adsorbed to the soil or sediment solids.

***Terrestrial Environmental Exposures***

Terrestrial species populations living near industrial and commercial facilities using methylene chloride may be exposed via multiple routes such as ingestion of surface waters and inhalation of outdoor air. As described in Section 2.3.3 methylene chloride is present and measurable through monitoring in a variety of environmental media including ambient and indoor air, surface water and ground water.

### 2.3.5 Human Exposures

In this section, EPA presents occupational, consumer and general population exposures. Subpopulations, including potentially exposed and susceptible subpopulations, within these exposure categories are also presented.

#### 2.3.5.1 Occupational Exposures

Exposure pathways and exposure routes are listed below for worker activities under the various conditions of use (industrial or commercial) described in Section 2.2. In addition, exposures to occupational non-users (ONU), who do not directly handle the chemical but perform work in an area where the chemical is present are listed. Engineering controls and/or personal protective equipment may impact the occupational exposure levels.

In the previous 2014 risk assessments (U.S. EPA, 2014b), EPA assessed inhalation exposures to methylene chloride for occupational use in paint and coating removal, which will be considered in the methylene chloride risk evaluation.

Workers and occupational non-users may be exposed to methylene chloride when performing activities associated with the conditions of use described in Section 2.2, including, but not limited to:

- Unloading and transferring methylene chloride to and from storage containers to process vessels;
- Using methylene chloride in process equipment (e.g., vapor degreasing machine, process equipment used to manufacture refrigerants);
- Applying formulations and products containing methylene chloride onto substrates (e.g., applying adhesive removers containing methylene chloride onto substrates requiring adhesive removal);
- Cleaning and maintaining equipment;
- Sampling chemical, formulations or products containing methylene chloride for quality control (QC);
- Repackaging chemical, formulations or products containing methylene chloride;
- Handling, transporting and disposing waste containing methylene chloride;
- Performing other work activities in or near areas where methylene chloride is used.

***Key Data***
Key data that inform occupational exposure assessment include: the OSHA Chemical Exposure Health Data (CEHD) and NIOSH Health Hazard Evaluation (HHE) program data. OSHA data are workplace monitoring data from OSHA inspections. OSHA data can be obtained through CEHD https://www.osha.gov/opengov/healthsamples.html. Table_Apx B-1 and Table_Apx B-2 in Appendix B provides a summary of industry sectors with methylene chloride personal monitoring air samples obtained from OSHA inspections conducted between 2011 and 2016. NIOSH HHEs are conducted at the request of employees, union officials, or employers and help inform potential hazards at the workplace. HHEs can be downloaded at https://www.cdc.gov/ niosh/hhe/. EPA identified several HHEs during the problem formulation; these HHEs are listed in Table_Apx B-3 in Appendix B. EPA also identified additional sources of potentially relevant occupational exposure data. These sources are listed in Table_Apx B-4 through Table_Apx B-7 in Appendix B, and EPA will review these data and evaluate their utility in the risk evaluation.

***Inhalation***
Based on these occupational exposure scenarios, inhalation exposure to vapor is expected. EPA anticipates this is the most important methylene chloride exposure pathway for workers and occupational nonusers based on the high volatility of methylene chloride. Based on the potential for spray application of some products containing methylene chloride exposures to mists are also expected for workers and ONU and will be incorporated into the occupational inhalation exposure estimates.

The United States has several regulatory and non-regulatory exposure limits for methylene chloride: an Occupational Safety and Health Administration (OSHA) Permissible Exposure Limit (PEL) of 25 ppm 8-hour time-weighted average (TWA) and Short-Term Exposure Limit (STEL) of 125 ppm 15-minute TWA (OSHA, 1997), and an American Conference of Government Industrial Hygienists (ACGIH) Threshold Limit Value (TLV) of 50 ppm 8-hour TWA (ACGIH, 2001). Also, the National Institute for Occupational Safety and Health (NIOSH) indicates that methylene chloride has an immediately dangerous to life and health (IDLH) value of 2,300 ppm based on effects that might occur from a 30-minute exposure, and NIOSH provides a notation that methylene chloride is a potential occupational carcinogen (NIOSH, 2011).

***Dermal***
Based on the conditions of use EPA expects workers to have potential for skin contact with liquids and vapors. Where workers may be exposed to methylene chloride, the OSHA standard requires that workers are protected from contact (e.g. gloves) (29 CFR 1910.1052). Occupational non-users are not directly handling methylene chloride; therefore, skin contact with liquid methylene chloride is not expected for occupational non-users but skin contact with vapors is expected for occupational nonusers.

***Oral***
Exposure may occur through mists that deposit in the upper respiratory tract however, based on physical chemical properties, mists of methylene chloride will likely be rapidly absorbed in the respiratory tract or evaporate and will be considered as an inhalation exposure.

#### 2.3.5.2 Consumer Exposures
Methylene chloride can be found in consumer products and/or commercial products that are readily available for public purchase at common retailers (EPA-HQ-OPPT-2016-0742-0003, Sections 3 and 4 and Table 2-3) and can therefore result in exposures to consumers and bystanders (non-product users that are incidentally exposed to the product).

In EPA's 2014 risk assessment for methylene chloride paint stripping use, consumer inhalation exposures in residential settings were assessed using a variety of indoor exposure scenarios (U.S. EPA, 2014b). Scenarios differed in their type of application (i.e., brush vs. spray), location of product application (workshop vs. bathroom), mass of methylene chloride emitted, user's location during the wait period and air exchange rate between the rest of the house with outdoor air.

***Inhalation***

EPA expects that inhalation exposure to vapor will be the most significant route of exposure for consumer and bystander exposure scenarios, in line with EPA's 2014 risk assessment of methylene chloride paint stripping use, which assumed that inhalation is the main exposure pathway based on the physical-chemical properties of methylene chloride (e.g. high vapor pressure) (U.S. EPA, 2014b). Based on the potential for spray application of some products containing methylene chloride exposures to mists are also expected. These exposures to consumers and bystanders through mists may deposit in the upper respiratory tract; EPA assumes these are absorbed via inhalation

***Dermal***

There is a potential for dermal exposures to methylene chloride in consumer uses. Dermal exposure may occur via contact with vapor or mist deposition onto the skin or via direct liquid contact during use. Exposures to skin would be expected to evaporate fairly quickly based on physical chemical properties including vapor pressure, water solubility and log $K_{OW}$ but some methylene chloride would also be dermally absorbed. When evaporation of methylene chloride is reduced such as in occluded scenarios (e.g. continued contact with a methylene chloride soaked rag) dermal absorption would be higher due to the longer duration of exposure. These dermal exposures would be concurrent with inhalation exposures and the overall contribution of dermal exposure to total exposure is expected to be smaller than via inhalation however there may be exceptions for the occluded scenarios. Overall, dermal exposures to consumers in occluded and non-occluded scenarios are expected. Bystanders will not have dermal contact with liquid methylene chloride but will have dermal exposures to methylene chloride vapor.

***Oral***

Consumers may be exposed to methylene chloride via transfer of methylene chloride from hand to mouth. This exposure pathway will be limited by a combination of dermal absorption and volatilization.

***Exposures from Disposal***

EPA does not expect exposure to consumers from disposal of consumer products. It is anticipated that most products will be disposed of in original containers, particularly those products that are purchased as aerosol cans. Liquid products may be recaptured in an alternate container following use (e.g. paint scrapings after paint removal as was done in EPA's 2014 risk assessment for methylene chloride paint stripping use).

#### 2.3.5.3 General Population Exposures

Wastewater/liquid wastes, solid wastes or air emissions of methylene chloride could result in potential pathways for oral, dermal or inhalation exposure to the general population.

***Inhalation***

Inhalation serves as the expected primary route of exposure for the general population due to both its high volatility and propensity to be released to air from ongoing commercial and industrial activities (U.S. EPA, 2014b, 2009; ATSDR, 2000). Between 1998 and 2006, >90% of all reported TRI releases of methylene chloride were air releases (U.S. EPA, 2014b) and levels of methylene chloride in the ambient air are widespread and shown to be increasing (Section 2.3.2). The 2011 NATA modeled concentrations at a census tract level found a maximum total methylene chloride concentration of 5,000 parts per

trillion (18 µg/$m^3$) and maximum human inhalation exposure concentrations of 3,900 parts per trillion (14 µg/$m^3$). Greater than 94% of all modeled tracts were less than 100 parts per trillion. While available indoor air measurements for methylene chloride are less prevalent, it may be present in this environment due to its variety of uses including consumer uses.

***Oral***

The general population may ingest methylene chloride via contaminated drinking water, ground water, and/or surface water. Ingestion of contaminated drinking water is expected to be the primary route of oral exposure. Oral ingestion may include exposure to contaminated breast milk or incidental ingestion of methylene chloride residue on the hand/body. Based on the presence of methylene chloride in water used for bathing or recreation, the oral ingestion of contaminated water could contribute, to a lesser degree, to oral exposures.

***Dermal***

General population exposures to methylene chloride through the dermal route may occur through contact with water such as while bathing in household water that has residual methylene chloride or public recreation in contaminated waterways. Methylene chloride can be absorbed through the skin; however, based on its physical and chemical properties, once exposed to air most of the amount on skin would be expected to volatize before being absorbed.

#### 2.3.5.4 Potentially Exposed or Susceptible Subpopulations

TSCA requires the determination of whether a chemical substance presents an unreasonable risk to "a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation" by EPA. TSCA § 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." General population is "the total of individuals inhabiting an area or making up a whole group" and refers here to the U.S. general population (U.S. EPA, 2011c).

As part of the Problem Formulation, EPA identified potentially exposed and susceptible subpopulations for further analysis during the development and refinement of the life cycle, conceptual models, exposure scenarios, and analysis plan. In this section, EPA addresses the potentially exposed or susceptible subpopulations identified as relevant based on greater exposure. EPA will address the subpopulations identified as relevant based on greater susceptibility in the hazard section.

EPA identifies the following as potentially exposed or susceptible subpopulations that EPA expects to consider in the risk evaluation due to their *greater exposure*:

- Workers and occupational non-users.
- Consumers and bystanders associated with consumer use. Methylene chloride has been identified in products available to consumers; however, only some individuals within the general population may use these products. Therefore, those who do use these products are a potentially exposed or susceptible subpopulation due to greater exposure.
- Other groups of individuals within the general population who may experience greater exposures due to their proximity to conditions of use identified in Section 2.2 that result in releases to the environment and subsequent exposures (e.g., individuals who live or work near manufacturing, processing, use or disposal sites).

In developing exposure scenarios, EPA will analyze available data to ascertain whether some human receptor groups may be exposed via exposure pathways that may be distinct to a particular subpopulation or lifestage and whether some human receptor groups may have higher exposure via identified pathways of exposure due to unique characteristics (e.g., activities, duration or location of exposure) when compared with the general population (U.S. EPA, 2006a).

In summary, in the risk evaluation for methylene chloride, EPA expects to analyze the following potentially exposed groups of human receptors: workers, occupational non-users, consumers, bystanders associated with consumer use, and other groups of individuals within the general population who may experience greater exposure. EPA may also identify additional potentially exposed or susceptible subpopulations that will be considered based on greater exposure.

## 2.4 Hazards (Effects)

For scoping, EPA conducted comprehensive searches for data on hazards of methylene chloride, as described in *Strategy for Conducting Literature Searches for Methylene Chloride: Supplemental File for the TSCA Scope Document* EPA-HQ-OPPT-2016-0742-0060 (U.S. EPA, 2017c). Based on initial screening, EPA expects to analyze the hazards of methylene chloride identified in this problem formulation document. However, when conducting the risk evaluation, the relevance of each hazard within the context of a specific exposure scenario will be judged for appropriateness. For example, hazards that occur only as a result of chronic exposures may not be applicable for acute exposure scenarios. This means that it is unlikely that every hazard identified will be analyzed for every exposure scenario.

### 2.4.1 Environmental Hazards

EPA identified the following sources of environmental hazard data for methylene chloride: (U.S. EPA, 2014b; OECD, 2011; WHO, 1996; Health and Environment Canada, 1993). Only the *on-topic* references listed in the Ecological Hazard Literature Search Results were considered as potentially relevant data/information sources for the risk evaluation. Inclusion criteria were used to screen the results of the ECOTOX literature search (as explained in the *Strategy for Conducting Literature Searches for Methylene Chloride: Supplemental Document to the TSCA Scope Document, CASRN:79-09-2*). Data from the screened literature are summarized below (Table 2-8) as ranges (min-max). EPA expects to review these data/information sources during risk evaluation using the data quality review evaluation metrics and the rating criteria described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018).

***Toxicity to Aquatic Organisms***

Fish exposed to methylene chloride between 24 hours and 9 days had $LC_{50}$ concentrations ranging from 34 mg/L to 1,100 mg/L(U.S. EPA, 2014b; OECD, 2011; Health and Environment Canada, 1993). In a 24-hour cytotoxicity test in cultured fish cells, protein content decreased 50% at a calculated *in vitro* concentration of 49,000 mg/L ((Dierickx, 1993). Amphibians exposed to methylene chloride from 48 hours to 9.5 days had $EC_{50}$ concentrations ranging from 16.92 mg/L to > 48 mg/L for mortality and teratogenicity and a no observed effect concentration range of 0.017 mg/L to 0.1 mg/L. Aquatic invertebrates exposed to methylene chloride between 4 hours to 12 days had $EC_{50}$ concentrations ranging from 27 mg/L to 69,160 mg/L (as needed, units were converted to mg/L based on the methylene chloride MW of 84.93 g/mol and density of 1.33 g/cm$^3$) and there was a 96-hour LOEC for developmental and teratogenic effects between concentrations of 0.0008 and 0.0009 mg/L. Aquatic plants exposed between 3 to 96 hours to methylene chloride had various effects, including biomass and growth inhibition and population-level effects, at concentrations ranging from 0.98 to 2,292 mg/L. Mortality to freshwater fungi was observed when exposed to methylene chloride at concentrations of

2400 mg/L for 2 to 30 hours. There were no available acute sediment toxicity studies, however, toxicity is expected to be similar to that of aquatic invertebrates when exposed to methylene chloride in sediment pore water.

For chronic exposures to methylene chloride, there was one fish study with 23 to 27-day $LC_{50}$ concentrations between 13.16 mg/L and 13.51 mg/L, respectively. Developmental and other effects in fish were observed at LOECs ranging from 5.5 mg/L to 209 mg/L. Aquatic plants had a 10-day LOEC of 0.002 mg/L for reduction in Chlorophyll A.

***Toxicity to Soil and Terrestrial Organisms***

Terrestrial mammals exposed to methylene chloride, by injection for 0.25 hours, had physiological effects with an $EC_{50}$ of 326.3 mg/kg-body weight. Mammals exposed via oral administration for up to 30 days had LOAELs ranging from 115 to 1720 mg/kg-body weight per day. In two studies, bird eggs injected with methylene chloride for 14 days had $LD_{50}$ concentration of > 8.5 and 14.1 mg/egg, respectively, but teratogenicity was not observed. Terrestrial invertebrates fumigated with methylene chloride for 24 hours had $LD_{50}$s ranging from 81.28 – 129.9 mg/L. Soil invertebrates had a 48-hr $LC_{50}$ of 0.304 mg/cm$^2$ after topical exposures to methylene chloride. The 48-hr $LC_{50}$ was >1.0 mg/cm$^2$ for invertebrates exposed to methylene chloride in soil. Fungi exposed in an assay to methylene chloride demonstrated cellular effects at LOECs ranging from 5.3 – 11.5 mg/L (converted from 62.4 to 135.7 mM).

Mammals with oral exposures to methylene chloride for 18-weeks to 31-weeks had a NOAEC of 225 mg/kg body weight per day with no mortality or reproductive effects at the highest concentrations tested. Mammals with inhalation exposures to methylene chloride over a two-year period had a NOAEC of 695 mg/m$^3$ and a LOAEC of 1737 mg/m$^3$. Terrestrial plants exposed to methylene chloride for 14-days had no growth effects.

**Table 2-8. Summary of Ecological Hazard Information for Methylene Chloride**

| Duration | Test Organism | Endpoint | Hazard Values* | Units | Effect Endpoint | References |
|---|---|---|---|---|---|---|
| **Aquatic Organisms and Amphibians** | | | | | | |
| **Acute** | Fish | $LC_{50}$ | 34 – 1,100 | mg/L | Mortality/ Immobility | U.S. EPA (2014b); OECD (2011); Health and Environment Canada (1993); Tsuji et al. (1986) |
| | | $EC_{50}$ (assay) | 49,000 | mg/L | Biochemical/ Protein Content | Dierickx (1993) |
| | Amphibians | $EC_{50}$ | 16.93 – > 48 | mg/L | Mortality/ Teratogenicity | Marquis et al. (2006); WHO (1996); Health and Environment Canada (1993) |
| | | NOEC | 0.017 – 0.1 | | | |
| | | LOEC | 0.822 – 0.981 | | | |
| | Aquatic invertebrates | $EC_{50}$ | 27 – 69,160 | mg/L | Mortality/ Immobility | U.S. EPA (2014b); OECD (2011); Rayburn and Fisher |

| Duration | Test Organism | Endpoint | Hazard Values* | Units | Effect Endpoint | References |
|---|---|---|---|---|---|---|
| **Acute** | Aquatic invertebrates | NOEC | 68 – 133,000 | mg/L | Mortality/ Immobility/ Development | (1999); Wilson (1998); Sanchez-Fortun et al. (1997); WHO (1996); Health and Environment Canada (1993) |
| | | LOEC | 0.0008 – 0.0009 | mg/L | Development/ Teratogenicity | |
| | Aquatic Plants | $EC_{50}$ | 0.98 – 2,292 | mg/L | Growth Rate/ Biomass/ Cellular/ Biochemical | U.S. EPA (2014b); Wu et al. (2014); OECD (2011); Tsai and Chen (2007); Ando et al. (2003); WHO (1996); Brack and Rottler (1994) |
| | | NOEC | 0.98 - 221 | mg/L | Population/ Cellular/ Biochemical | Wu et al. (2014); Tsai and Chen (2007); Ando et al. (2003); Brack and Rottler (1994) |
| | | LOEC | 0.98 –403 | | | |
| | Fungi | $LT_{50}$ | 2400 | mg/L | Mortality | Steiman et al. (1995) |
| **Chronic** | Fish | $LC_{50}$ | 13.16 – 13.51 | mg/L | Mortality | WHO (1996); Health and Environment Canada (1993) |
| | | LOEC | 5.5 – 209 | mg/L | Mortality/Development/Body Weight | U.S. EPA (2014b); OECD (2011); WHO (1996); Health and Environment Canada (1993) |
| | | MATC | 108 | mg/L | Body Weight | U.S. EPA (2014b); WHO (1996) |
| | Aquatic Plants | NOEC | 2 | mg/L | Population/ Cellular | Wu et al. (2014); Tsai and Chen (2007); Ando et al. (2003); Brack and Rottler (1994) |
| | | LOEC | 0.002 | | | |
| **Terrestrial Organisms** | | | | | | |
| **Acute** | Mammals | $EC_{50}$ | 326.3 | mg/kg bdwt/d | Mortality/Growth /Physiological | Sasaki et al. (1998); Herr and Boyes (1997) |
| | | NOAEC | 25 - 600 | | | |
| | | LOAEC | 75 - 1720 | | | |
| | Avian | $LD_{50}$ | >8.5 – 14.1 | mg/egg | Mortality | Health and Environment Canada (1993) |
| | Terrestrial Invertebrates | $LD_{50}$ | 81.28 – 129.9 | mg/L | Mortality | Health and Environment Canada (1993) |

| Duration | Test Organism | Endpoint | Hazard Values* | Units | Effect Endpoint | References |
|---|---|---|---|---|---|---|
| **Acute** | Soil Invertebrates | $LC_{50}$ | 0.304 – >1.0 | $mg/cm^2$ | Mortality | OECD (2011); WHO (1996) |
| | Fungi | LOEC | 5300 – 11,525 | mg/L | Cellular/Genetic | Crebelli et al. (1995) |
| **Chronic** | Mammals | NOAEC | 225 - 695 | $mg/m^3$ | Mortality/Liver/ CNS | OECD (2011); U.S. EPA (2011b); WHO (1996) |

* Values in the tables are presented as reported by the study authors, unless units were converted for consistency.

Based on the information listed in Table 2-8, fish and aquatic invertebrates with acute exposures to methylene chloride resulted in mortality or immobilization. Mortality and other adverse effects were observed to amphibians with acute exposures. When algae were exposed to methylene chloride, adverse effects to biomass, growth rate, and cellular effects were observed. There was mortality and/or developmental effects in fish, aquatic invertebrates and amphibians with acute and chronic exposures. The most sensitive taxa in the dataset were:

- aquatic invertebrates, including insect larvae, had $EC_{50}$s as low as 27 mg/L and developmental effects with a 96-h LOEC of 0.0008 mg/L
- amphibians had $EC_{50}$s as low as 16.93 mg/L and LOECs from 0.822 mg/L to 0.981 mg/L
- aquatic plants had a LOEC of 0.002 mg/L for reduction in Chlorophyll A

Based on the studies listed in Table 2-8, acute toxicity to terrestrial species was observed, including cellular effects in mammals, mortality in soil and terrestrial invertebrates, growth and cellular effects in terrestrial plants and cellular effects in fungi. There was mortality in mammals and bird embryos with acute exposures to methylene chloride and effects chronic exposures had growth effects. The most sensitive taxa in the dataset were:

- soil invertebrates had a $LC_{50}$ of 0.304 $mg/cm^2$ from topical application of methylene chloride
- terrestrial mammals with an oral LOAEC of 115 mg/kg bdwt/day and a NOAEC of 25 mg/kg bdwt/day and an inhalation LOAEC of 1737 $mg/m^3$ and NOAEC of 695 $mg/m^3$
- terrestrial invertebrates with a $LD_{50}$ of 81.28 mg/L

Environmental hazard data will be further reviewed for overall data quality confidence and integrated during the risk evaluation phase. The lowest values were used for hazard levels of concern to estimate lower bound effect levels that would likely encompass more sensitive species not specifically represented by the available experimental data. It should be noted that these hazard levels of concern do not account for differences in inter- and intra-species variability, as well as laboratory-to-field variability and are dependent upon the availability of datasets that can be used to characterize relative sensitivities across multiple species within a given taxa or species group, since the data available for most industrial chemicals are limited.

### 2.4.2 Human Health Hazards

Methylene chloride has an existing EPA IRIS Assessment (U.S. EPA, 2011b), an ATSDR Toxicological Profile (ATSDR, 2010, 2000), and assessments of the effects of acute exposures in the AEGL

(NAC/AEGL, 2008), Spacecraft Maximum Allowable Concentrations (SMAC) for Methylene Chloride (NRC, 1996a) and an acute Recommended Exposure Limit (REL) published by the Office of Environmental Health Hazard Assessment (OEHHA) (OEHHA, 2008); hence, many of the hazards of methylene chloride have been previously compiled and reviewed. EPA expects to use these previous analyses as a starting point for identifying key and supporting studies to inform the human health hazard assessment, including dose-response analysis. The relevant studies will be evaluated using the data quality criteria in the *Application of Systematic Review in TSCA Risk Evaluations* document (U.S. EPA, 2018). EPA also expects to consider other studies (e.g., more recently published, alternative test data) that have been published since these reviews, as identified in the literature search conducted by the Agency for methylene chloride [*Methylene Chloride (CASRN 75-09-2) Bibliography: Supplemental File for the TSCA Scope Document* EPA-HQ-OPPT-2016-0742-0059 (U.S. EPA, 2017a)]. Based on reasonably available information, the following sections describe the potential hazards associated with methylene chloride.

#### 2.4.2.1 Non-Cancer Hazards

***Acute Toxicity***

Neurotoxicity indicative of CNS depression is a primary effect of methylene chloride in humans following acute oral and inhalation exposures (U.S. EPA, 2011b). CNS depressive effects may be a result of methylene chloride or its metabolite carbon monoxide and will be evaluated. Identified CNS depressive symptoms include drowsiness, confusion, headache, dizziness and neurobehavioral deficits when performing various tasks. Acute and/or short-term inhalation and oral exposure by animals to methylene chloride has also resulted in CNS depressant effects; decreased motor activity; impaired learning and memory; and changes in responses to sensory stimuli. CNS depressant effects can result in loss of consciousness and respiratory depression, resulting in irreversible coma, hypoxia and eventual death (NAC/AEGL, 2008).

***Liver Toxicity***

The liver is a sensitive target organ for inhalation and oral exposure (U.S. EPA, 2011b). Based on studies of workers there is limited evidence of liver effects. Following chronic repeated inhalation and oral exposures to methylene chloride, rats and mice exhibited hepatocyte vacuolation, necrosis and degeneration (U.S. EPA, 2011b).

***Neurotoxicity***

The brain is often affected by exposures to methylene chloride (U.S. EPA, 2011b). As noted above, acute non-lethal effects in humans include general CNS depressive symptoms. There is some limited evidence of increased prevalence of neurological symptoms among workers and possible detriments in attention and reaction time in complex tasks in retired workers after longer-term exposures (U.S. EPA, 2011b).

***Irritation***

Following exposures to methylene chloride vapors, irritation has been observed in the respiratory tract and eyes (ATSDR, 2000). Direct contact with liquid methylene chloride on the skin has caused chemical burns in workers and gastrointestinal irritation in individuals who ingested methylene chloride (U.S. EPA, 2011b; ATSDR, 2000).

#### 2.4.2.2 Genotoxicity and Cancer Hazards

Methylene chloride and some of its key metabolites have been extensively evaluated in carcinogenicity, genotoxicity and other MOA studies. Most of these studies have been thoroughly reviewed in the EPA IRIS Assessment (U.S. EPA, 2011b). Studies in humans provide evidence for an association between occupational exposure to methylene chloride and increased risk for some specific cancers, including

brain cancer, liver cancer, non-Hodgkin's lymphoma and multiple myeloma (U.S. EPA, 2011b). In addition, several cancer bioassays in animals have identified the liver and lung as the most sensitive target organs for methylene chloride-induced tumor development (U.S. EPA, 2011b). In the IRIS assessment, EPA hypothesized that methylene chloride induced lung and liver tumors through a mutagenic mode of carcinogenic action. A weight-of-evidence analysis of *in vivo* and *in vitro* data provide support to the proposed mutagenicity of methylene chloride (U.S. EPA, 2011b).

In the 2011 IRIS assessment, following U.S. EPA (2005) *Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 2005) using a weight-of-evidence judgment of the likelihood that methylene chloride is a human carcinogen, EPA concluded that methylene chloride is "likely to be carcinogenic in humans by all routes of exposure" (U.S. EPA, 2011b).

#### 2.4.2.3 Potentially Exposed or Susceptible Subpopulations

TSCA requires that the determination of whether a chemical substance presents an unreasonable risk include consideration of unreasonable risk to "a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation" by EPA. TSCA § 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." In developing the hazard assessment, EPA will evaluate available data to ascertain whether some human receptor groups may have greater susceptibility than the general population to the chemical's hazard(s).

## 2.5 Conceptual Models

EPA risk assessment guidance (U.S. EPA, 2014a, 1998), defines Problem Formulation as the part of the risk assessment framework that identifies the major factors to be considered in the assessment. It draws from the regulatory, decision-making and policy context of the assessment and informs the assessment's technical approach.

A conceptual model describes the actual or predicted relationships between the chemical substance and receptors, either human or environmental. These conceptual models are integrated depictions of the conditions of use, exposures (pathways and routes), hazards and receptors. The initial conceptual models describing the scope of the assessment for methylene chloride, have been refined during problem formulation. The changes to the conceptual models in this problem formulation are described along with the rationales.

In this section, EPA outlines those pathways that will be included and further analyzed in the risk evaluation; will be included but will not be further analyzed in risk evaluation; and will not be included in the TSCA risk evaluation; and the underlying rationale for these decisions.

EPA determined as part of problem formulation that it is not necessary to conduct further analysis on certain exposure pathways that were identified in the methylene chloride scope document and that remain in the risk evaluation. Each risk evaluation will be "fit-for-purpose," meaning not all conditions of use will warrant the same level of evaluation and the Agency may be able to reach some conclusions without comprehensive or quantitative risk evaluations 82 FR 33726, 33734, 33739 (July 20, 2017).

As part of this problem formulation, EPA also identified exposure pathways under regulatory programs of other environmental statutes, administered by EPA, which adequately assess and effectively manage exposures and for which long-standing regulatory and analytical processes already exist, i.e., the Clean

Air Act (CAA), the Safe Drinking Water Act (SDWA), the Clean Water Act (CWA) and the Resource Conservation and Recovery Act (RCRA). OPPT worked closely with the offices within EPA that administer and implement the regulatory programs under these statutes. In some cases, EPA has determined that chemicals present in various media pathways (i.e., air, water, land) fall under the jurisdiction of existing regulatory programs and associated analytical processes carried out under other EPA-administered statutes and have been assessed and effectively managed under those programs. EPA believes that the TSCA risk evaluation should generally focus on those exposure pathways associated with TSCA conditions of use that are not adequately assessed and effectively managed under the regulatory regimes discussed above because these pathways are likely to represent the greatest areas of risk concern. As a result, EPA does not expect to include in the risk evaluation certain exposure pathways identified in the methylene chloride scope document.

### 2.5.1 Conceptual Model for Industrial and Commercial Activities and Uses: Potential Exposures and Hazards

The revised conceptual model (Figure 2-2) describes the pathways of exposure from industrial and commercial activities and uses of methylene chloride that EPA expects to include in the risk evaluation. There are exposures to workers and/or occupational non-users via inhalation routes and/or exposures to workers via dermal routes for all conditions of use identified in this problem formulation. In the (U.S. EPA, 2014b) risk assessment, inhalation exposures to vapor were assessed as the most likely exposure route; however, there are potential dermal exposures for some conditions of use, such as maintenance of industrial degreasing tanks and manual handling of metal parts removed from industrial degreasing tanks. In addition to the pathways illustrated in the figure, EPA will evaluate activities resulting in exposures associated with distribution in commerce (e.g. loading, unloading) throughout the various lifecycle stages and conditions of use (e.g. manufacturing, processing, industrial use, commercial use, disposal) rather than a single distribution scenario.

***Inhalation***

EPA/OPPT's 2014 risk assessment of methylene chloride paint stripping use assumed that inhalation is the main exposure pathway based on the physical-chemical properties of methylene chloride (e.g. high vapor pressure) (U.S. EPA, 2014b). Inhalation exposures for workers are regulated by OSHA's occupational safety and health standards for methylene chloride which include a PEL of 25 ppm TWA, exposure monitoring, control measures and respiratory protection (29 CFR 1910.1052 App. A). EPA expects that for workers and occupational non-users exposure via inhalation will be the most significant route of exposure for most exposure scenarios. EPA expects to further analyze inhalation exposures to vapors and mists for workers and occupational non-users in the risk evaluation.

***Dermal***

There is the potential for dermal exposures to methylene chloride in many worker scenarios. Where workers may be exposed to methylene chloride, the OSHA standard requires that workers are protected from contact (e.g. gloves) (29 CFR 1910.1052). EPA's 2014 risk assessment of methylene chloride paint stripping use included the potential dermal exposures to methylene chloride as an area of uncertainty that may underestimate the total exposures (U.S. EPA, 2014b). These dermal exposures would be concurrent with inhalation exposures and the overall contribution of dermal exposure to the total exposure is expected to be small however there may be exceptions for occluded scenarios. Occupational non-users are not directly handling methylene chloride; therefore, skin contact with liquid methylene chloride is not expected for occupational non-users and EPA does not expect to further analyze this pathway in the risk evaluation. EPA expects to further analyze dermal exposures for skin contact with liquids in occluded situations for workers.

Workers and occupational non-users can have skin contact with methylene chloride vapor concurrently with inhalation exposures. The parameters determining the absorption of methylene chloride vapor are based on the concentration of the vapor, the duration of exposure and absorption. The concentration of the vapor and the duration of exposure are the same for concurrent dermal and inhalation exposures. Therefore, the differences between dermal and inhalation exposures depend on the absorption. The dermal absorption can be estimated from the skin permeation coefficient (0.28 cm/hr for methylene chloride vapor (ATSDR, 2010, 2000)) and exposed skin surface area (on the order of 0.2 $m^2$ (U.S. EPA, 2011a)). The absorption of inhaled vapors can be estimated from the volumetric inhalation rate (approximately 1.25 $m^3$/hr for a person performing light activity (U.S. EPA, 2011a) adjusted by a retention factor such as 0.75. Based on these parameters the absorption of methylene chloride vapor via skin will be orders of magnitude lower than via inhalation and will not be further analyzed.

***Waste Handling, Treatment and Disposal***

Figure 2-2 shows that waste handling, treatment and disposal is expected to lead to the same pathways as other industrial and commercial activities and uses. The path leading from the "Waste Handling, Treatment and Disposal" box to the "Hazards Potentially Associated with Acute and/or Chronic Exposures See Section 2.4.2" box was re-routed to accurately reflect the expected exposure pathways, routes, and receptors associated with these conditions of use of methylene chloride.

For each condition of use identified in Table 2-3, a determination was made as to whether or not each unique combination of exposure pathway, route, and receptor will be further analyzed in the risk evaluation. The results of that analysis along with the supporting rationale are presented in Appendix C and Appendix E.

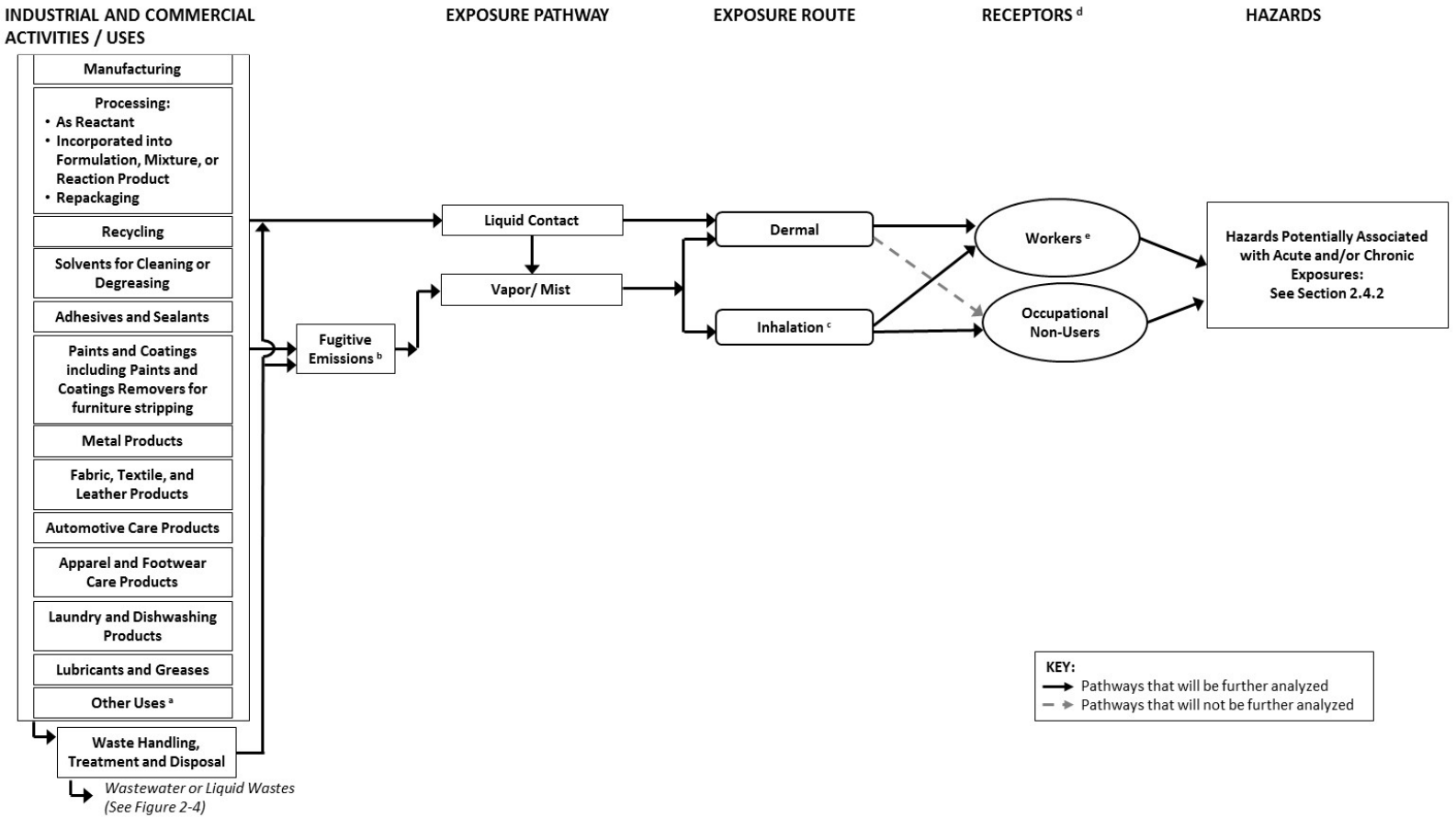


**Figure 2-2. Methylene Chloride Conceptual Model for Industrial and Commercial Activities and Uses: Potential Exposures and Hazards**

The conceptual model presents the exposure pathways, exposure routes and hazards to human receptors from industrial and commercial activities and uses of methylene chloride.

[a] Some products are used in both commercial and consumer applications such adhesives and sealants. Additional uses of methylene chloride are included in Table 2-3.

[b] Fugitive air emissions are those that are not stack emissions and include fugitive equipment leaks from valves, pump seals, flanges, compressors, sampling connections and open-ended lines; evaporative losses from surface impoundment and spills; and releases from building ventilation systems.

[c] Exposure may occur through mists that deposit in the upper respiratory tract however, based on physical chemical properties, mists of methylene chloride will likely be rapidly absorbed in the respiratory tract or evaporate and will be considered as an inhalation exposure.

[d] Receptors include potentially exposed or susceptible subpopulations.

[e] When data and information are available to support the analysis, EPA also considers the effect that engineering controls and/or personal protective equipment have on occupational exposure levels.

### 2.5.2 Conceptual Model for Consumer Activities and Uses: Potential Exposures and Hazards

The revised conceptual model (Figure 2-3) illustrates the pathways of exposure from consumer uses of methylene chloride that EPA expects to include in the risk evaluation. In the (U.S. EPA, 2014b) risk assessment, inhalation exposures to vapor and mist were assessed as the most likely exposure route; however, there are potential dermal exposures for some conditions of use. It should be noted that some consumers may purchase and use products primarily intended for commercial use.

***Inhalation***

As mentioned above, EPA/OPPT's 2014 risk assessment of methylene chloride paint stripping use assumed that inhalation of methylene chloride vapor is the main exposure pathway based on the physical-chemical properties of methylene chloride (e.g. high vapor pressure) (U.S. EPA, 2014b). EPA expects inhalation to be the primary route of exposure and expects to further analyze inhalation exposures to methylene chloride vapor and mist for consumers and bystanders.

***Dermal***

There is potential for dermal exposures to methylene chloride from consumer uses. Dermal exposure may occur via contact with vapor or mist deposition onto the skin or via direct liquid contact during use. Direct contact with liquid methylene chloride would be concurrent with inhalation exposures and dermal exposures to consumers in occluded and non-occluded scenarios are expected. Bystanders will not have direct dermal contact with liquid methylene chloride. EPA expects to further analyze direct dermal contact with liquid methylene chloride for consumers.

Consumers and bystanders can have skin contact with methylene chloride vapor concurrently with inhalation exposures. Similar to workers (see Section 2.5.1) the parameters determining the absorption of methylene chloride vapor are based on the concentration of the vapor, the duration of exposure and absorption. The concentration of the vapor and the duration of exposure are the same for concurrent dermal and inhalation exposures. Therefore, the differences between dermal and inhalation exposures depend on the absorption. The dermal absorption can be estimated from the skin permeation coefficient (0.28 cm/hr for methylene chloride vapor (ATSDR, 2010, 2000)) and exposed skin surface area (on the order of 0.2 $m^2$ (U.S. EPA, 2011a)). The absorption of inhaled vapors can be estimated from the volumetric inhalation rate (approximately 1.25 $m^3$/hr for a person performing light activity (U.S. EPA, 2011a) adjusted by a retention factor such as 0.75. Based on these parameters the absorption of methylene chloride vapor via skin will be orders of magnitude lower than via inhalation and will not be further analyzed.

***Oral***

Consumers may be exposed to methylene chloride via transfer of methylene chloride from hand to mouth. This exposure pathway will be limited by a combination of dermal absorption and volatilization; therefore, this pathway will not be further evaluated.

Furthermore, based on available toxicological data, EPA does not expect that considering separate oral routes of exposure for incidental ingestion would have significantly different toxicity, rather skin contact will be included as part of consumer dermal exposures. Bystanders are not directly handling methylene chloride; therefore, incidental ingestion via contact with methylene chloride is not expected for bystanders. Therefore, this pathway will not be further evaluated for consumers or bystanders.

***Disposal***

EPA does not expect to further analyze exposure to consumers from disposal of consumer products. It is anticipated that most products will be disposed of in original containers, particularly those products that are purchased as aerosol cans. Liquid products may be recaptured in an alternate container following use (e.g. paint scrapings after paint removal as was done in EPA's 2014 risk assessment for methylene chloride paint stripping use) (U.S. EPA, 2014b).

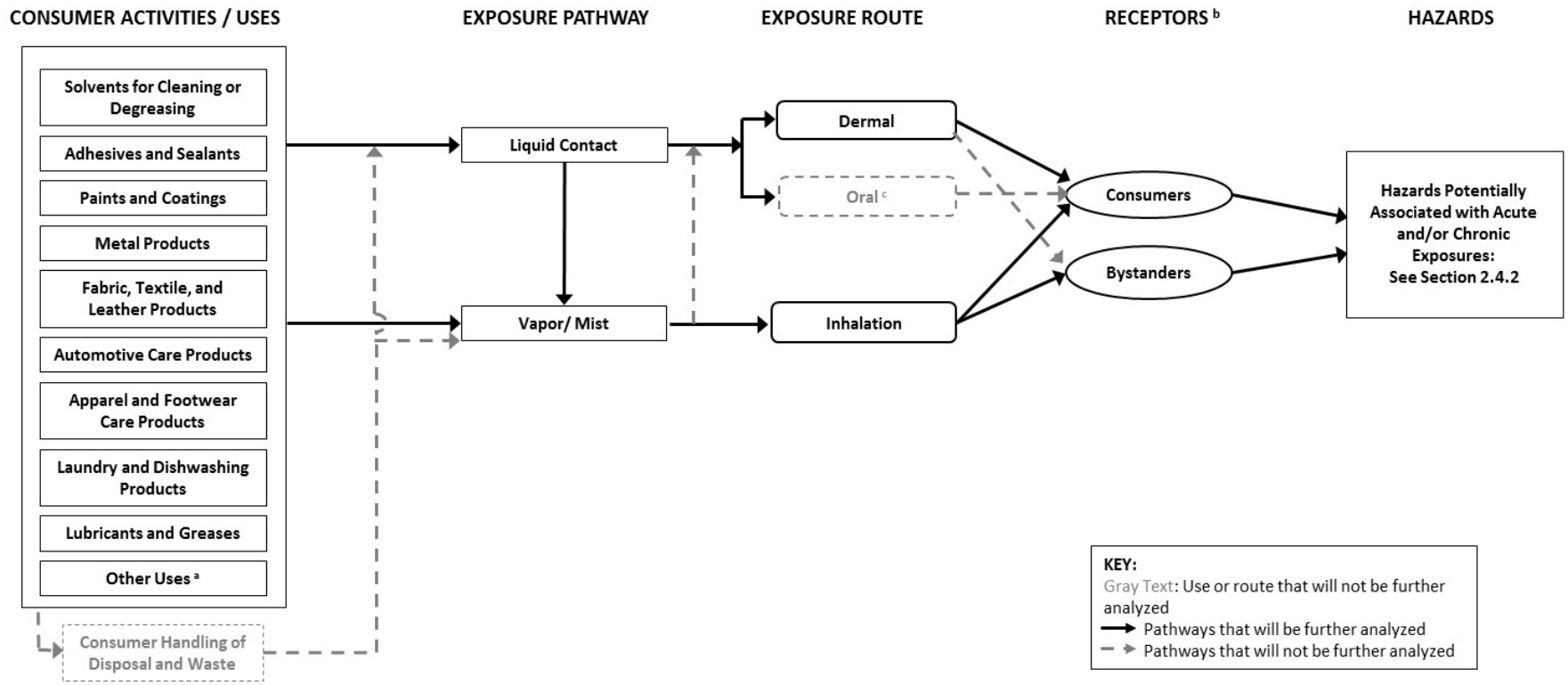


**Figure 2-3. Methylene Chloride Conceptual Model for Consumer Activities and Uses: Potential Exposures and Hazards**

The conceptual model presents the exposure pathways, exposure routes and hazards to human receptors from consumer activities and uses of methylene chloride.

[a] Some products are used in both commercial and consumer applications. Additional uses of methylene chloride are included in Table 2-3.

[b] Receptors include potentially exposed or susceptible subpopulations.

[c] Exposure may occur via transfer of methylene chloride from hand to mouth however this exposure pathway will be limited by a combination of dermal absorption and volatilization; therefore, this pathway will not be further evaluated

### 2.5.3 Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards

The revised conceptual model (Figure 2-4) illustrates the expected exposure pathways to human and ecological receptors from environmental releases and waste streams associated with industrial and commercial activities for methylene chloride that EPA expects to include in the risk evaluation. The pathway that EPA expects to include and analyze further in the risk evaluation is described in Section 2.5.3.1 and shown in the conceptual model Figure 2-4. The pathways that EPA expects to include but not further analyze in risk evaluation are described in Section 2.5.3.2 and shown in the conceptual model Figure 2-4. The pathways that EPA does not expect to include in risk evaluation are described in Section 2.5.3.3.

#### 2.5.3.1 Pathways That EPA Expects to Include and Further Analyze in Risk Evaluation

EPA expects to analyze aquatic invertebrates and aquatic plants exposed via contaminated surface water.

There are no national recommended water quality criteria for the protection of aquatic life for methylene chloride and as a result EPA does not believe that methylene chloride exposure to aquatic organisms in surface water has been adequately assessed or effectively managed under other EPA statutory authorities (see Section 2.5.3.3). Based on the national-scale environmental monitoring data for methylene chloride described in Section 2.3.4 methylene chloride was detected in 14.6% of all surface water samples with a median of 0.035 µg/L and ranged from 0.0055 to 34 µg/L ($99^{th}$ percentile = 1.55 µg/L). As summarized in Section 2.4.1 methylene chloride demonstrated hazard at concentrations as low as 0.9 µg/L for aquatic invertebrate developmental delays/non-development and 2 µg/L for aquatic plant reduction in Chlorophyll A. These hazard levels are not sufficiently below the range of monitored concentrations to eliminate risk concerns. Therefore, EPA expects to evaluate risks to aquatic invertebrates and aquatic plants from exposures to methylene chloride in surface waters.

#### 2.5.3.2 Pathways That EPA Expects to Include in Risk Evaluation But Not Further Analyze

Species in the environment including aquatic organisms, amphibians and terrestrial organisms may come into contact with methylene chloride-contaminated biosolids and soil pore water when the biosolids are land applied. Methylene chloride is not expected to adsorb to soil and sediment due to its low partitioning to organic matter (estimated log $K_{OC}$ = 1.4), so methylene chloride detected in biosolids is in the aqueous phase associated with the biosolids, not adsorbed to the organic matter. Thus, methylene chloride concentrations in surface waters and soil pore water are representative of exposures to amphibians and terrestrial organisms since only limited amounts of methylene chloride will be adsorbed to the organic matter in associated sediments and soils. Based on methylene chloride concentrations in surface waters and soil pore water described in Section 2.3.4 and hazard information summarized in Section 2.4.1, the exposures are orders of magnitude below levels observed to cause effects in amphibians and terrestrial organisms, including mammals, soil invertebrates and birds.

If methylene chloride-contaminated biosolids are released to the environment, including when the biosolids are land applied, methylene chloride will be present mainly in aqueous compartments based on its physical-chemical properties (water solubility, organic carbon:water partition coefficient [log $K_{OC}$], Henry's Law constant, vapor pressure). Overall, methylene chloride in land-applied biosolids is expected to be mobile in soil, volatilizing to air or migrating into surface and groundwater in the aqueous phase. However, methylene chloride concentrations in biosolids-associated water are expected to be no greater than the concentrations in the WWTP effluent, which represents a much larger fraction of the water released from WWTP (the volume of water removed with biosolids represents < 2% of

wastewater treatment plant influent volume (U.S. EPA, 1974), and is < 1% of influent volume when the sludge is dewatered and the excess water is returned to treatment, a process that is commonly used (NRC, 1996b)). Concentrations of methylene chloride in biosolids-associated water will further decrease through volatilization to air during transport, processing (including dewatering), handling, and application to soil (which may include spraying, which increases surface area and can enhance volatilization). Overall, the exposures to surface water from biosolids will be negligible compared to the direct release of WWTP effluent to surface water, and therefore exposures of aquatic organisms to methylene chloride from surface water due to land-applied biosolids will not be further analyzed.

#### 2.5.3.3 Pathways That EPA Does Not Expect to Include in the Risk Evaluation

Exposures to receptors (i.e. general population, terrestrial species) may occur from industrial and/or commercial uses; industrial releases to air, water or land; and other conditions of use. As described in section 2.5, EPA does not expect to include in the risk evaluation pathways under programs of other environmental statutes, administered by EPA, which adequately assess and effectively manage exposures and for which long-standing regulatory and analytical processes already exist. These pathways are described below.

**Ambient Air Pathway**

The Clean Air Act (CAA) contains a list of hazardous air pollutants (HAP) and provides EPA with the authority to add to that list pollutants that present, or may present, a threat of adverse human health effects or adverse environmental effects. For stationary source categories emitting HAP, the CAA requires issuance of technology-based standards and, if necessary, additions or revisions to address developments in practices, processes, and control technologies, and to ensure the standards adequately protect public health and the environment. The CAA thereby provides EPA with comprehensive authority to regulate emissions to ambient air of any hazardous air pollutant.

Methylene chloride is a HAP. EPA has issued a number of technology-based standards for source categories that emit perchloroethylene to ambient air and, as appropriate, has reviewed, or is in the process of reviewing remaining risks. Because stationary source releases of methylene chloride to ambient air are adequately assessed and any risks effectively managed when under the jurisdiction of the CAA, EPA does not expect to evaluate emission pathways to ambient air from commercial and industrial stationary sources or associated inhalation exposure of the general population or terrestrial species in this TSCA evaluation.

**Drinking Water Pathway**

EPA has regular analytical processes to identify and evaluate drinking water contaminants of potential regulatory concern for public water systems under the Safe Drinking Water Act (SDWA). Under SDWA, EPA must also review and revise “as appropriate” existing drinking water regulations every 6 years.

EPA has promulgated National Primary Drinking Water Regulations (NPDWRs) for methylene chloride under the Safe Drinking Water Act. EPA has set an enforceable Maximum Contaminant Level (MCL) as close as feasible to a health based, non-enforceable Maximum Contaminant Level Goal (MCLG). Feasibility refers to both the ability to treat water to meet the MCL and the ability to monitor water quality at the MCL, SDWA Section 1412(b)(4)(D), and public water systems are required to monitor for the regulated chemical based on a standardized monitoring schedule to ensure compliance with the maximum contaminant level (MCL).

Hence, because the drinking water exposure pathway for methylene chloride is currently addressed in the SDWA regulatory analytical process for public water systems, EPA does not expect to include this

pathway in the risk evaluation for methylene chloride under TSCA. EPA's Office of Water and Office of Pollution Prevention and Toxics will continue to work together providing understanding and analysis of the SDWA regulatory analytical processes and to exchange information related to toxicity and occurrence data on chemicals undergoing risk evaluation under TSCA.

**Ambient Water Pathways**

EPA develops recommended water quality criteria under section 304(a) of the CWA for pollutants in surface water that are protective of aquatic life or human health designated uses. EPA develops and publishes water quality criteria based on priorities of states and others that reflect the latest scientific knowledge. A subset of these chemicals are identified as "priority pollutants" (103 human health and 27 aquatic life). The CWA requires states adopt numeric criteria for priority pollutants for which EPA has published recommended criteria under section 304(a), the discharge or presence of which in the affected waters could reasonably be expected to interfere with designated uses adopted the state. When states adopt criteria that EPA approves as part of state's regulatory water quality standards, exposure is considered when state permit writers determine if permit limits are needed and at what level for a specific discharger of a pollutant to ensure protection of the designated uses of the receiving water. Once states adopt criteria as water quality standards, the CWA requires National Pollutant Discharge Elimination System (NPDES) discharge permits include effluent limits as stringent as necessary to meet standards. CWA section 301(b)(1)(C). This is the process used under the CWA to address risk to human health and aquatic life from exposure to a pollutant in ambient waters.

EPA has identified methylene chloride as a priority pollutant and EPA has developed recommended water quality criteria for protection of human health for methylene chloride which are available for adoption into state water quality standards for the protection of human health and are available for use by NPDES permitting authorities in deriving effluent limits to meet state narrative criteria. As such, EPA does not expect to include this pathway in the risk evaluation under TSCA. EPA's Office of Water and Office of Pollution Prevention and Toxics will continue to work together providing understanding and analysis of the CWA water quality criteria development process and to exchange information related to toxicity of chemicals undergoing risk evaluation under TSCA. EPA may update its CWA section 304(a) water quality criteria for methylene chloride in the future under the CWA.

EPA has not developed CWA section 304(a) recommended water quality criteria for the protection of aquatic life for methylene chloride, so there are no national recommended criteria for this use available for adoption into state water quality standards and available for use in NPDES permits. As a result, this pathway will undergo aquatic life risk evaluation under TSCA (see Section 2.5.3.1). EPA may publish CWA section 304(a) aquatic life criteria for methylene chloride in the future if it is identified as a priority under the CWA.

**Disposal Pathways**

Methylene chloride is included on the list of hazardous wastes pursuant to RCRA 3001 (40 CFR §§ 261.33) as a listed waste on the F, K, and U lists. The general standard in section RCRA 3004(a) for the technical criteria that govern the management (treatment, storage, and disposal) of hazardous waste are those "necessary to protect human health and the environment," RCRA 3004(a). The regulatory criteria for identifying "characteristic" hazardous wastes and for "listing" a waste as hazardous also relate solely to the potential risks to human health or the environment. 40 C.F.R. §§ 261.11, 261.21-261.24. RCRA statutory criteria for identifying hazardous wastes require EPA to "tak[e] into account toxicity, persistence, and degradability in nature, potential for accumulation in tissue, and other related factors such as flammability, corrosiveness, and other hazardous characteristics." Subtitle C controls cover not only hazardous wastes that are landfilled, but also hazardous wastes that are incinerated (subject to joint control under RCRA Subtitle C and the Clean Air Act (CAA) hazardous waste combustion MACT) or

injected into UIC Class I hazardous waste wells (subject to joint control under Subtitle C and the Safe Drinking Water Act (SDWA)).

EPA does not expect to include emissions to ambient air from municipal and industrial waste incineration and energy recovery units in the risk evaluation, as they are regulated under section 129 of the Clean Air Act. CAA section 129 requires EPA to review and, if necessary, add provisions to ensure the standards adequately protect public health and the environment. Thus, combustion by-products from incineration treatment of methylene chloride wastes (the majority of the 37.8 million lbs identified as treated in Table 2-6) would be subject to these regulations, as would methylene chloride burned for energy recovery (15.6 million lbs).

EPA does not expect to include on-site releases to land that go to underground injection in its risk evaluation. TRI reporting in 2016 indicated 59,711 pounds released to underground injection to a Class I well and no releases to underground injection wells of Classes II-VI. Environmental disposal of methylene chloride injected into Class I well types are managed and prevented from further environmental release by RCRA and SDWA regulations. Therefore, disposal of methylene chloride via underground injection is not likely to result in environmental and general population exposures.

EPA does not expect to include on-site releases to land from RCRA Subtitle C hazardous waste landfills or exposures of the general population or terrestrial species from such releases in the TSCA evaluation. Based on 2015 reporting to TRI, the majority of the land disposals occur in Subtitle C landfills (30,757 lbs on-site and 5,334 lbs off site). Design standards for Subtitle C landfills require double liner, double leachate collection and removal systems, leak detection system, run on, runoff, and wind dispersal controls, and a construction quality assurance program. They are also subject to closure and post-closure care requirements including installing and maintaining a final cover, continuing operation of the leachate collection and removal system until leachate is no longer detected, maintaining and monitoring the leak detection and groundwater monitoring system. Bulk liquids may not be disposed in Subtitle C landfills. Subtitle C landfill operators are required to implement an analysis and testing program to ensure adequate knowledge of waste being managed, and to train personnel on routine and emergency operations at the facility. Hazardous waste being disposed in Subtitle C landfills must also meet RCRA waste treatment standards before disposal. Given these controls, general population exposure to methylene chloride in groundwater from Subtitle C landfill leachate is not expected to be a significant pathway.

EPA does not expect to include on-site releases to land from RCRA Subtitle D municipal solid waste (MSW) landfills or exposures of the general population (including susceptible populations) or terrestrial species from such releases in the TSCA evaluation. While permitted and managed by the individual states, municipal solid waste landfills are required by federal regulations to implement some of the same requirements as Subtitle C landfills. MSW landfills generally must have a liner system with leachate collection and conduct groundwater monitoring and corrective action when releases are detected. MSW landfills are also subject to closure and post-closure care requirements, and must have financial assurance for funding of any needed corrective actions. MSW landfills have also been designed to allow for the small amounts of hazardous waste generated by households and very small quantity waste generators (less than 220 lbs per month). Bulk liquids, such as free solvent, may not be disposed of at MSW landfills.

EPA does not expect to include on-site releases to land from industrial non-hazardous waste and construction/demolition waste landfills in the methylene chloride risk evaluation. Industrial non-hazardous and construction/demolition waste landfills are primarily regulated under state regulatory programs. States must also implement limited federal regulatory requirements for siting, groundwater

monitoring and corrective action and a prohibition on open dumping and disposal of bulk liquids. States may also establish additional requirements such as for liners, post-closure and financial assurance, but are not required to do so.  Therefore, EPA does not expect to include this pathway in the risk evaluation.

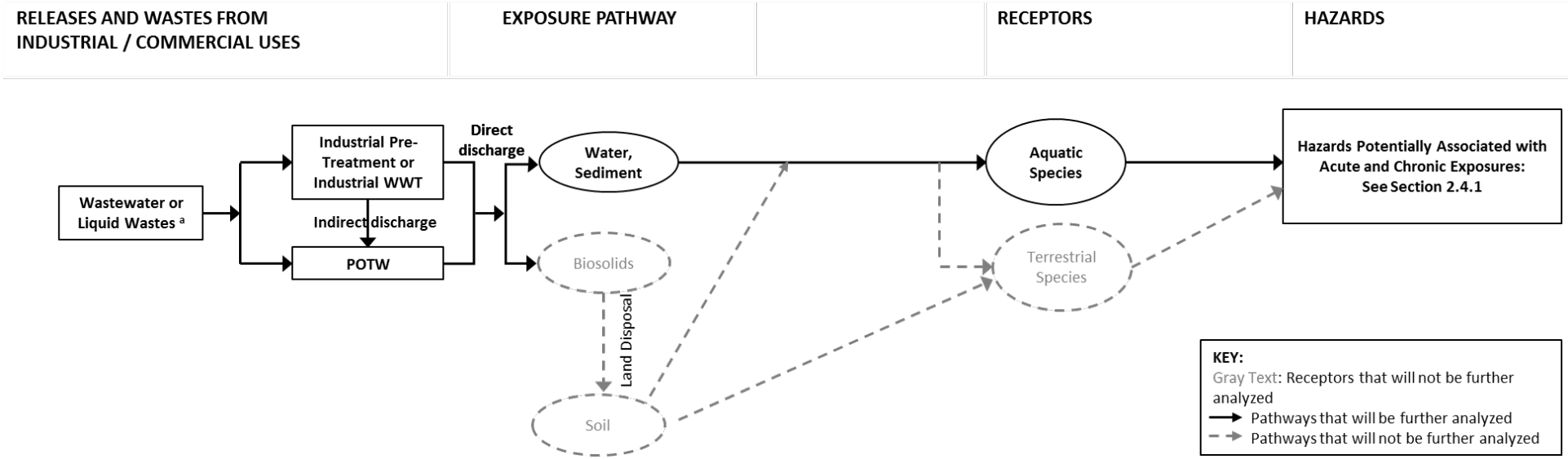


**Figure 2-4. Methylene Chloride Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards**

The conceptual model presents the exposure pathways, exposure routes and hazards to human and environmental receptors from environmental releases and wastes of methylene chloride.

[a] Industrial wastewater may be treated on-site and then released to surface water (direct discharge), or pre-treated and released to POTW (indirect discharge).

## 2.6 Analysis Plan

The analysis plan presented in the problem formulation is a refinement of the initial analysis plan that was published in the *Scope of the Risk Evaluation for Methylene Chloride (Dichloromethane)*.

The analysis plan outlined here is based on the conditions of use for methylene chloride, as described in Section 2.2 of this problem formulation. EPA is implementing systematic review approaches to identify, select, assess, integrate and summarize the findings of studies supporting the TSCA risk evaluation. The analytical approaches and considerations in the analysis plan are used to frame the scope of the systematic review activities for this assessment. The supplemental document, *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018), provides additional information about criteria and methods that have been and will be applied to the first 10 chemical risk evaluations.

While EPA has conducted a comprehensive search for reasonably available data as described in the Scope of the Risk Evaluation for Methylene Chloride, EPA encourages submission of additional existing data, such as full study reports or workplace monitoring from industry sources, that may be relevant for refining conditions of use, exposures, hazards and potentially exposed or susceptible subpopulations during the risk evaluation. EPA will continue to consider new information submitted by the public.

During risk evaluation, EPA will rely on the comprehensive literature results [*Methylene Chloride (CASRN 75-09-2) Bibliography: Supplemental File for the TSCA Scope Document* EPA-HQ-OPPT-2016-0742-0059 (U.S. EPA, 2017a)] or supplemental literature searches to address specific questions. Further, EPA may consider any relevant confidential business information (CBI) in the risk evaluation in a manner that protects the confidentiality of the information from public disclosure. The analysis plan is based on EPA's knowledge of methylene chloride to date, which includes partial, but not complete review of identified literature. If additional data or approaches become available, EPA may refine its analysis plan based on this information.

### 2.6.1 Exposure

Based on their physical-chemical properties, expected sources, and transport and transformation within the outdoor and indoor environment chemical substances are more likely to be present in some media and less likely to be present in others. Media-specific levels will vary based on the chemical substance of interest. For most chemical substances level(s) can be characterized through a combination of available monitoring data and modeling approaches.

#### 2.6.1.1 Environmental Releases

EPA expects to consider and analyze releases to relevant environmental media as follows:

1) Review reasonably available published literature or information on processes and activities associated with the conditions of use to evaluate the types of releases and wastes generated. EPA has reviewed some key data sources containing information on processes and activities resulting in releases, and the information found is shown in Appendix B.1. EPA will continue to review potentially relevant data sources identified in Table_Apx B-4 in Appendix B during risk evaluation.

   EPA plans to review the following key data sources in Table 2-9 for additional information on activities resulting in environmental releases. The evaluation strategy for engineering and occupational data sources discussed in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018) describes how data, information, and studies will be reviewed.

**Table 2-9. Potential Sources of Environmental Release Data**

| |
|---|
| U.S. EPA TRI Data (Reporting Year 2016 only) |
| U.S. EPA Generic Scenarios |
| OECD Emission Scenario Documents |
| EU Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) Specific Environmental Release Categories (SpERC) factsheets |
| Discharge Monitoring Report (DMR) surface water discharge data for methylene chloride from NPDES-permitted facilities |

2) Review reasonably available chemical-specific release data, including measured or estimated release data (e.g., data collected under the TRI program). EPA has reviewed key release data sources including the Toxics Release Inventory (TRI), and the data from this source is summarized in Section 2.3.2 above and also in Appendix B. EPA will continue to review relevant data sources as identified in Table_Apx B-5 in Appendix B during risk evaluation. EPA will match identified data to applicable conditions of use and identify data gaps where no data are found for particular conditions of use. EPA will attempt to address data gaps identified as described in steps 3 and 4 below by considering potential surrogate data and models.
3) Review reasonably available measured or estimated release data for surrogate chemicals that have similar uses and chemical and physical properties. Data for solvents that are used in the same types of applications may be considered as surrogate data for methylene chloride. As with methylene chloride, trichloroethylene is used in paints and coatings, in adhesives and sealants, and as solvents for cleaning and degreasing. EPA will evaluate the use of data for solvents such as trichloroethylene as surrogates to fill data gaps where uses of methylene chloride and other solvents align. If surrogate data are used, EPA normally converts air concentrations using the ratio of the vapor pressures of the two chemicals. EPA will review literature sources identified and if surrogate data are found, EPA will match these data to applicable conditions of use for potentially filling data gaps.
4) Understand and consider regulatory limits that may inform estimation of environmental releases. EPA has identified information from various EPA statutes (including, for example, regulatory limits, reporting thresholds or disposal requirements) that may be relevant to release estimation. Some of the information has informed revision of the conceptual models during problem formulation. EPA will further consider relevant regulatory requirements in estimating releases during risk evaluation.
5) Review and determine applicability of OECD Emission Scenario Documents (ESDs) and EPA Generic Scenarios to estimation of environmental releases. Potentially relevant OECD Emission Scenario Documents (ESDs) and EPA Generic Scenarios (GS) have been identified that correspond to some conditions of use. For example, the ESD on Industrial Use of Adhesives for Substrate Bonding, the ESD on the Coating Industry (Paints, Lacquers and Varnishes), and the GS on the Use of Vapor Degreasers are some of the ESDs and GSs that EPA may use to assess potential releases. EPA will need to critically review these generic scenarios and ESDs to determine their applicability to the conditions of use assessed. EPA was not able to identify ESDs or GSs corresponding to several conditions of use, including manufacture and import of methylene chloride, use of methylene chloride as an anti-spatter welding aerosol, and use of methylene chloride in pharmaceutical manufacturing. EPA will perform additional targeted research to understand those conditions of use which may inform identification of release scenarios. EPA may also need to perform targeted research for applicable models and associated parameters that EPA may use to estimate releases for certain conditions of use. If ESDs and GSs are not available, other methods may be considered. Additionally, for conditions of use where no measured data on releases are

available, EPA may use a variety of methods including the application of default assumptions such as standard loss fractions associated with drum cleaning (3%) or single process vessel cleanout (1%).

6) Map or group each condition(s) of use to a release assessment scenario. EPA has identified release scenarios and mapped them to some conditions of use. For example, some scenario groupings include Contractor Adhesive Removal and Industrial In-line Vapor Degreasing. EPA grouped similar conditions of use (based on factors including process equipment and handling, release sources and usage rates of methylene chloride and formulations containing methylene chloride, or professional judgment) into scenario groupings but may further refine these groupings as additional information becomes available during risk evaluation.
   EPA was not able to identify release scenarios corresponding to several conditions of use due to a lack of general knowledge of those conditions of use. EPA will perform additional targeted research to understand those uses which may inform identification of release scenarios.

7) Complete the weight of the evidence of environmental release data.
   EPA will rely on the weight of the scientific evidence when evaluating and integrating environmental release data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

#### 2.6.1.2 Environmental Fate

EPA expects to consider and analyze fate and transport in environmental media as follows:

1) Review reasonably available measured or estimated environmental fate endpoint data collected through the literature search.

   A general overview of persistence and bioaccumulation was presented in the TSCA Work Plan Chemical Risk Assessment Methylene Chloride: Paint Stripping Use (U.S. EPA, 2014b). Key environmental fate characteristics were included in the TSCA Scope for Methylene Chloride (U.S. EPA, 2017b) and in previous assessments of methylene chloride, including those conducted by the EPA Integrated Risk Information System (U.S. EPA, 2011b), EPA Office of Water (OW, 2015), US Agency for Toxic Substances and Disease Registry (ATSDR, 2010, 2000), Environment Canada (Health and Environment Canada, 1993), and Organization for Economic Cooperation and Development Cooperative Chemicals Assessment Program (OECD, 2011). These information sources will be used as a starting point for the environmental fate assessment. Other sources that will be consulted include those that are identified through the systematic review process. Studies will be evaluated using the evaluation strategies laid out in *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018).

   If measured values resulting from sufficiently high-quality studies are not available (to be determined through the systematic review process), chemical properties will be estimated using EPI Suite, SPARC, and other chemical parameter estimation models. Estimated fate properties will be reviewed for applicability and quality.

2) Using measured environmental fate data and/or environmental fate modeling, determine the influence of environmental fate endpoints (e.g., persistence, bioaccumulation, partitioning, transport) on exposure pathways and routes of exposure to environmental receptors.

Measured fate data including volatilization from water, sorption to organic matter in soil and sediments, aqueous and atmospheric photolysis rates, and aerobic and anaerobic biodegradation rates, along with physical-chemical properties and models such as the EPI Suite™ STP model (which estimates removal in wastewater treatment due to adsorption to sludge and volatilization to air) and volatility model (which estimates half-life from volatilization from a model river and model lake), will be used to characterize the movement of methylene chloride within and among environmental media and the persistence of methylene chloride in media.

3) Evaluate the weight of the evidence of environmental fate data.
   EPA will rely on the weight of the scientific evidence when evaluating and integrating environmental fate data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

#### 2.6.1.3 Environmental Exposures

EPA expects to consider the following in developing its environmental exposure assessment of methylene chloride:

1) Refine and finalize exposure scenarios for environmental receptors by considering unique combinations of sources (use descriptors), exposure pathways, exposure settings, populations exposed, and exposure routes. For methylene chloride, exposure scenarios for environmental receptors include exposures from surface water.
2) Review reasonably available environmental and biological monitoring data for environmental exposure to surface water. EPA will rely on databases (see examples below) and literature obtained during systematic review to include ranges and trends of chemical in surface water, including any trends seen in concentrations and spatial trends.
   - STORET and NWIS (USGS/EPS): https://www.epa.gov/waterdata/storage-and-retrieval-and-water-quality-exchange#portal
   - OPPT monitoring database
3) Review reasonably available information on releases to determine how modeled estimates of concentrations near industrial point sources compare with available monitoring data. Available exposure models that estimate surface water (e.g. E-FAST) will be evaluated and considered alongside available surface water data to characterize environmental exposures. Modeling approaches to estimate surface water concentrations generally consider the following inputs: direct release into surface water and transport (partitioning within media) and characteristics of the environment (river flow, volume of pond, meteorological data).
4) Determine applicability of existing additional contextualizing information for any monitored data or modeled estimates during risk evaluation. For example, site/location, time period, and conditions under which monitored data were collected will be evaluated to determine relevance and applicability to wider scenario development. Any studies which relate levels of methylene chloride in the environment or biota with specific sources or groups of sources will be evaluated.
5) Evaluate the weight of evidence of environmental occurrence data and modeled estimates.
   EPA will rely on the weight of the scientific evidence when evaluating and integrating environmental exposure data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

#### 2.6.1.4 Occupational Exposures

EPA expects to consider and analyze both worker and occupational nonuser exposures as follows:

1) Review reasonably available exposure monitoring data for specific condition(s) of use. Exposure data to be reviewed may include workplace monitoring data collected by government agencies such as OSHA and NIOSH, and monitoring data found in published literature (e.g., personal exposure monitoring data (direct measurements) and area monitoring data (indirect measurements)). Data, information, and studies will be evaluated using the evaluation strategies laid out in *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018). For some OSHA data, NAICS codes included with the data will be matched with potentially applicable conditions of use, and data gaps will be identified where no data are found for particular conditions of use. EPA will attempt to address data gaps identified as described in steps 2 and 3 below. Where possible, job descriptions may be useful in distinguishing exposures to different subpopulations within a particular condition of use. EPA has also identified additional data sources that may contain relevant monitoring data for the various conditions of use. EPA will review these sources, identified in Table 2-10 and in Table_Apx B-6 in Appendix B, and will extract relevant data for consideration and analysis during risk evaluation.

**Table 2-10. Potential Sources of Occupational Exposure Data**

| |
|---|
| 2014 TSCA Work Plan Chemical Risk Assessment Report for Methylene Chloride (Paint Stripping use) |
| U.S. NIOSH Health Hazard Evaluation (HHE) Program reports |
| U.S. OSHA Chemical Exposure Health Data (CEHD) program data |
| U.S. EPA Generic Scenarios |
| OECD Emission Scenario Documents |
| Sector-specific Worker Exposure Descriptions (SWEDs) |
| 2000 ATSDR Tox Profile |

2) Review reasonably available exposure data for surrogate chemicals that have uses and chemical and physical properties similar to methylene chloride. If surrogate data are identified, these data will be matched with applicable conditions of use for potentially filling data gaps. For several uses including use of adhesives, cleaners, and laundry and dishwashing products, EPA believes that trichloroethylene and other similar solvents may share the same or similar conditions of use and may be considered as surrogates for methylene chloride.
3) For conditions of use where data are limited or not available, review existing exposure models that may be applicable in estimating exposure levels. Models may be generic, broadly applicable models or may be specific to conditions of use (e.g., some OECD Emission Scenario Documents and US EPA Generic Scenarios may be identified as potentially mapping to some conditions of use). EPA has identified potentially relevant OECD ESDs and EPA GSs corresponding to some conditions of use. For example, the ESD on Industrial Use of Adhesives for Substrate Bonding, the ESD on the Industrial Use of Industrial Cleaners, and the GS on Textile Finishing are some of the ESDs and GSs that EPA may use to estimate occupational exposures. Where mappings are identified, the scenario documents will be reviewed for whether they contain exposure models that may apply to the conditions of use. An example of a generic model that has been used in addressing data gaps in some conditions of use is the Near-Field/ Far-Field (NF/FF) model e.g. in the recent trichloroethylene risk evaluation (U.S. EPA, 2014c). This or other models, including the assumption of compliance with the OSHA PEL for methylene chloride, may be explored where models specific to conditions of use are not found. If any models are identified as applicable, EPA will search for appropriate model parameter data. If parameter data can be located or assumed,

exposure estimates generated from these models may be used for potentially filling data gaps. EPA was not able to identify ESDs or GSs corresponding to several conditions of use, including recycling of methylene chloride and solvent mixtures containing methylene chloride, and processing and formulation of methylene chloride into industrial, commercial and consumer products. EPA will perform additional targeted research to understand those conditions of use, which may inform identification of exposure scenarios. EPA may also need to perform targeted research to identify applicable models that EPA may use to estimate exposures for certain conditions of use.

4) Review reasonably available data that may be used in developing, adapting or applying exposure models to the particular risk evaluation. This step will be performed after Steps #2 and #3 above. Based on information developed from Step #2 and Step #3, EPA will evaluate relevant data to determine whether the data can be used to develop, adapt, or apply models for specific conditions of use (and corresponding exposure scenarios).
5) Consider and incorporate applicable engineering controls and/or personal protective equipment into exposure scenarios. EPA will review potentially relevant data sources on engineering controls and personal protective equipment as identified in Table 2-10 and in Table_Apx B-7 in Appendix B and determine their applicability for incorporation into exposure scenarios during risk evaluation.
6) Map or group each condition of use to occupational exposure assessment scenario(s). For scenarios and worker exposure estimates, some key information and data to consider for grouping include per-site throughput or use rates of methylene chloride and formulations containing methylene chloride, process equipment and handling, and worker exposure activities and factors impacting exposures/ doses (routes, exposure factors or modeling). These main drivers must be similar enough between uses to allow for uses to be grouped for worker exposure. EPA has identified occupational exposure scenarios and mapped them to conditions of use. For example, one scenario grouping is commercial aerosol degreasing, where cleaning products containing methylene chloride are applied to substrates via spraying methods in a commercial setting. EPA grouped similar conditions of use (based on factors including process equipment and handling, usage rates of methylene chloride and formulations containing methylene chloride, exposure/release sources, or professional judgment) into scenario groupings but may further refine these groupings as additional information is identified during risk evaluation.
7) EPA was not able to identify occupational exposure scenarios corresponding to several conditions of use due to a lack of understanding of those conditions of use. EPA will perform targeted research to understand those uses which may inform identification of occupational exposure scenarios. If no data are available EPA may use appropriate conservative default assumptions in assessing occupational exposure.
8) Evaluate the weight of the evidence of occupational exposure data. EPA will rely on the weight of the scientific evidence when evaluating and integrating occupational exposure data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

#### 2.6.1.5 Consumer Exposures

EPA expects to consider and analyze both consumers using a consumer product and bystanders associated with the consumer using the product as follows:

1) Refine and finalize exposure scenarios for consumers by mapping sources of exposure (i.e., consumer products), exposure pathways, exposure settings, exposure routes, and populations exposed. Considerations for constructing exposure scenarios for consumers:

- Reasonably available data on consumer products or products available for consumer use including the weight fraction of methylene chloride in products;
- Information characterizing the use patterns of consumer products containing methylene chloride including the following: intended or likely consumer activity, method of application (e.g., spray-applied, brush-applied, dip), formulation type, amount of product used, frequency and duration of individual use events, and room or setting of use;
- The associated route of exposure for consumers; and
- Populations who may be exposed to products as users or bystanders in the home, including potentially exposed and susceptible subpopulations such as children or women of child bearing age and subsets of consumers who may use commercially-available products or those who may use products more frequently than typical consumers.

During consumer exposure modeling, these factors determine the resulting exposure route and magnitude. For example, while the product with the highest weight fraction in a given consumer product scenario could be run early on to indicate preliminary levels of exposure, that product may not actually result in the highest potential exposure due to having a lower frequency of use.

2) Evaluate the relative potential and magnitude of exposure routes based on available data. For methylene chloride, inhalation of vapor is expected to result in higher exposure to consumers and bystanders as compared to other pathways due to fate and exposure properties. We expect to comprehensively evaluate the data sources to effectively evaluate these pathways moving forward, but quantitative comparisons across exposure pathways or in relation to toxicity thresholds are not yet possible.
3) Review and use existing indoor exposure models that may be applicable in estimating indoor air (vapor). For example, U.S. EPA (2014b) used the Multi-Chamber Concentration and Exposure Model (MCCEM) to estimate and evaluate indoor exposures to methylene chloride-based paint strippers. EPA anticipates using similar models and approaches to evaluate indoor exposures moving forward.
9) Review reasonably available empirical data that may be used in developing, adapting or applying exposure models to the particular risk evaluation. For example, existing models developed for a chemical assessment may be applicable to another chemical assessment if model parameter data are available. For methylene chloride, existing scenarios and data parameters associated with modeling exposure from the use of methylene chloride-based paint strippers have already been developed (U.S. EPA, 2014b). EPA anticipates using this and other developed models for evaluation moving forward.
10) Review reasonably available consumer product-specific sources to determine how those exposure estimates compare with each other and with indoor monitoring data reporting methylene chloride in dust or indoor air.
11) Review reasonably available population- or subpopulation-specific exposure factors and activity patterns to determine if potentially exposed or susceptible subpopulations need to be further refined.
12) Evaluate the weight of the evidence of consumer exposure estimates based on different approaches. EPA will rely on the weight of the scientific evidence when evaluating and integrating consumer exposure data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

#### 2.6.1.6 General Population

EPA does not expect to include general population exposures in the risk evaluation for methylene chloride. EPA has determined that the existing regulatory programs and associated analytical processes adequately assess and effectively manage the risks of methylene chloride that may be present in various

media pathways (e.g., air, water, land) for the general population. For these cases, EPA believes that the TSCA risk evaluation should focus not on those exposure pathways, but rather on exposure pathways associated with TSCA conditions of use that are not subject to those regulatory processes, because the latter pathways are likely to represent the greatest areas of concern to EPA.

### 2.6.2 Hazards (Effects)

#### 2.6.2.1 Environmental Hazards

EPA will conduct an environmental hazard assessment of methylene chloride as follows:

1) Review reasonably available environmental hazard data, including data from alternative test methods (e.g., computational toxicology and bioinformatics; high-throughput screening methods; data on categories and read-across; *in vitro* studies).
   Environmental hazard data will be evaluated using the ecological toxicity data quality criteria outlined in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018). The study evaluation results will be documented in the risk evaluation phase and data from suitable studies will be extracted and integrated in the risk evaluation process.

   Conduct hazard identification (the qualitative process of identifying acute and chronic endpoints) and concentration-response assessment (the quantitative relationship between hazard and exposure) for all identified environmental hazard endpoints. Suitable environmental hazard data will be reviewed for acute and chronic endpoints for mortality and other effects (e.g. growth, immobility, reproduction, etc.). EPA will evaluate the character of the concentration-response relationship (*i.e.* positive, negative or no response) as part of the review.

   Sufficient environmental hazard studies are available to assess the hazards of environmental concentrations of methylene chloride to terrestrial and aquatic species. EPA did not find suitable sediment invertebrate hazard data, but will use hazard information from aquatic invertebrates to infer hazards to sediment invertebrates from exposures to methylene chloride in sediment pore water.

2) Derive aquatic and terrestrial concentrations of concern (COC) for acute and, where possible, chronic endpoints.
   The aquatic environmental hazard studies may be used to derive acute and chronic concentrations of concern (COC) for mortality, behavioral, developmental and reproductive or other endpoints determined to be detrimental to environmental populations. Depending on the robustness of the evaluated data for a particular organism (*e.g.* aquatic invertebrates), environmental hazard values (e.g. ECx/LCx/NOEC/LOEC, etc.) may be derived and used to further understand the hazard characteristics of methylene chloride to aquatic species.
3) Evaluate the weight of the evidence of environmental hazard data.

   EPA will rely on the weight of the scientific evidence when evaluating and integrating environmental hazard data. The data integration strategy will be designed to be fit-for-purpose. EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

4) Consider the route(s) of exposure, available biomonitoring data and available approaches to integrate exposure and hazard assessments.

EPA believes there is sufficient information to evaluate the potential risks to aquatic invertebrates, aquatic plants and amphibians from exposures to methylene chloride in ground water and surface water.

#### 2.6.2.2 Human Health Hazards

EPA expects to consider and analyze human health hazards as follows:

1) Review reasonably available human health hazard data, including data from alternative test methods as needed (e.g., computational toxicology and bioinformatics; high-throughput screening methods; data on categories and read-across; in vitro studies; systems biology).

   For the methylene chloride risk evaluation, EPA will evaluate information in the IRIS assessment and human health studies using OPPT's structured process described in the document, *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018). Human and animal data will be identified and included as described in the inclusion and exclusion criteria in Appendix F. EPA plans to prioritize the evaluation of mechanistic evidence. Specifically, EPA does not plan to evaluate mechanistic studies unless needed to clarify questions about associations between methylene chloride and health effects and its relevance to humans. The *Applications of Systematic Review* document (U.S. EPA, 2018) describes the process of how studies will be evaluated using specific data evaluation criteria and a predetermined approach. Study results will be extracted and presented in evidence tables by hazard endpoint. EPA plans to evaluate relevant studies identified in the Integrated Risk Information System (IRIS) *Toxicological Review of Dichloromethane (Methylene Chloride)* (U.S. EPA, 2011b) and the *TSCA Work Plan Chemical Risk Assessment - Methylene Chloride: Paint Striping Use* (U.S. EPA, 2014b). In addition for identifying human and animal data, EPA intends to review studies published after the most recent of the multiple acute reference values were published (e.g. AEGLs). These studies were published from January 1, 2008 to March 2, 2017 and are captured in the comprehensive literature search conducted by the Agency for methylene chloride (see *Methylene Chloride (CASRN 75-09-2) Bibliography: Supplemental File for the TSCA Scope Document*; EPA-HQ-OPPT-2016-0742-0059 (U.S. EPA, 2017a)) using the approaches described in *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018). To more fully understand circumstances related to deaths by individuals using methylene chloride, EPA/OPPT will review case reports, case series and ecological studies related to deaths and effects that may imminently lead to death (respiratory distress). EPA/OPPT will not be evaluating case reports and series or ecological studies for endpoints that appear to be less severe endpoints (e.g., nausea).

2) In evaluating reasonably available data, determine whether particular human receptor groups may have greater susceptibility to the chemical's hazard(s) than the general population.

   Reasonably available human health hazard data will be evaluated to ascertain whether some human receptor groups may have greater susceptibility than the general population to methylene chloride hazard(s).

3) Conduct hazard identification (the qualitative process of identifying non-cancer and cancer endpoints) and dose-response assessment (the quantitative relationship between hazard and exposure) for all identified human health hazard endpoints.

Human health hazards from acute and chronic exposures will be identified by evaluating the human and animal data that meet the data quality criteria described in *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018). Data quality evaluation will be performed on relevant studies identified in the IRIS assessment (U.S. EPA, 2011b), the TSCA work plan risk assessment (U.S. EPA, 2014b), and assessments of the effects of acute exposures in the (NAC/AEGL, 2008), SMAC for methylene chloride (NRC, 1996a) and an acute REL published by (OEHHA, 2008). Data quality evaluation will also be performed on studies published from January 1, 2008 to March 2, 2017 that were identified in the comprehensive literature search and that met the inclusion criteria for full-text screening (see *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018). Hazards identified by studies meeting data quality criteria will be grouped by routes of exposure relevant to humans (oral, inhalation) and by cancer and noncancer endpoints.

Dose-response assessment will be performed in accordance with EPA guidance (U.S. EPA, 2012a, 2011a, 1994). Dose-response analyses performed to support the U.S. EPA (2011b) IRIS oral and inhalation reference dose determinations and for the cancer unit risk and slope factor may be used if the data meet data quality criteria and if additional information on the identified hazard endpoints or additional hazard endpoints would not alter the analysis.

4) Derive points of departure (PODs) where appropriate; conduct benchmark dose modeling depending on the available data. Adjust the PODs as appropriate to conform (e.g., adjust for duration of exposure) to the specific exposure scenarios evaluated.

   Hazard data will be evaluated to determine the type of dose-response modeling that is applicable, if the dose-response modeling requires updating. Where modeling is feasible, a set of dose-response models that are consistent with a variety of potentially underlying biological processes will be applied to empirically model the dose-response relationships in the range of the observed data consistent with the EPA *Benchmark Dose Technical Guidance Document* (U.S. EPA, 2012a). Where dose-response modeling is not feasible, NOAELs or LOAELs will be identified.

   EPA will evaluate whether the available physiologically-based pharmacokinetic (PBPK) and empirical kinetic models are adequate for route-to-route and interspecies extrapolation of the POD, or for extrapolation of the POD to appropriate exposure durations for the risk evaluation.

5) Consider the route(s) of exposure (oral, inhalation, dermal), available route-to-route extrapolation approaches, available biomonitoring data and available approaches to correlate internal and external exposures to integrate exposure and hazard assessment.

   EPA believes there are sufficient data to conduct dose-response analysis with benchmark dose modeling or NOAELs or LOAELs for both inhalation and oral routes of exposure.

   A route-to-route extrapolation from the inhalation and oral toxicity studies is needed to assess systemic risks from dermal exposures. Without an adequate PBPK model, the approaches described in the EPA guidance document *Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part E, Supplemental Guidance for Dermal Risk Assessment)* could be applied. These approaches may be able to further inform the relative importance of dermal exposures compared with other routes of exposure.

6) Evaluate the weight of the evidence of human health hazard data.

EPA will rely on the weight of the scientific evidence when evaluating and integrating human health hazard data. The strategy will be designed to be fit-for-purpose. EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

### 2.6.3 Risk Characterization

Risk characterization is an integral component of the risk assessment process for both ecological and human health risks. EPA will derive the risk characterization in accordance with EPA's *Risk Characterization Handbook* (U.S. EPA, 2000). As defined in EPA's *Risk Characterization Policy*, "the risk characterization integrates information from the preceding components of the risk evaluation and synthesizes an overall conclusion about risk that is complete, informative and useful for decision makers." Risk characterization is considered to be a conscious and deliberate process to bring all important considerations about risk, not only the likelihood of the risk but also the strengths and limitations of the assessment, and a description of how others have assessed the risk into an integrated picture.

Risk characterization at EPA assumes different levels of complexity depending on the nature of the risk assessment being characterized. The level of information contained in each risk characterization varies according to the type of assessment for which the characterization is written. Regardless of the level of complexity or information, the risk characterization for TSCA risk evaluations will be prepared in a manner that is transparent, clear, consistent, and reasonable (TCCR) (U.S. EPA, 2000). EPA will also present information in this section consistent with approaches described in the Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act (82 FR 33726). For instance, in the risk characterization summary, EPA will further carry out the obligations under TSCA section 26; for example, by identifying and assessing uncertainty and variability in each step of the risk evaluation, discussing considerations of data quality such as the reliability, relevance and whether the methods utilized were reasonable and consistent, explaining any assumptions used, and discussing information generated from independent peer review. EPA will also be guided by EPA's Information Quality Guidelines (U.S. EPA, 2002) as it provides guidance for presenting risk information. Consistent with those guidelines, in the risk characterization, EPA will also identify: (1) Each population addressed by an estimate of applicable risk effects; (2) the expected risk or central estimate of risk for the potentially exposed or susceptible subpopulations affected; (3) each appropriate upper-bound or lower bound estimate of risk; (4) each significant uncertainty identified in the process of the assessment of risk effects and the studies that would assist in resolving the uncertainty; and (5) peer reviewed studies known to the Agency that support, are directly relevant to, or fail to support any estimate of risk effects and the methodology used to reconcile inconsistencies in the scientific information.

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# APPENDICES

# Appendix A REGULATORY HISTORY

## A.1 Federal Laws and Regulations

**Table_Apx A-1. Federal Laws and Regulations**

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| **EPA Regulations** | | |
| TSCA – Section 6(a) | Provides EPA with the authority to prohibit or limit the manufacture (including import), processing, distribution in commerce, use or disposal of a chemical if EPA evaluates the risk and concludes that the chemical presents an unreasonable risk to human health or the environment. | Proposed rule (82 FR 7464, January 19, 2017) regulating certain uses of methylene chloride and N-methylpyrrolidone in paint and coating removal.<br>EPA intends to finalize the methylene chloride rule (https://www.epa.gov/newsreleases/epa-announces-action-methylene-chloride) |
| TSCA – Section 6(b) | Directs EPA to promulgate regulations to establish processes for prioritizing chemicals and conducting risk evaluations on priority chemicals. In the meantime, EPA directed to identify and begin risk evaluations on 10 chemical substances drawn from the 2014 update of the TSCA Work Plan for Chemical Assessments. | Methylene chloride is on the initial list of chemicals to be evaluated for unreasonable risk under TSCA (81 FR 91927, December 19, 2016). |
| TSCA – Section 8(a) | The TSCA section 8(a) CDR Rule requires manufacturers (including importers) to give EPA basic exposure-related information on the types, quantities and uses of chemical substances produced domestically and imported into the United States. | Methylene chloride manufacturing (including importing), processing, and use information is reported under the CDR rule (76 FR 50816, August 16, 2011). |
| TSCA – Section 8(b) | EPA must compile, keep current and publish a list (the TSCA Inventory) of each chemical | Methylene chloride was on the initial TSCA Inventory and therefore was not subject to EPA's new chemicals review |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | substance manufactured, processed or imported in the United States. | process under TSCA section 5 (60 FR 16309, March 29, 1995). |
| TSCA – Section 8(d) | Provides EPA with authority to issue rules requiring producers, importers, and (if specified) processors of a chemical substance or mixture to submit lists and/or copies of ongoing and completed, unpublished health and safety studies. | One submission received in 2001 (U.S. EPA, Chemical Data Access Tool. Accessed April 24, 2017). |
| TSCA – Section 8(e) | Manufacturers (including importers), processors, and distributors must immediately notify EPA if they obtain information that supports the conclusion that a chemical substance or mixture presents a substantial risk of injury to health or the environment. | Sixteen submissions received 1992-1994 (U.S. EPA, ChemView. Accessed April 24, 2017). |
| TSCA – Section 4 | Provides EPA with authority to issue rules and orders requiring manufacturers (including importers) and processors to test chemical substances and mixtures. | Five chemical data from test rules (Section 4) from 1974 and (U.S. EPA, ChemView. Accessed April 24, 2017). |
| EPCRA – Section 313 | Requires annual reporting from facilities in specific industry sectors that employ 10 or more full-time equivalent employees and that manufacture, process or otherwise use a TRI-listed chemical in quantities above threshold levels. A facility that meets reporting requirements must submit a reporting form for each chemical for which it triggered reporting, providing data across a variety of categories, including activities and uses of the chemical, releases and other waste management (e.g., quantities | Methylene chloride is a listed substance subject to reporting requirements under 40 CFR 372.65 effective as of January 01, 1987. |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | recycled, treated, combusted) and pollution prevention activities (under section 6607 of the Pollution Prevention Act). These data include on- and off-site data as well as multimedia data (i.e., air, land and water). | |
| Federal Food, Drug, and Cosmetic Act (FFDCA) –Section 408 | FFDCA governs the allowable residues of pesticides in food. Section 408 of the FFDCA provides EPA with the authority to set tolerances (rules that establish maximum allowable residue limits), or exemptions from the requirement of a tolerance, for pesticide residues (including inert ingredients) on food. Prior to issuing a tolerance or exemption from tolerance, EPA must determine that the pesticide residues permitted under the action are "safe." Section 408(b) of the FFDCA defines "safe" to mean a reasonable certainty that no harm will result from aggregate, nonoccupational exposures to the pesticide. Pesticide tolerances or exemptions from tolerance that do not meet the FFDCA safety standard are subject to revocation under FFDCA section 408(d) or (e). In the absence of a tolerance or an exemption from tolerance, a food containing a pesticide residue is considered adulterated and may not be distributed in interstate commerce. | Methylene chloride was registered as an antimicrobial, conventional chemical in 1974.<br>In 1998, EPA removed methylene chloride from its list of pesticide product inert ingredients that are currently used in pesticide products (63 FR 34384). The tolerance exemptions for methylene chloride were revoked in 2002 (67 FR 16027, April 4, 2002). |
| CAA – Section 112(b) | Defines the original list of 189 HAPs. Under 112(c) of the CAA, EPA must identify and list source categories that emit HAP and then set emission standards for those | Methylene chloride is listed as a HAP (42 U.S. Code section 7412), and is considered an "urban air toxic" (CAA Section 112(k)). |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | listed source categories under CAA section 112(d). CAA section 112(b)(3)(A) specifies that any person may petition the Administrator to modify the list of HAP by adding or deleting a substance. Since 1990, EPA has removed two pollutants from the original list leaving 187 at present. | |
| CAA – Section 112(d) | Directs EPA to establish, by rule, NESHAPs for each category or subcategory of listed major sources and area sources of HAPs (listed pursuant to Section 112(c)). The standards must require the maximum degree of emission reduction that the EPA determines is achievable by each particular source category. This is generally referred to as maximum achievable control technology (MACT). | There are a number of source-specific NESHAPs for methylene chloride, including:<br>• Foam production and fabrication process (68 FR 18062, April 14, 2003; 72 FR 38864, July 16, 20027; 73 FR 15923, March 26, 2008; 79 FR 48073, August 15, 2014).<br>• Aerospace (60 FR 45948, September 1, 1995).<br>• Boat manufacturing (66 FR 44218, August 22, 2001).<br>• Chemical manufacturing industry (agricultural chemicals and pesticides, cyclic crude and intermediate production, industrial inorganic chemicals, industrial and miscellaneous organic chemicals, inorganic pigments, plastic materials and resins, pharmaceutical production, synthetic rubber) (74 FR 56008, October 29, 2009).<br>• Fabric printing, coating and dyeing (68 FR 32172, May 29, 2003).<br>• Halogenated Solvent Cleaning (72 FR 25138, May 3, 2007).<br>• Miscellaneous organic chemical production and processes (MON) (68 FR 63852, November 10, 2003).<br>• Paint and allied products manufacturing (area sources) (74 FR 63504, December 3, 2009). |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | | • Paint stripping and miscellaneous surface coating operations (area sources) (73 FR 1738, January 9, 2008).<br>• Paper and other web surface coating (67 FR 72330, December 4, 2002).<br>• Pesticide active ingredient production (64 FR 33550, June 23, 1999; 67 FR 38200, June 3, 2002).<br>• Pharmaceutical production (63 FR 50280, September 21, 1998).<br>• Publicly Owned Treatment Works (64 FR 57572, October 26, 1999).<br>• Reciprocating Internal Combustion Engines (RICE) (75 FR 51570, August 20, 2010).<br>• Reinforced plastic composites production (68 FR 19375, April 21, 2003).<br>• Wood preserving (area sources) (72 FR 38864, July 16, 2007).) |
| CAA sections 112(d) and 112(f) | Risk and technology review (RTR) of section 112(d) MACT standards. Section 112(f)(2) requires EPA to conduct risk assessments for each source category subject to section 112(d) MACT standards, and to determine if additional standards are needed to reduce remaining risks. Section 112(d)(6) requires EPA to review and revise the MACT standards, as necessary, taking into account developments in practices, processes and control technologies. | EPA has promulgated a number of RTR NESHAP (e.g., the RTR NESHAP for Halogenated Solvent Cleaning (72 FR 25138; May 3, 2007) and will do so, as required, for the remaining source categories with NESHAP. |
| CAA – Section 612 | Under Section 612 of the CAA, EPA's Significant New Alternatives Policy (SNAP) program reviews substitutes for ozone-depleting substances within | Under the SNAP program, EPA listed methylene chloride as an acceptable substitute in multiple industrial end-uses, including as a blowing agent in polyurethane foam, in cleaning |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | a comparative risk framework. EPA publishes lists of acceptable and unacceptable alternatives. A determination that an alternative is unacceptable, or acceptable only with conditions, is made through rulemaking. | solvents, in aerosol solvents and in adhesives and coatings (59 FR 13044, March 18, 1994). In 2016, methylene chloride was listed as an unacceptable substitute for use as a blowing agent in the production of flexible polyurethane foam (81 FR 86778, December 1, 2016). |
| CWA – Section 301(b), 304(b), 306, and 307(b) | Requires establishment of Effluent Limitations Guidelines and Standards for conventional, toxic, and nonconventional pollutants. For toxic and non-conventional pollutants, EPA identifies the best available technology that is economically achievable for that industry after considering statutorily prescribed factors and sets regulatory requirements based on the performance of that technology. | Methylene chloride is designated as a toxic pollutant under section 307(a)(1) of the CWA and as such is subject to effluent limitations. Under CWA section 304, methylene chloride is included in the list of total toxic organics (TTO) (40 CFR 413.02(i)). |
| CWA – Section 307(a) | Establishes a list of toxic pollutants or combination of pollutants under the CWA. The statue specifies a list of families of toxic pollutants also listed in the Code of Federal Regulations at 40 CFR Part 401.15. The “priority pollutants” specified by those families are listed in 40 CFR Part 423 Appendix A. These are pollutants for which best available technology effluent limitations must be established on either a national basis through rules (Sections 301(b), 304(b), 307(b), 306) or on a case-by-case best professional judgement basis in NPDES permits, see Section 402(a)(1)(B). | |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| SDWA – Section 1412 | Requires EPA to publish non-enforceable maximum contaminant level goals (MCLGs) for contaminants which 1. may have an adverse effect on the health of persons; 2. are known to occur or there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern; and 3. in the sole judgement of the Administrator, regulation of the contaminant presents a meaningful opportunity for health risk reductions for persons served by public water systems. When EPA publishes an MCLG, EPA must also promulgate a National Primary Drinking Water Regulation (NPDWR) which includes either an enforceable maximum contaminant level (MCL), or a required treatment technique. Public water systems are required to comply with NPDWRs. | Methylene chloride is subject to NPDWR under the SDWA with a MCLG of zero and an enforceable MCL of 0.005 mg/L or 5 ppb (Section 1412). |
| CERCLA – Sections 102(a) and 103 | Authorizes EPA to promulgate regulations designating as hazardous substances those substances which, when released into the environment, may present substantial danger to the public health or welfare or the environment. EPA must also promulgate regulations establishing the quantity of any hazardous substance the release of which must be reported under Section 103.<br>Section 103 requires persons in charge of vessels or facilities to | Methylene chloride is a hazardous substance under CERCLA. Releases of methylene chloride in excess of 1,000 pounds must be reported (40 CFR 302.4). |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | report to the National Response Center if they have knowledge of a release of a hazardous substance above the reportable quantity threshold. | |
| RCRA – Section 3001 | Directs EPA to develop and promulgate criteria for identifying the characteristics of hazardous waste, and for listing hazardous waste, taking into account toxicity, persistence, and degradability in nature, potential for accumulation in tissue and other related factors such as flammability, corrosiveness, and other hazardous characteristics. | Methylene chloride is included on the list of hazardous wastes pursuant to RCRA 3001.<br>RCRA Hazardous Waste Code: F001, F002, U080; see 40 CFR 261.31, 261.32.<br>In 2013, EPA modified its hazardous waste management regulations to conditionally exclude solvent-contaminated wipes that have been cleaned and reused from the definition of solid waste under RCRA and to conditionally exclude solvent-contaminated wipes that are disposed from the definition of hazardous waste (78 FR 46448, July 31, 2013, 40 CFR 261.4(a)(26)). |
| **Other Federal Regulations** | | |
| Federal Hazardous Substance Act (FHSA) | Requires precautionary labeling on the immediate container of hazardous household products and allows the Consumer Product Safety Commission (CPSC) to ban certain products that are so dangerous or the nature of the hazard is such that labeling is not adequate to protect consumers. | Certain household products that contain methylene chloride are hazardous substances required to be labelled under the FHSA (52 FR 34698, September 14, 1987). In 2016, the Halogenated Solvents Industry Alliance petitioned the CPSC to amend the CPSC's labeling interpretation and policy on those products (81 FR 60298, September 1, 2016). In 2018, CPSC updated the labelling policy for paint strippers containing methylene chloride (83 FR 12254, March 21, 2018 and 83 FR 18219, April 26, 2018) |
| Hazardous Materials Transportation Act (HMTA) | Section 5103 of the Act directs the Secretary of Transportation to: | Methylene chloride is listed as a hazardous material with regard to transportation and is subject to |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | • Designate material (including an explosive, radioactive material, infectious substance, flammable or combustible liquid, solid or gas, toxic, oxidizing or corrosive material, and compressed gas) as hazardous when the Secretary determines that transporting the material in commerce may pose an unreasonable risk to health and safety or property.<br>• Issue regulations for the safe transportation, including security, of hazardous material in intrastate, interstate and foreign commerce. | regulations prescribing requirements applicable to the shipment and transportation of listed hazardous materials (70 FR 34381, June 14 2005). |
| FFDCA | Provides the FDA with authority to oversee the safety of food, drugs and cosmetics. | Methylene chloride is banned by the FDA as an ingredient in all cosmetic products (54 FR 27328, June 29, 1989). |
| Occupational Safety and Health Act | Requires employers to provide their workers with a place of employment free from recognized hazards to safety and health, such as exposure to toxic chemicals, excessive noise levels, mechanical dangers, heat or cold stress or unsanitary conditions (29 U.S.C section 651 et seq.). | In 1997, OSHA revised an existing occupational safety and health standards for methylene chloride, to include an 8-hour TWA PEL of 25 ppm TWA, exposure monitoring, control measures and respiratory protection (29 CFR 1910.1052 App. A). |

## A.2 State Laws and Regulations

**Table_Apx A-2. State Laws and Regulations**

| State Actions | Description of Action |
|---|---|
| State PELs | California (PEL of 25 ppm and a STEL of 100) (Cal Code Regs. title 8, section 5155) |
| State Right-to-Know Acts | Massachusetts (454 Code Mass. Regs. section 21.00), New Jersey (8:59 N.J. Admin. Code section 9.1) and Pennsylvania (34 Pa. Code section 323). |

| State Actions | Description of Action |
|---|---|
| State Drinking Water Standards and Guidelines | Arizona (14 Ariz. Admin. Register 2978, August 1, 2008), California (Cal Code Regs. Title 26, section 22-64444), Delaware (Del. Admin. Code Title 16, section 4462), Connecticut (Conn. Agencies Regs. section 19-13-B102), Florida (Fla. Admin. Code R. Chap. 62-550), Maine (10 144 Me. Code R. Chap. 231), Massachusetts (310 Code Mass. Regs. section 22.00), Minnesota (Minn R. Chap. 4720), New Jersey (7:10 N.J Admin. Code section 5.2), Pennsylvania (25 Pa. Code section 109.202), Rhode Island (14 R.I. Code R. section 180-003), Texas (30 Tex. Admin. Code section 290.104). |
| Chemicals of High Concern to Children | Several states have adopted reporting laws for chemicals in children's products that include methylene chloride, including Maine (38 MRSA Chapter 16-D), Minnesota (Minnesota Statutes 116.9401 to 116.9407), Oregon (Toxic-Free Kids Act, Senate Bill 478, 2015), Vermont (18 V.S.A section 1776) and Washington State (WAC 173-334-130). |
| Volatile Organic Compound (VOC) Regulations for Consumer Products | Many states regulate methylene chloride as a VOC. These regulations may set VOC limits for consumer products and/or ban the sale of certain consumer products as an ingredient and/or impurity. Regulated products vary from state to state, and could include contact and aerosol adhesives, aerosols, electronic cleaners, footwear or leather care products and general degreasers, among other products. California (Title 17, California Code of Regulations, Division 3, Chapter 1, Subchapter 8.5, Articles 1, 2, 3 and 4), Connecticut (R.C.S.A Sections 22a-174-40, 22a-174-41, and 22a-174-44), Delaware (Adm. Code Title 7, 1141), District of Columbia (Rules 20-720, 20-721, 20-735, 20-736, 20-737), Illinois (35 Adm Code 223), Indiana ( 326 IAC 8-15), Maine (Chapter 152 of the Maine Department of Environmental Protection Regulations), Maryland (COMAR 26.11.32.00 to 26.11.32.26), Michigan (R 336.1660 and R 336. 1661), New Hampshire (Env-A 4100) New Jersey (Title 7, Chapter 27, Subchapter 24), New York (6 CRR-NY III A 235), Rhode Island (Air Pollution Control Regulation No. 31) and Virginia (9VAC5 CHAPTER 45) all have VOC regulations or limits for consumer products. Some of these states also require emissions reporting. |
| Other | California listed methylene chloride on Proposition 65 (Cal Code Regs. title 27, section 27001)<br>Massachusetts designated methylene chloride as a Higher Hazard Substance which will require reporting starting in 2014 (301 CMR 41.00). |

## A.3 International Laws and Regulations

**Table_Apx A-3. Regulatory Actions by other Governments and Tribes**

| Country/ Organization | Requirements and Restrictions |
|---|---|
| Canada | Methylene chloride is on the Canadian List of Toxic Substances (CEPA 1999 Schedule 1). Canada required pollution prevention plan implementation for methylene chloride in 2003 for aircraft paint stripping; flexible polyurethane foam blowing; pharmaceuticals and chemical intermediates manufacturing and tablet coating; industrial cleaning; and adhesive formulations. The overall reduction objective of 85% was exceeded (*Canada Gazette*, Part I, Saturday, February 28, 2004; Vol. 138, No. 9, p. 409). |
| European Union | In 2010, a restriction of sale and use of paint removers containing 0.1% or more methylene chloride was added to Annex XVII of regulation (EC) No 1907/2006 - REACH (Registration, Evaluation, Authorization and Restriction of Chemicals). The restriction included provisions for individual member states to issue a derogation for professional uses if they have completed proper training and demonstrate they are capable of safely use the paint removers containing methylene chloride (European Chemicals Agency (ECHA) database. Accessed April 18, 2017). |
| Australia | Methylene chloride was assessed under Human Health Tier II of the Inventory Multi-Tiered Assessment and Prioritisation (IMAP). Uses reported include solvent in paint removers, adhesives, detergents, print developing, aerosol propellants (products not specified), cold tank degreasing and metal cleaning, as well as uses in waterproof membranes, in urethane foam and plastic manufacturing, and as an extraction solvent for spices, caffeine and hops (NICNAS, 2017, *Human Health Tier II assessment for Methane, dichloro-*. Accessed April, 18 2017*)*. |
| Japan | Methylene chloride is regulated in Japan under the following legislation: Act on the Evaluation of Chemical Substances and Regulation of Their Manufacture, etc. (Chemical Substances Control Law; CSCL)<br>• Act on Confirmation, etc. of Release Amounts of Specific Chemical Substances in the Environment and Promotion of Improvements to the Management Thereof<br>• Industrial Safety and Health Act (ISHA)<br>• Air Pollution Control Law<br>• Water Pollution Control Law<br>• Soil Contamination Countermeasures Act<br>(National Institute of Technology and Evaluation [NITE] Chemical Risk Information Platform [CHIRP]. Accessed April 17, 2017). |
| Basel Convention | Halogenated organic solvents (Y41) are listed as a category of waste under the Basel Convention. Although the United States is not currently |

| Country/ Organization | Requirements and Restrictions |
|---|---|
| | a party to the Basel Convention, this treaty still affects U.S. importers and exporters. |
| OECD Control of Transboundary Movements of Wastes Destined for Recovery Operations | Halogenated organic solvents (A3150) are listed as a category of waste subject to The Amber Control Procedure under Council Decision C (2001) 107/Final. |
| Australia, Austria, Belgium, Canada, Denmark, European Union, Finland, France, Germany, Hungary, Ireland, Israel, Japan, Latvia New Zealand, People's Republic of China, Poland, Singapore, South Korea, Spain, Sweden, Switzerland, United Kingdom | Occupational exposure limits for methylene chloride (GESTIS International limit values for chemical agents (Occupational exposure limits, OELs) database. Accessed April 18, 2017). |

# Appendix B PROCESS, RELEASE AND OCCUPATIONAL EXPOSURE INFORMATION

This appendix provides information and data found in preliminary data gathering for methylene chloride.

## B.1 Process Information

Process-related information potentially relevant to the risk evaluation may include process diagrams, descriptions and equipment. Such information may inform potential release sources and worker exposure activities.

Note that the processing information below is representative of methylene chloride, but not inclusive of all uses. EPA will consider this information and data in combination with other data and methods for use in the risk evaluation.

### B.1.1 Manufacturing (Including Import)

According to 2016 public CDR data, methylene chloride is both manufactured in and imported into the United States (U.S. EPA, 2016b).

#### B.1.1.1 Domestic Manufacturing

Methylene chloride is primarily manufactured through the gas-phase reaction of hydrogen chloride with methanol to produce methyl chloride, which is then reacted with chlorine to produce methylene chloride, along with chloroform and carbon tetrachloride as coproducts. This reaction is typically driven by high temperature, but may also be driven through catalysis or photolysis. This reaction may alternatively be conducted in the liquid phase at low temperatures and high pressures, which can yield high selectivities of methylene chloride (Holbrook, 2003).

An antiquated production method of methylene chloride is the reaction of excess methane with chlorine at temperatures of approximately 400 to 500°C. Lower reaction temperatures are possible through the use of catalysis or photolysis. This reaction produces methylene chloride with methyl chloride, chloroform and carbon tetrachloride as coproducts and unreacted methane with hydrogen chloride as byproducts. The unreacted methane and hydrogen chloride are removed through a water wash, dried, and recycled. The liquid stream of chlorinated organic products is washed, alkali scrubbed, dried and fractionated (Holbrook, 2003).

Other minor production methods of methylene chloride exist, such as: the reduction of chloroform or carbon tetrachloride with hydrogen over a platinum catalyst; the molten salt oxychlorination of methane; the reaction of phosgene and formaldehyde over an activated carbon catalyst; and the reduction of carbon tetrachloride with ferrous hydroxide in the presence of alkaline hydroxides or carbonates (Holbrook, 2003).

#### B.1.1.2 Import

Based on EPA's knowledge of the chemical industry, typical import activities include storage in warehouses prior to distribution for further processing and use and QC sampling.
Methylene chloride may be transported in drums, trucks, railcars, barges and oceangoing ships. Storage contains should be constructed of galvanized or otherwise suitably lined mild or plain steel. Bulk storage tanks should include a vent equipped with a desiccant-packed dryer, such as calcium chloride, or an inert gas pad with pressure/vacuum relief valve (Holbrook, 2003).

### B.1.2 Processing

#### B.1.2.1 Reactant or Intermediate

Processing as a reactant or intermediate is the use of methylene chloride as a feedstock in the production of another chemical product via a chemical reaction in which methylene chloride is consumed to form the product. Methylene chloride is used as an intermediate for the production of difluoromethane, also known as HFC-32, which is used in fluorocarbon blends for refrigerants (Marshall and Pottenger, 2016).

Methylene chloride is also a feedstock in the production of bromochloromethane. Bromochloromethane is produced through a halogen exchange reaction with methylene chloride and either bromine or hydrogen bromide with an aluminum or aluminum trihalide catalyst. Alternative processes include the gas-phase bromination of methylene chloride with hydrogen bromide and the liquid-phase displacement reaction of methylene chloride with inorganic bromides (Ioffe and Frim, 2011).

#### B.1.2.2 Incorporating into Formulation, Mixture, or Reaction Product

Incorporation into a formulation, mixture or reaction product refers to the process of mixing or blending of several raw materials to obtain a single product or preparation. The uses of methylene chloride that may require incorporation into a formulation include paint removers; adhesives and sealants; paints and coatings; degreasers, cleaners, and spot removers; and lubricants. Methylene chloride-specific formulation processes were not identified; however, several ESDs published by the OECD have been identified that provide general process descriptions for some of these types of products. The formulation of paints and coatings typically involves dispersion, milling, finishing and filling into final packages (OECD, 2009b). Adhesive formulation involves mixing together volatile and non-volatile chemical components in sealed, unsealed or heated processes (OECD, 2009a). Sealed processes are most common for adhesive formulation because many adhesives are designed to set or react when exposed to ambient conditions (OECD, 2009a). Lubricant formulation typically involves the blending of two or more components, including liquid and solid additives, together in a blending vessel (OECD, 2004).

#### B.1.2.3 Repackaging

Based on EPA's knowledge of the chemical industry, typical repackaging sites receive the chemical in bulk containers and transfer the chemical from the bulk container into another smaller container in preparation for distribution in commerce.

#### B.1.2.4 Recycling

TRI data from 2015 indicate that many sites ship methylene chloride for off-site recycling. A general description of waste solvent recovery processes was identified. Waste solvents are generated when it becomes contaminated with suspended and dissolved solids, organics, water, or other substance (U.S. EPA, 1980). Waste solvents can be restored to a condition that permits reuse via solvent reclamation/recycling (U.S. EPA, 1980). The recovery process involves an initial vapor recovery (e.g., condensation, adsorption, and absorption) or mechanical separation (e.g., decanting, filtering, draining, setline, and centrifuging) step followed by distillation, purification, and final packaging (U.S. EPA, 1980).

### B.1.3 Uses

In this scope document, EPA has grouped uses based on CDR categories and identified examples within these categories as subcategories. Note that some subcategories may be grouped under multiple CDR categories. The differences between these uses will be further investigated and defined during risk evaluation.

### B.1.3.1 Solvents for Cleaning or Degreasing

EPA has gathered information on different types of cleaning and degreasing systems from recent trichloroethylene risk evaluation (U.S. EPA, 2014c) and risk management (82 FR 7432, January 19, 2017; 81 FR 91592, December 16, 2016) activities and 1-Bromopropane Draft Risk Assessment (U.S. EPA, 2016c) activities. Provided below are descriptions of three cleaning and degreasing uses of methylene chloride.

***Vapor Degreasers***

Vapor degreasing is a process used to remove dirt, grease and surface contaminants in a variety of metal cleaning industries. Vapor degreasing may take place in batches or as part of an in-line (i.e., continuous) system. Vapor degreasing equipment can generally be categorized into one of three degreaser types described below:

1) Batch vapor degreasers – In batch machines, each load (parts or baskets of parts) is loaded into the machine after the previous load is completed. Individual organizations, regulations and academic studies have classified batch vapor degreasers differently. For the purposes of the scope document, EPA categories the batch vapor degreasers into five types: open-top vapor degreasers (OTVDs); OTVDs with enclosures; closed-loop degreasing systems (airtight); airless degreasing systems (vacuum drying); and airless vacuum-to-vacuum degreasing systems.
2) Conveyorized vapor degreasers – In conveyorized systems, an automated parts handling system, typically a conveyor, continuously loads parts into and through the vapor degreasing equipment and the subsequent drying steps. Conveyorized degreasing systems are usually fully enclosed except for the conveyor inlet and outlet portals. Conveyorized degreasers are likely used in shops where there are a large number of parts being cleaned. There are seven major types of conveyorized degreasers: monorail degreasers; cross-rod degreasers; vibra degreasers; ferris wheel degreasers; belt degreasers; strip degreasers; and circuit board degreasers (U.S. EPA, 1977).
3) Continuous web vapor degreasers – Continuous web cleaning machines are a subset of in-line degreasers but differ in that they are specifically designed for cleaning parts that are coiled or on spools such as films, wires and metal strips (Kanegsberg and Kanegsberg, 2011; U.S. EPA, 2006b). In continuous web degreasers, parts are uncoiled and loaded onto rollers that transport the parts through the cleaning and drying zones at speeds >11 feet/minute (U.S. EPA, 2006b). The parts are then recoiled or cut after exiting the cleaning machine (Kanegsberg and Kanegsberg, 2011; U.S. EPA, 2006b).

***Cold Cleaners***

Methylene chloride can also be used as a solvent in cold cleaners, which are non-boiling solvent degreasing units. Cold cleaning operations include spraying, brushing, flushing and immersion; the use process and worker activities associated with cold cleaning have been previously described in (U.S. EPA, 2016c) 1-Bromopropane Draft Risk Assessment.

***Aerosol Spray Degreasers and Cleaners***

Aerosol degreasing is a process that uses an aerosolized solvent spray, typically applied from a pressurized can, to remove residual contaminants from fabricated parts. Products containing methylene chloride may be used in aerosol degreasing applications such as brake cleaning, engine degreasing and metal product cleaning (see the *Preliminary Information on Manufacturing, Processing, Distribution, Use and Disposal for Methylene Chloride* EPA-HQ-OPPT-2016-0742-0003). This use has been previously described in (U.S. EPA, 2016c) 1-Bromopropane Draft Risk Assessment. Aerosol degreasing may occur at either industrial facilities or at commercial repair shops to remove contaminants on items being serviced. Aerosol degreasing products may also be purchased and used by consumers for various applications.

### B.1.3.2 Adhesives and Sealants

Based on products identified in EPA's *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal for Methylene Chloride* (EPA-HQ-OPPT-2016-0742-0003) and 2016 CDR reporting (U.S. EPA, 2016b), methylene chloride may be used in adhesives and sealants for industrial, commercial and consumer applications. The *Preliminary Information on Manufacturing, Processing, Distribution, Use and Disposal for Methylene Chloride* (EPA-HQ-OPPT-2016-0742-0003) identifies aerosol and canister adhesive products that contain methylene chloride. In these applications, the methylene chloride likely serves as a propellant or solvent and evaporates during adhesive drying. These adhesive products are identified for use on substrates such as metal, foam, plastic, rubber, fabric, leather, wood and fiberglass. The types of adhesives identified in the *Preliminary Information on Manufacturing, Processing, Distribution, Use and Disposal for Methylene Chloride* (EPA-HQ-OPPT-2016-0742-0003) include contact adhesives, crosslinking adhesives, pressure sensitive adhesives, sealers and cements.

The OECD (2013) ESD for Use of Adhesives provides general process descriptions and worker activities for industrial adhesive uses. Given the identified applications of methylene chloride in aerosol and canister adhesives, EPA anticipates workers spray apply the adhesive to substrates. The adhesives are likely sold and used in sealed containers such as spray cans or canister tanks.

### B.1.3.3 Paints and Coatings

Based on the *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: Methylene Chloride* and *Use and Market Profile for Methylene Chloride*, both available in the public docket (EPA-HQ-OPPT-2016-0742), methylene chloride may be used in various paints and coatings for industrial, commercial and consumer applications. Typical process descriptions and worker activities for industrial and commercial uses in coating applications include manual application with roller or brush, air spray systems, airless and air-assisted airless spray systems, electrostatic spray systems, electrodeposition/electrocoating and autodeposition, dip coating, curtain coating systems, roll coating systems and supercritical carbon dioxide systems (OECD, 2009b). After application, solvent-based coatings typically undergo a drying stage in which the solvent evaporates from the coating (OECD, 2009b).

Methylene chloride is used for paint removal in a variety of industries, such as the automotive, aircraft, construction and refinishing industries. Application methods include manual or automated application, with techniques such as spray application, pouring, wiping and rolling. Additional details on this use of methylene chloride can be found in EPA's 2014 TSCA Work Plan Chemical Risk Assessment for the use of methylene chloride as a paint remover (U.S. EPA, 2014b). The Agency proposed restrictions under TSCA section 6 to address the risks from methylene chloride in paint and coating removal by consumers and most commercial users except for commercial furniture stripping (82 FR 7464, January 19, 2017). While paint and coating removal falls under the conditions of use for methylene chloride, based on the intention to finalize the rulemaking the scenarios already assessed in the 2014 risk assessment these uses will not be re-evaluated and EPA will rely on the 2014 risk evaluation (https://www.epa.gov/newsreleases/epa-announces-action-methylene-chloride) see Section 2.2.2.1.

### B.1.3.4 Laundry and Dishwashing Products

***Spot Cleaner***

Methylene chloride is found in products used to spot clean garments (EPA-HQ-OPPT-2016-0742-0003). Spot cleaning products can be applied to the garment either before or after the garment is dry cleaned.

The process and worker activities associated with commercial dry cleaning and spot cleaning have been previously described in (U.S. EPA, 2016c) 1-Bromopropane Draft Risk Assessment.

#### B.1.3.5 Lubricants and Greases

EPA identified several commercial and consumer lubricant products that contain methylene chloride. These lubricants are used to reduce friction and wear and prevent seizing where metal-to-metal contact is possible and inhibit rusting and corrosion by displacing water in a wide variety of applications, including machinery, hardware, cables, and chains. The majority of these lubricant products are aerosol lubricants (available in aerosol cans), although one liquid-based lubricant product (available in pails and drums) was also identified. Aerosol lubricants are sprayed directly onto metal substrates, while liquid lubricants may be brushed or spray applied to metal substrates. The methylene chloride is anticipated to completely evaporate during the drying phase, leaving behind a lubricating film (*Use and Market Profile for Methylene Chloride* EPA-HQ-OPPT-2016-0742-0003)

#### B.1.3.6 Other Uses

Methylene chloride is a U-listed hazardous waste under RCRA code U080 (40 CFR § 261.33(f)). Additionally, methylene chloride is included in multiple waste codes under the F-list of non-specific source wastes (40 CFR § 261.31(a)).

### B.1.4 Disposal

Methylene chloride is a U-listed hazardous waste under code U080 under RCRA; therefore, discarded, unused pure and commercial grades of methylene chloride are regulated as a hazardous waste under RCRA (40 CFR § 261.33(f)). Additionally, methylene chloride is included in multiple waste codes under the F-list of non-specific source wastes (40 CFR § 261.31(a)).

## B.2 Occupational Exposure Data

EPA presents below examples of occupational exposure-related information from the preliminary data gathering. EPA will consider this information and data in combination with other data and methods for use in the risk evaluation.

Table_Apx B-1and Table_Apx B-2 show mappings of release and worker exposure scenarios to industry sectors with available OSHA data for methylene chloride, obtained from OSHA inspections between 2002 and 2016 for personal monitoring data and area monitoring data, respectively. EPA attempted to group industry sectors according to possible release/exposure scenarios, but there is a great degree of uncertainty where and how methylene chloride may be used in these industries. The industry sectors in Table_Apx B-1and Table_Apx B-2 were extracted from the OSHA CEHD (OSHA, 2017).

EPA also found some NIOSH HHE data since 2000 that are summarized and included in Table_Apx B-3.

**Table_Apx B-1 Mapping of Scenarios to Industry Sectors with Methylene Chloride Personal Monitoring Air Samples Obtained from OSHA Inspections Conducted Between 2002 and 2016**

| Possible Release / Exposure Scenarios | NAICS | NAICS Description (Job Titles from OSHA) |
|---|---|---|
| Manufacture of methylene chloride; Processing as a Reactant; Incorporated into Formulation, Mixture or Reaction Product | 325199 | All Other Basic Organic Chemical Manufacturing (Operator) |
| | 325998 | All Other Miscellaneous Chemical Product and Preparation Manufacturing (Technician) |

**Table_Apx B-1 Mapping of Scenarios to Industry Sectors with Methylene Chloride Personal Monitoring Air Samples Obtained from OSHA Inspections Conducted Between 2002 and 2016**

| Possible Release / Exposure Scenarios | NAICS | NAICS Description (Job Titles from OSHA) |
|---|---|---|
| Solvents (for cleaning and degreasing); Metal products not covered elsewhere | 331316 | Aluminum Extruded Product Manufacturing (2007 NAICS - 2012 is 331318 Other Aluminum Rolling, Drawing, and Extruding) (Poly-Pour Setup) |
| | 331513 | Steel Foundries (except Investment) (Machine Operator, Industrial Hygienist) |
| | 332710 | Machine Shops (Shipping and Receiving) |
| | 332811 | Metal Heat Treating (Controller) |
| | 332999 | All Other Miscellaneous Fabricated Metal Product Manufacturing (Welder) |
| | 333132 | Oil and Gas Field Machinery and Equipment Manufacturing (Laborer) |
| | 336211 | Motor Vehicle Body Manufacturing (Welder) |
| | 334416 | Capacitor, Resistor, Coil, Transformer, and Other Inductor Manufacturing (Operator) |
| | 327390 | Other Concrete Product Manufacturing (Rspecta Machine Cleaner, Rspecta Machine Operator) |
| Application of Adhesives; Solvents (for cleaning and degreasing); Metal products not covered elsewhere | 332321 | Metal Window and Door Manufacturing (Adhesive Sprayer) |
| | 335121 | Residential Electric Lighting Fixture Manufacturing (Glue Application) |
| | 333921 | Elevator and Moving Stairway Manufacturing (Carpenter, Adhesive Sprayer) |
| Paint and Coating Application; Solvents (for cleaning and degreasing); Metal products not covered elsewhere | 332312 | Fabricated Structural Metal Manufacturing (Painter) |
| Paint and Coating Application | 238320 | Painting and Wall Covering Contractors (apprentice painter employee) |
| | 238390 | Other Building Finishing Contractors (laborer) |
| | 713110 | Amusement and Theme Parks (Painter) |
| | 811420 | Reupholstery and Furniture Repair (Owner, Refinisher, Laborer, Stripper) |
| | 448190 | Other Clothing Stores (Screen Printer) |
| | 451110 | Sporting Goods Stores (Screen Printing) |
| | 323113 | Commercial Screen Printing (Quality Control, Production/Sprayer, Screen Print Lead) |
| Fabric Finishing | 313312 | Textile and Fabric Finishing (except Broadwoven Fabric) Mills (2007 NAICS - 2012 is 313310 Textile and Fabric Finishing Mills) (Production specialist) |
| | 315240 | Women's, Girls', and Infants' Cut and Sew Apparel Manufacturing (Presser, Supervisor – Finishing Dept) |
| | 316998 | All Other Leather Good and Allied Product Manufacturing (Spray Finishing, Sprayer of Methylene Chloride, Press Operator, Miscellaneous) |
| Plastic product manufacturing (converting) | 325211 | Plastics Material and Resin Manufacturing (Plastic Fabricator, CSHO, Assistant Supervisor, Extruder Operator) |
| | 326199 | All Other Plastics Product Manufacturing (ADA Area, Hop Area Operator, Injection Molding Operator, Assembler) |
| | 325991 | Custom Compounding of Purchased Resins (Fabricator) |
| Rubber product manufacturing (converting); Solvents (for cleaning and degreasing) | 325212 | Synthetic Rubber Manufacturing (Insert Prep / Degreaser Operator, Compliance Officer) |

**Table_Apx B-1 Mapping of Scenarios to Industry Sectors with Methylene Chloride Personal Monitoring Air Samples Obtained from OSHA Inspections Conducted Between 2002 and 2016**

| Possible Release / Exposure Scenarios | NAICS | NAICS Description (Job Titles from OSHA) |
|---|---|---|
| Pharmaceutical product manufacturing; Processing aid, not otherwise listed; Laboratory use | 325412 | Pharmaceutical Preparation Manufacturing (Laboratory Technician) |
| Polyurethane foam blowing; Application of Adhesives | 326150 | Urethane and Other Foam Product (except Polystyrene) Manufacturing (Molder/Painter, Mold Machine Operator, Blue Zone, Adhesive Application) |
| Paint and Coating Application; Automotive care products (Functional fluids for air conditioners: refrigerant, treatment, leak sealer, Interior car care – spot remover, degreasers) | 811111 | General Automotive Repair (Paint, Production) |
| Automotive care products (Functional fluids for air conditioners: refrigerant, treatment, leak sealer, Interior car care – spot remover, degreasers); Aerosol degreasing/ cleaning by contractors | 811310 | Commercial and Industrial Machinery and Equipment (except Automotive and Electronic) Repair and Maintenance (Mechanic) |
| | 811121 | Automotive Body, Paint, and Interior Repair and Maintenance (Manager) |
| Laboratory use | 541380 | Testing Laboratories (Analyst, Lab Tech) |
| | 621511 | Medical Laboratories (Lab Tech) |
| Paint and Coating Application; Application of Adhesives | 339950 | Sign Manufacturing (Gluer, Floor Manager, Painter, Laminator, OSHA CSHO, Acrylic Production, Production, Industrial Hygienist, Sign Maker, Lettering) |
| Unknown / Other Uses | 327991 | Cut Stone and Stone Product Manufacturing (Carpenter, Postform) |
| | 321211 | Hardwood Veneer and Plywood Manufacturing (Lamination, Operator, CSHO) |
| | 321911 | Wood Window and Door Manufacturing (stripper) |
| | 321999 | All Other Miscellaneous Wood Product Manufacturing (Floater: stripper and refinisher, Fabricator) |
| | 337110 | Wood Kitchen Cabinet and Countertop Manufacturing (Glue Sprayer, CSHO, Cabinet Assembler, Spray Painter, Fabricator) |
| | 337212 | Custom Architectural Woodwork and Millwork Manufacturing (Shop worker) |
| | 423930 | Recyclable Material Merchant Wholesalers (Fingers) |
| | 339999 | All Other Miscellaneous Manufacturing (Glass decorator) |
| | 423810 | Construction and Mining (except Oil Well) Machinery and Equipment Merchant Wholesalers (Technician) |
| | 424610 | Plastics Materials and Basic Forms and Shapes Merchant Wholesalers (Fabricator) |
| | 424990 | Other Miscellaneous Nondurable Goods Merchant Wholesalers (Plant Worker) |
| | 443112 | Radio, Television, and Other Electronics Stores (2007 NAICS - 2012 is 443142 Electronic Stores) (Press Operator) |
| | 443141 | Household Appliance Stores (Metal Shop Worker) |
| | 322121 | Paper (except Newsprint) Mills (Operators, Mechanics) |
| | 485410 | School and Employee Bus Transportation (Service Worker) |
| | 532299 | All Other Consumer Goods Rental (Warehouse Help, Industrial Hygienist) |
| | 811490 | Other Personal and Household Goods Repair and Maintenance (Laborer) |

**Table_Apx B-1 Mapping of Scenarios to Industry Sectors with Methylene Chloride Personal Monitoring Air Samples Obtained from OSHA Inspections Conducted Between 2002 and 2016**

| Possible Release / Exposure Scenarios | NAICS | NAICS Description (Job Titles from OSHA) |
|---|---|---|
| N/A | 926150 | Regulation, Licensing, and Inspection of Miscellaneous Commercial Sectors (Compliance Officer, Industrial Hygienist, CSHO) |

**Table_Apx B-2 Mapping of Scenarios to Industry Sectors with Methylene Chloride Area Monitoring Air Samples Obtained from OSHA Inspections Conducted Between 2013 and 2016**

| Possible Release / Exposure Scenarios | NAICS | NAICS Description |
|---|---|---|
| Polyurethane foam blowing | 326150 | Urethane and Other Foam Product (except Polystyrene) Manufacturing (Blue Zone, Adhesive Application) |
| Paint and Coating Application; Application of Adhesives | 339950 | Sign Manufacturing (Production Area) |

### *NIOSH HHEs*

EPA found a total of 122 HHEs that contained methylene chloride on NIOSH's website. Limiting the search to reports done since 2000 (~16 years) resulted in three HHEs. The following subsections provide summaries of the facilities inspected, the findings of the inspection, and any recommendations for using the data.

#### *Federal Crime Lab, Unidentified Location (2016) (2012-0238-3257)*

The Health Hazard Evaluation Program received a request from the health and safety director at a Federal Bureau of Investigation (FBI) crime laboratory (lab) to evaluate workplace health hazards. Inspectors sampled employees in the Operational Projects Unit, which builds crime scene models to display in court hearings. Activities included woodcutting, spray painting, laser cutting of plastics, assembling plastics parts, and 3-dimensional printing. The inspectors used Dräger direct-reading colorimetric detector tubes to evaluate employee exposures to methylene chloride during the following tasks:

1. Manually transferring methylene chloride from a 1-quart container to a 30-mL squeeze bottle in the paint spray booth. This task took approximately 2 minutes and was done 1–2 times per month.
2. Hand assembling Plexiglas® parts without local exhaust ventilation. A small amount of methylene chloride was squeezed from a 30-mL container onto the parts. The employee then held the pieces together for a few seconds.

Employees voluntarily wore lab coats, Sperian® N95 filtering facepiece respirators, ear plugs or earmuffs, and nitrile gloves. No methylene chloride was detected during sampling activities (< 20 ppm).

EPA notes that these exposure data may be compared with alternative data that are available for the risk evaluation before use. The methodology and results for this study are limited, and/or may not be representative of typical occupational use.

***Woodworking Studio, Brooklyn College, Brooklyn, New York (2009) (HETA 2007-0167-3078)***

NIOSH received a confidential employee request for an HHE at Brooklyn College in Brooklyn, New York, to investigate health and safety concerns in the sculpture studios, including the ceramic, woodworking, and metalworking studios. In the woodworking studio, the inspectors observed methylene chloride being used as an adhesive for plexiglass bonding and being applied using a 4-ounce squeeze bottle. The inspectors performed PBZ air sampling for VOCs, but methylene chloride was not measurable at quantifiable levels (LOD unknown). The inspectors recommended that the college substitute a less toxic plastics adhesive for methylene chloride.

EPA notes that these exposure data be compared with alternative data that are available for the risk evaluation before use. The methodology and results for this study are limited, and/or may not be representative of typical occupational use.

***Human Performance International, Inc., Charlotte, North Carolina (2001) (HETA 2000-0110-2849)***

The Hazard Evaluation and Technical Assistance Branch (HETAB) of the National Institute for Occupational Safety and Health (NIOSH) collaborated with the Division of Applied Research and Technology (DART) within NIOSH to conduct a pilot research study evaluating occupational exposure to noise and potential ototoxic agents, such as solvents, metals, and asphyxiants, among a stock car racing team.

Methylene chloride was present in the lacquer thinner used to clean the paint guns. In between each coat of primer, sealer, or paint that is applied, the painter leaves the paint booth to clean the paint gun in a lacquer thinner bath that is located directly adjacent to the paint booth. After cleaning, the primer or paint is mixed and poured into the paint gun. Coveralls and an organic vapor cartridge half-face respirator are worn inside the paint booth. The respirator is removed when the painter exits the paint booth, and is not worn while the paint gun is cleaned, or while the paint is mixed. The painter reported that the respirator filters are changed every two months and the respirator is discarded when it gets dirty. It was not cleaned on a daily basis after use. A chemical solutions glove was occasionally worn while cleaning the paint gun in the lacquer thinner bath and while mixing paint.

Full-shift area samples were taken in the paint booth, outside the paint booth door, in the paint storage and mixing area, and the body shop area. Concentrations of methylene chloride were non-detectable (LOD = 0.045 ppm).

This use of methylene chloride as a paint thinner used to clean paint guns may be a previously unidentified activity that occurs in automotive refinishing shops. Paint stripping in automotive refinishing shops was previously assessed in EPA's 2014 risk assessment.

Table_Apx B-3 summarizes information from the NIOSH HHEs described above.

**Table_Apx B-3 Summary of NIOSH HHEs Since 2000**

| Exposure/Release Scenario | Facility Description | Number of Exposure Samples | Minimum of Exposure Values (ppm) | Maximum of Exposure Values (ppm) | Comments | Data Source |
|---|---|---|---|---|---|---|
| **Manual adhesive application** | Model Building Shop | Unknown | ND | ND | PBZ samples; LOD = 20 ppm | (NIOSH, 2016) |
| **Manual adhesive application** | Woodworking Studio | Unknown | ND | ND | PBZ samples; LOD unknown | (NIOSH, 2009) |
| **Paint and coating (use of paint thinner to clean paint guns may be a not-previously identified activity in auto refinish shops)** | Race Shop – Paint Booth, Paint Mixing, Body Shop | Unknown | ND | ND | Area samples; LOD = 0.045 ppm | (Gwin et al., 2001) |

## B.3 Sources Containing Potentially Relevant Data or Information

Some sources of information and data related to releases and worker exposure were found during the systematic review literature search. Sources of data or information identified in the Analysis Plan Sections 2.6.1.1 Environmental Releases and 2.6.1.5 Occupational Exposures are shown in the four tables below. The data sources identified are based on preliminary results to date of the full-text screening step of the systematic review process. Further screening and quality evaluation are on-going. These sources will be reviewed to determine the utility of the data and information in the Risk Evaluation.

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**Table_Apx B-7 Potentially Relevant Data Sources for Engineering Controls and Personal Protective Equipment**

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|---|---|
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| HSIA (2008). Chlorinated solvents - The key to surface cleaning performance. | https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3982144 |
| HESIS (2006). Methylene chloride: How to find out if you are working with methylene chloride: Fact sheet. Richmond, CA. | https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3982224 |
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| DHHS (1992). In- Depth Survey Report: The Control of Methylene Chloride in Furniture Stripping at The JM Murray Center, Inc. Atlanta, GA, CDC. | https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/3986433 |

# Appendix C SUPPORTING TABLE FOR INDUSTRIAL AND COMMERCIAL ACTIVITIES AND USES CONCEPTUAL MODEL

**Table_Apx C-1 Industrial and Commercial Activities and Uses Conceptual Model Supporting Table**
(Note that rows shaded in gray are not proposed for further analysis)

| Life Cycle Stage | Category | Subcategory | Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| Manufacturing | Domestic Manufacture | Domestic Manufacture | Manufacture of methylene chloride | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29 CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. Furthermore, vapor dermal exposures are expected to be much smaller than concurrent inhalation exposures for workers and ONU |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | No | Mist generation not expected |
| Manufacturing | Import | Import | Repackaging of Import Containers | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |

| Life Cycle Stage | Category | Subcategory | Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. Furthermore, vapor dermal exposures are expected to be much smaller than concurrent inhalation exposures for workers and ONU |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | No | Mist generation not expected |
| Processing | Processing as a reactant | Intermediate in industrial gas manufacturing (e.g. manufacture of fluorinated gases used as refrigerants); Intermediate for pesticide, fertilizer, and other agricultural chemical manufacturing; CBI function for petrochemical manufacturing; Intermediate for other chemicals | Industrial gas manufacturing; Agricultural chemical manufacturing; Petrochemical manufacturing; Chemical manufacturing | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. Furthermore, vapor dermal exposures are expected to be much smaller than concurrent inhalation exposures for workers and ONU |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | No | Mist generation not expected |
| Processing | Incorporated into formulation, mixture, or reaction product | Solvents[3]; Propellants and blowing agents; Paint additives and coating additives; Laboratory chemicals; Processing aid, | Formulation of:<br>• chemical mixtures;<br>• cleaning fluids;<br>• Paints and Coatings;<br>• laboratory chemicals; | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |

[3] Solvents (for cleaning or degreasing), Solvents (which become part of product formulation or mixture); Propellants and blowing agents for all other chemical product and preparation manufacturing; and Propellants and blowing agents for plastics product manufacturing; Paint additives and coating additives; Laboratory chemicals for all other chemical product and preparation manufacturing; Processing aid, not otherwise listed for petrochemical manufacturing; Adhesive and sealant chemicals in adhesive manufacturing; Unknown function for oil and gas drilling, extraction, and support

| Life Cycle Stage | Category | Subcategory | Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | not otherwise listed; Adhesive and sealant chemicals in adhesive manufacturing; Unknown function for oil and gas drilling, extraction, and support activities | • petrochemical products;<br>• adhesives;<br>• oil and gas drilling and extraction products;<br>Use of blowing agents in chemical product manufacturing and plastics product manufacturing; | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. Furthermore, vapor dermal exposures are expected to be much smaller than concurrent inhalation exposures for workers and ONU |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | No | Mist generation not expected |
| Processing | Repackaging | Solvents (which become part of product formulation or mixture) for all other chemical product and preparation manufacturing; Laboratory chemicals; CBI functions for all other chemical product and preparation manufacturing; | Repackaging | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. Furthermore, vapor dermal exposures are expected to be much smaller than concurrent inhalation exposures for workers and ONU |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | No | Mist generation not expected |
| Processing | Recycling | Recycling | Process solvent recycling | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |

| Life Cycle Stage | Category | Subcategory | Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. Furthermore, vapor dermal exposures are expected to be much smaller than concurrent inhalation exposures for workers and ONU |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | No | Mist generation not expected |
| Distribution in commerce | Distribution | Distribution | Distribution of bulk shipments of methylene chloride; Distribution of formulated products | Liquid Contact, Vapor | Dermal/ Inhalation | Workers, ONU | No | Activities related to distribution (e.g., loading and unloading) will be considered throughout the methylene chloride life cycle, rather than using a single distribution scenario. |
| Industrial, commercial and consumer uses | Solvents (for cleaning or degreasing) | Batch vapor degreaser (e.g., open-top, closed-loop)<br><br>In-line vapor degreaser (e.g., conveyorized, web cleaner) | Open top vapor degreasing (OTVD); OTVD with enclosures; Airtight closed-loop degreasing system; Airless vacuum drying degreasing system; Airless vacuum-to-vacuum degreasing system<br><br>Conveyorized vapor degreasing; Cross-rod and ferris wheel vapor degreasing; Web vapor degreasing | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. Furthermore, vapor dermal exposures are expected to be much smaller than concurrent inhalation exposures for workers and ONU |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | No | Mist generation not expected |
| Industrial, commercial and consumer uses | Solvents (for cleaning or degreasing) | Cold cleaner; Aerosol spray degreaser/ cleaner | Spray use in cold cleaning - maintenance (manual spray; spray sink; dip tank); Aerosol degreasing/ cleaning by contractors | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |

| Life Cycle Stage | Category | Subcategory | Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. Furthermore, vapor dermal exposures are expected to be much smaller than concurrent inhalation exposures for workers and ONU |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | Yes | EPA will further analyze to determine whether mist generation is applicable. |
| Industrial, commercial and consumer uses | Adhesives and sealants | Single component glues and adhesives and sealants and caulks | Manual non-spray (paste/roller/brush) application | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. Furthermore, vapor dermal exposures are expected to be much smaller than concurrent inhalation exposures for workers and ONU |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | No | Mist generation not expected |
| Industrial, commercial and consumer uses | Adhesives and sealants | Single component glues and adhesives and sealants and caulks | Manual spray application | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. Furthermore, vapor dermal exposures are expected to be much smaller than concurrent inhalation exposures for workers and ONU |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | Yes | Public comments indicate aerosol spray application occurs. |

| Life Cycle Stage | Category | Subcategory | Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| Industrial, commercial and consumer uses | Paints and coatings including paint and coating removers for furniture stripping | Paints and coatings removers for furniture stripping | Paint and coating remover application and removal | Liquid Contact Vapor Mist | Dermal Inhalation | Workers ONU | No | EPA intends to finalize the methylene chloride rulemaking addressing paint stripping uses of methylene chloride, scenarios already assessed in the 2014 risk assessment will not be re-evaluated and will rely on the in the 2014 risk evaluation (U.S. EPA, 2014b) (https://www.epa.gov/newsreleases/epa-announces-action-methylene-chloride) |
| Industrial, commercial and consumer uses | Paints and coatings | Paints and coatings use | Manual spray application | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | Yes | EPA will further analyze to determine whether mist generation is applicable. |
| Industrial, commercial and consumer uses | Paints and coatings | Paints and coatings use | Manual non-spray (paste/roller/brush) application | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |

| Life Cycle Stage | Category | Subcategory | Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. Furthermore, vapor dermal exposures are expected to be much smaller than concurrent inhalation exposures for workers and ONU |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | No | Mist generation not expected |
| Industrial, commercial and consumer uses | Adhesives and sealants including adhesives and sealants removers | Adhesive/caulk removers | Adhesive/caulk removal by contractors | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. Furthermore, vapor dermal exposures are expected to be much smaller than concurrent inhalation exposures for workers and ONU |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | Yes | EPA will further analyze to determine whether mist generation is applicable. |
| Industrial, commercial and consumer uses | Metal products not covered elsewhere | Degreasers – aerosol and non-aerosol degreasers and cleaners e.g., coil cleaners | Spray use in cold cleaning - maintenance (manual spray; spray sink) | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. Furthermore, vapor dermal exposures are expected to be much smaller than concurrent inhalation exposures for workers and ONU |

| Life Cycle Stage | Category | Subcategory | Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | Mist | Dermal/Inhalation | Workers, ONU | Yes | EPA will further analyze to determine whether mist generation is applicable. |
| Industrial, commercial and consumer uses | Metal products not covered elsewhere | Degreasers – aerosol and non-aerosol degreasers and cleaners e.g., coil cleaners | Dip tank use in cold cleaning - manufacturing (dip tank) | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. Furthermore, vapor dermal exposures are expected to be much smaller than concurrent inhalation exposures for workers and ONU |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | No | Mist generation not expected |
| Industrial, commercial and consumer uses | Fabric, textile and leather products not covered elsewhere | Textile finishing and impregnating/ surface treatment products e.g. water repellant | Fabric finishing | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. Furthermore, vapor dermal exposures are expected to be much smaller than concurrent inhalation exposures for workers and ONU |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | Yes | EPA will further analyze to determine whether mist generation is applicable. |
| Industrial, commercial and consumer uses | Automotive care products | Functional fluids for air conditioners: refrigerant, | Charging air conditioners during automotive original equipment | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |

| Life Cycle Stage | Category | Subcategory | Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | treatment, leak sealer; Interior car care – spot remover; Degreasers: gasket remover, transmission cleaners, carburetor cleaner, brake quieter/cleaner; Degreasers: gasket remover, transmission cleaners, carburetor cleaner, brake quieter/cleaner | manufacture; Servicing automotive air conditioners (refrigerant, leak sealer); Commercial interior car care; Commercial automotive servicing; Commercial brake servicing | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. Furthermore, vapor dermal exposures are expected to be much smaller than concurrent inhalation exposures for workers and ONU |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | Yes | Automotive Care Products are generally used in aerosol form. |
| Industrial, commercial and consumer uses | Apparel and footwear care products | Post-market waxes and polishes applied to footwear e.g. shoe polish | Commercial shoe care | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | Yes | EPA will further analyze to determine whether mist generation is applicable. |
| Industrial, commercial and consumer uses | Laundry and dishwashing products | Spot remover for apparel and textiles | Spot cleaning at commercial dry cleaners | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |

| Life Cycle Stage | Category | Subcategory | Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. Furthermore, vapor dermal exposures are expected to be much smaller than concurrent inhalation exposures for workers and ONU |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | Yes | EPA will further analyze to determine whether mist generation is applicable. |
| Industrial, commercial and consumer uses | Lubricants and greases | Liquid and spray lubricants and greases; Degreasers – aerosol and non-aerosol degreasers and cleaners | | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | Yes | EPA will further analyze to determine whether mist generation is applicable. |
| Industrial, commercial and consumer uses | Building/ construction materials not covered elsewhere | Cold pipe insulation | | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. Furthermore, vapor dermal exposures are expected to be much smaller than concurrent inhalation exposures for workers and ONU |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | Yes | EPA will further analyze to determine whether mist generation is applicable. |

| Life Cycle Stage | Category | Subcategory | Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| Industrial, commercial and consumer uses | Solvents (which become part of product formulation or mixture) | All other chemical product and preparation manufacturing | Unspecified chemical product manufacturing | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. Furthermore, vapor dermal exposures are expected to be much smaller than concurrent inhalation exposures for workers and ONU |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | No | Mist generation not expected |
| Industrial, commercial and consumer uses | Processing aid not otherwise listed | In multiple manufacturing sectors | | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. Furthermore, vapor dermal exposures are expected to be much smaller than concurrent inhalation exposures for workers and ONU |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | No | Mist generation not expected |
| Industrial, commercial and consumer uses | Propellants and blowing agents | Flexible polyurethane foam manufacturing | Polyurethane foam blowing | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |

| Life Cycle Stage | Category | Subcategory | Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. Furthermore, vapor dermal exposures are expected to be much smaller than concurrent inhalation exposures for workers and ONU |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | No | Mist generation not expected |
| Industrial, commercial and consumer uses | Other Uses | Other non-aerosol uses, e.g. Laboratory chemicals - all other chemical product and preparation manufacturing; Electrical equipment, appliance, and component manufacturing; Plastic and rubber products; Oil and gas drilling, extraction, and support activities; Functional fluids (closed systems) in pharmaceutical and medicine manufacturing; Carbon remover, lithographic printing cleaner, wood floor cleaner, brush cleaner | Laboratory use; Electrical equipment, appliance, and component manufacturing; Plastic product manufacturing (compounding and converting); Use in oil and gas drilling, extraction, and support activities; Pharmaceutical product manufacturing; Use as carbon remover, lithographic printing cleaner, wood floor cleaner, brush cleaner | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. Furthermore, vapor dermal exposures are expected to be much smaller than concurrent inhalation exposures for workers and ONU |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | No | Mist generation not expected |

| Life Cycle Stage | Category | Subcategory | Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| Industrial, commercial and consumer uses | Other Uses | Other aerosol uses, e.g. Anti-adhesive agent - anti-spatter welding aerosol | Use as anti-adhesive agent - anti-spatter welding aerosol | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. Furthermore, vapor dermal exposures are expected to be much smaller than concurrent inhalation exposures for workers and ONU |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | Yes | EPA will further analyze to determine whether mist generation is applicable. |
| Disposal | Waste Handling, Treatment and Disposal | Disposal of methylene chloride wastes | Worker handling of wastes | Liquid Contact | Dermal | Workers | Yes | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected however occluded exposures may significantly contribute to total exposure. Occluded exposures will be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | Workers, ONU | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | Vapor | Dermal | Workers, ONU | No | Based on OSHA standard (29CFR 1910.1052) workers are required to be protected and exposure to vapors are not expected to be occluded. Furthermore, vapor dermal exposures are expected to be much smaller than concurrent inhalation exposures for workers and ONU |
| | | | | Mist | Dermal/Inhalation | Workers, ONU | No | Mist generation not expected |

# Appendix D SUPPORTING TABLE FOR CONSUMER ACTIVITIES AND USES CONCEPTUAL MODEL

**Table_Apx D-1 Consumer Activities and Uses Conceptual Model Supporting Table**
(Note that rows shaded in gray are not proposed for further analysis)

| Category | Subcategory | Form | Exposure Pathway / Media | Exposure Scenario | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| Solvents for Cleaning and Degreasing | Brush Cleaner | Liquid | Liquid Contact | Dermal contact with liquid product on the skin | Dermal | Consumer | Yes | Based on conditions of use, consumers may have direct dermal contact with methylene chloride. Occluded exposures may be higher. |
| | | | Vapor/Mist | Evaporation from the surface | Inhalation | Consumer | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystander | | |
| Solvents for Cleaning and Degreasing | Carbon Remover | Aerosol | Liquid Contact | Dermal contact with liquid product on the skin | Dermal | Consumer | Yes | Based on conditions of use, consumers may have direct dermal contact with methylene chloride. Occluded exposures may be higher. |
| | | | Vapor/Mist | Spray application (stationary) | Inhalation | Consumer | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, |
| | | | | | | Bystander | | |

| Category | Subcategory | Form | Exposure Pathway / Media | Exposure Scenario | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | | inhalation pathway will be further analyzed. |
| | | | | | Oral | Consumer | No | Based on physical chemical properties, mists of methylene chloride will likely be rapidly absorbed in the respiratory tract or evaporate |
| | | | | | | Bystander | | |
| | | | | Evaporation from the surface | Inhalation | Consumer | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystander | | |
| Solvents for Cleaning and Degreasing | Coil Cleaner | Aerosol | Liquid Contact | Dermal contact with liquid product on skin | Dermal | Consumer | Yes | Based on conditions of use, consumers may have direct dermal contact with methylene chloride. Occluded exposures may be higher. |
| | | | Vapor/Mist | Spray application (stationary) | Inhalation | Consumer | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystander | | |

| Category | Subcategory | Form | Exposure Pathway / Media | Exposure Scenario | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | | Oral | Consumer | No | Based on physical chemical properties, mists of methylene chloride will likely be rapidly absorbed in the respiratory tract or evaporate |
| | | | | | | Bystander | | |
| | | | | Evaporation from the surface | Inhalation | Consumers | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystanders | | |
| Solvents for Cleaning and Degreasing | Degreaser | Liquid | Liquid Contact | Dermal contact with liquid product on the skin | Dermal | Consumer | Yes | Based on conditions of use, consumers may have direct dermal contact with methylene chloride. Occluded exposures may be higher. |
| | | | Vapor/Mist | Evaporation from the surface | Inhalation | Consumer | | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystander | | |
| | | Aerosol | Liquid Contact | Dermal contact with liquid product on skin | Dermal | Consumer | Yes | Based on conditions of use, consumers may have direct |

| Category | Subcategory | Form | Exposure Pathway / Media | Exposure Scenario | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | | dermal contact with methylene chloride. Occluded exposures may be higher. |
| | | | Vapor/Mist | Spray application (stationary) | Inhalation | Consumer | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystander | | |
| | | | | | Oral | Consumer | No | Based on physical chemical properties, mists of methylene chloride will likely be rapidly absorbed in the respiratory tract or evaporate |
| | | | | | | Bystander | | |
| | | | | Evaporation from the surface | Inhalation | Consumers | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystanders | | |
| Adhesives and Sealants | Single component glues and adhesives and sealants and caulks | Liquid | Liquid Contact | Dermal contact with liquid product on the skin | Dermal | Consumer | Yes | Based on conditions of use, consumers may have direct dermal contact with methylene chloride. Occluded |

| Category | Subcategory | Form | Exposure Pathway / Media | Exposure Scenario | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | | exposures may be higher. |
| | | | Vapor/Mist | Evaporation from the surface | Inhalation | Consumer | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystander | | |
| Adhesives and Sealants | Sealant | Aerosol | Liquid Contact | Dermal contact with liquid product on skin | Dermal | Consumer | Yes | Based on conditions of use, consumers may have direct dermal contact with methylene chloride. Occluded exposures may be higher. |
| | | | Vapor/Mist | Spray application (stationary) | Inhalation | Consumer | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystander | | |
| | | | | | Oral | Consumer | No | Based on physical chemical properties, mists of methylene chloride will likely be rapidly absorbed in the respiratory tract or evaporate |
| | | | | | | Bystander | | |

| Category | Subcategory | Form | Exposure Pathway / Media | Exposure Scenario | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | Evaporation from the surface | Inhalation | Consumers | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystanders | | |
| Paints and Coatings including removers | Adhesive Remover | Liquid | Liquid Contact | Dermal contact with liquid product on the skin | Dermal | Consumer | Yes | Based on conditions of use, consumers may have direct dermal contact with methylene chloride. Occluded exposures may be higher. |
| | | | Vapor/Mist | Evaporation from the surface | Inhalation | Consumer | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystander | | |
| Metal Products | | | | | | | No | None of the uses are for consumers |
| Fabric, Textile, and Leather Products | Textile Treatment | Liquid primarily | | | | | No | None of the uses are for consumers |
| Automotive care products | Function fluids for air conditioners: refrigerant, | Aerosol | Liquid Contact | Dermal contact with liquid product on skin | Dermal | Consumer | Yes | Based on conditions of use, consumers may have direct dermal contact with methylene |

| Category | Subcategory | Form | Exposure Pathway / Media | Exposure Scenario | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | treatment, leak sealer | | | | | | | chloride. Occluded exposures may be higher. |
| | | | Vapor/Mist | Spray application (stationary) | Inhalation | Consumer | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystander | | |
| | | | | | Oral | Consumer | No | Based on physical chemical properties, mists of methylene chloride will likely be rapidly absorbed in the respiratory tract or evaporate |
| | | | | | | Bystander | | |
| | | | | Inhalation of gas as comes through A/C | Inhalation | Consumer | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystander | | |
| Automotive care products | Interior car care, spot remover | Liquid | Liquid Contact | Dermal contact with liquid product on skin | Dermal | Consumers | Yes | Based on conditions of use, consumers may have direct dermal contact with methylene chloride. Occluded exposures may be higher. |
| | | | | | | Bystanders | | |

| Category | Subcategory | Form | Exposure Pathway / Media | Exposure Scenario | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | Vapor/Mist | Evaporation from the surface | Inhalation | Consumers | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystanders | | |
| Automotive Care Products | Auto Products - Engine Cleaner/ Degreaser | Aerosol | Liquid Contact | Dermal contact with liquid product on skin | Dermal | Consumer | Yes | Based on conditions of use, consumers may have direct dermal contact with methylene chloride. Occluded exposures may be higher. |
| | | | Vapor/Mist | Spray application (stationary) | Inhalation | Consumer | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystander | | |
| | | | | | Oral | Consumer | No | Based on physical chemical properties, mists of methylene chloride will likely be rapidly absorbed in the respiratory tract or evaporate |
| | | | | | | Bystander | | |
| | | | | Evaporation from the surface | Inhalation | Consumers | Yes | Due to high volatility (VP = 435 mmHg) at room |
| | | | | | | Bystanders | Yes | |

| Category | Subcategory | Form | Exposure Pathway / Media | Exposure Scenario | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | | temperature, inhalation pathway will be further analyzed. |
| Automotive Care Products | Auto Products - Brake Cleaner | Aerosol | Liquid Contact | Dermal contact with liquid product on skin | Dermal | Consumer | Yes | Based on conditions of use, consumers may have direct dermal contact with methylene chloride. Occluded exposures may be higher. |
| | | | Vapor/Mist | Spray application (stationary) | Inhalation | Consumer | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystander | | |
| | | | | | Oral | Consumer | No | Based on physical chemical properties, mists of methylene chloride will likely be rapidly absorbed in the respiratory tract or evaporate |
| | | | | | | Bystander | | |
| | | | | Evaporation from the surface | Inhalation | Consumers | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystanders | | |

| Category | Subcategory | Form | Exposure Pathway / Media | Exposure Scenario | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| Automotive Care Products | Auto Products - Carburetor Cleaner | Aerosol | Liquid Contact | Dermal contact with liquid product on skin | Dermal | Consumer | Yes | Based on conditions of use, consumers may have direct dermal contact with methylene chloride. Occluded exposures may be higher. |
| | | | Vapor/Mist | Spray application (stationary) | Inhalation | Consumer | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystander | | |
| | | | | | Oral | Consumer | No | Based on physical chemical properties, mists of methylene chloride will likely be rapidly absorbed in the respiratory tract or evaporate |
| | | | | | | Bystander | | |
| | | | | Evaporation from the surface | Inhalation | Consumer | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystander | | |
| Automotive Care Products | Auto Products - Fuel system cleaner | Unclear on product form | Liquid Contact | Dermal contact with liquid product on skin | Dermal | Consumer | Yes | Based on conditions of use, consumers may have direct |

| Category | Subcategory | Form | Exposure Pathway / Media | Exposure Scenario | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | | dermal contact with methylene chloride. Occluded exposures may be higher. |
| | | | Vapor/Mist | Spray application (stationary) | Inhalation | Consumer | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystander | | |
| | | | | | Oral | Consumer | No | Based on physical chemical properties, mists of methylene chloride will likely be rapidly absorbed in the respiratory tract or evaporate |
| | | | | | | Bystander | | |
| | | | | Evaporation from the surface | Inhalation | Consumer | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystander | | |
| Automotive Care Products | Auto Products - Gasket Remover | Aerosol | Liquid Contact | Dermal contact with liquid product on skin | Dermal | Consumer | Yes | Based on conditions of use, consumers may have direct dermal contact with methylene chloride. Occluded |

| Category | Subcategory | Form | Exposure Pathway / Media | Exposure Scenario | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | | exposures may be higher. |
| | | | Vapor/Mist | Spray application (stationary) | Inhalation | Consumer | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystander | | |
| | | | | | Oral | Consumer | No | Based on physical chemical properties, mists of methylene chloride will likely be rapidly absorbed in the respiratory tract or evaporate |
| | | | | | | Bystander | | |
| | | | | Evaporation from the surface | Inhalation | Consumer | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystander | | |
| Apparel and Footwear Care Products | Textile Treatment | | | | | | No | None of the listed products are consumer products |
| Laundry and Dishwashing Products | | | | | | | No | None of the listed products are consumer products |
| Lubricants and Greases | Lubricant | Aerosol or Liquid | | | | | No | None of the listed products are |

| Category | Subcategory | Form | Exposure Pathway / Media | Exposure Scenario | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | | consumer products |
| Other Uses | Cold Pipe Insulation Spray | Aerosol | Liquid Contact | Dermal contact with liquid product on skin | Dermal | Consumer | Yes | Based on conditions of use, consumers may have direct dermal contact with methylene chloride. Occluded exposures may be higher. |
| | | | Vapor/Mist | Spray application (stationary) | Inhalation | Consumer | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystander | | |
| | | | | | Oral | Consumer | No | Based on physical chemical properties, mists of methylene chloride will likely be rapidly absorbed in the respiratory tract or evaporate |
| | | | | | | Bystander | | |
| | | | | Evaporation from the surface | Inhalation | Consumer | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystander | | |

| Category | Subcategory | Form | Exposure Pathway / Media | Exposure Scenario | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| Other Uses | Weld Spatter Protectant | Aerosol | Liquid Contact | Dermal contact with liquid product on skin | Dermal | Consumer | Yes | Based on conditions of use, consumers may have direct dermal contact with methylene chloride. Occluded exposures may be higher. |
| | | | Vapor/Mist | Spray application (stationary) | Inhalation | Consumer | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystander | | |
| | | | | | Oral | Consumer | No | Based on physical chemical properties, mists of methylene chloride will likely be rapidly absorbed in the respiratory tract or evaporate |
| | | | | | | Bystander | | |
| | | | | Evaporation from the surface | Inhalation | Consumer | Yes | Due to high volatility (VP = 435 mmHg) at room temperature, inhalation pathway will be further analyzed. |
| | | | | | | Bystander | | |

| Category | Subcategory | Form | Exposure Pathway / Media | Exposure Scenario | Exposure Routes | Receptor / Population | Proposed for Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|
| Solvents for Cleaning and Degreasing | Brush Cleaner | Liquid | Liquid Contact | Dermal contact with liquid product on the skin | Dermal | Consumer | Yes | Based on conditions of use, consumers may have direct dermal contact with methylene chloride. Occluded exposures may be higher. |

# Appendix E SUPPORTING TABLE FOR ENVIRONMENTAL RELEASES AND WASTES CONCEPTUAL MODEL

**Table_Apx E-1 Environmental Releases and Wastes Conceptual Model Supporting Table**

| Life Cycle Stage | Use Category | Category | Release | Exposure Pathway | Receptor | Further Analysis? | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|
| Disposal | Disposal | Wastewater or Liquid Wastes | Industrial WWT operations | Water, Sediment | Aquatic Species | Yes | Aquatic species may be exposed to MC in water and sediment pore water at hazardous concentrations. |
| | | | | | Terrestrial Species | No | Terrestrial species exposures to MC in water are orders of magnitude below hazardous concentrations. |
| | | | Industrial wastewater pre treatment operations, then transfer to POTW | Water, Sediment | Aquatic Species | Yes | EPI Suite STP model estimates 43% of MC in wastewater will not be removed during treatment and will be present in the WWTP effluent. The Henry's Law constant of MC (3.25E-3 atm-$m^3$/mol) indicates that MC will volatilize from water. Aquatic species may be exposed to MC in water and sediment pore water at hazardous concentrations. |
| | | | | | Terrestrial Species | No | Terrestrial species exposures to MC in water are orders of magnitude below hazardous concentrations. |
| | | | Publicly owned treatment works (POTW) | Water, Sediment | Aquatic Species | Yes | EPI Suite STP model estimates 43% of MC in wastewater will not be removed during treatment and will be present in the WWTP effluent. Aquatic species may be exposed to MC in water and sediment pore water at hazardous concentrations. |

| Life Cycle Stage | Use Category | Category | Release | Exposure Pathway | Receptor | Further Analysis? | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|
| | | | | | Terrestrial Species | No | Terrestrial species exposures to MC in water are orders of magnitude below hazardous concentrations. |
| | | | Biosolids and land disposal to soil | Migration from biosolids via soil deposition | Terrestrial Species | No | Terrestrial species exposures to MC in water are orders of magnitude below hazardous concentrations. |

# Appendix F INCLUSION AND EXCLUSION CRITERIA FOR FULL TEXT SCREENING

Appendix F contains the eligibility criteria for various data streams informing the TSCA risk evaluation: environmental fate; engineering and occupational exposure; exposure to consumers; and human health hazard. The criteria are applied to the *on-topic* references that were identified following title and abstract screening of the comprehensive search results published on June 22, 2017.

Systematic reviews typically describe the study eligibility criteria in the form of PECO statements or a modified framework. PECO stands for Population, Exposure, Comparator and Outcome and the approach is used to formulate explicit and detailed criteria about those characteristics in the publication that should be present in order to be eligible for inclusion in the review. EPA/OPPT adopted the PECO approach to guide the inclusion/exclusion decisions during full text screening.

Inclusion and exclusion criteria were also used during the title and abstract screening, and documentation about the criteria can be found in the *Strategy for Conducting Literature Searches* document published in June 2017 along with each of the TSCA Scope documents. The list of *on-topic* references resulting from the title and abstract screening is undergoing full text screening using the criteria in the PECO statements. The overall objective of the screening process is to select the most relevant evidence for the TSCA risk evaluation. As a general rule, EPA is excluding non-English data/information sources and will translate on a case by case basis.

The inclusion and exclusion criteria for ecotoxicological data have been documented in the ECOTOX SOPs. The criteria can be found at https://cfpub.epa.gov/ecotox/help.cfm?helptabs=tab4) and in the *Strategy for Conducting Literature Searches* document published along with each of the TSCA Scope documents.

## F.1 Inclusion Criteria for Data Sources Reporting Environmental Fate Data

EPA/OPPT developed a generic PESO statement to guide the full text screening of environmental fate data sources. PESO stands for Pathways and Processes, Exposure, Setting or Scenario, and Outcomes. Subsequent versions of the PESO statement may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the inclusion criteria in the PESO statement are eligible for inclusion, considered for evaluation, and possibly included in the environmental fate assessment. On the other hand, data sources are excluded if they do not meet the criteria in the PESO statement.

Assessors seek information on various chemical-specific fate endpoints and associated fate processes, environmental media and exposure pathways as part of the process of developing the environmental fate assessment (Table_Apx F-2). Those that will be the focus of the environmental fate assessment for methylene chloride have been indicated in Table_Apx F-2. The PESO statement and information in Table_Apx F-1 will be used when screening the fate data sources to ensure complete coverage of the processes, pathways and data relevant to the fate of the chemical substance of interest.

| Table_Apx F-1. Inclusion Criteria for Data Sources Reporting Environmental Fate Data | |
|---|---|
| **PESO Element** | **Evidence** |
| **P**athways and **P**rocesses | • Environmental fate, transport, partitioning and degradation behavior across environmental media to inform exposure pathways of the chemical substance of interest<br>• Media of interest may include:<br>– Surface water<br>Please refer to the conceptual models for more information about the exposure pathways included in the TSCA risk evaluation. |
| **E**xposure | • Environmental exposure of ecological receptors (i.e., aquatic organisms) to the chemical substance of interest and/or its degradation products and metabolites<br><br>Please refer to the conceptual models for more information about the ecological and human receptors included in the TSCA risk evaluation. |
| **S**etting or **S**cenario | Any setting or scenario resulting in releases of the chemical substance of interest into the natural or built environment (e.g., wastewater treatment facilities) that would expose ecological receptors (i.e., aquatic organisms) |
| **O**utcomes | • Fate properties which allow assessments of exposure pathways:<br>o Abiotic and biotic degradation rates, mechanisms, pathways, and products<br>o Bioaccumulation magnitude and metabolism rates<br>o Partitioning within and between environmental media (see Pathways and Processes) |

| Table_Apx F-2. Fate Endpoints and Associated Processes, Media and Exposure Pathways Considered in the Development of the Environmental Fate Assessment | | |
|---|---|---|
| **Fate Data Endpoint** | **Associated Process(es)** | **Associated Media/Exposure Pathways** |
| | | **Surface water, Sediment** |
| **Abiotic reduction rates or half-lives** | Abiotic reduction, Abiotic dehalogenation | X |
| **Aerobic biodegradation rates or half-lives** | Aerobic biodegradation | X |
| **Anaerobic biodegradation rates or half-lives** | Anaerobic biodegradation | X |
| **Aqueous photolysis (direct and indirect) rates or half-lives** | Aqueous photolysis (direct and indirect) | X |
| **Bioconcentration factor (BCF), Bioaccumulation factor (BAF)** | Bioconcentration, Bioaccumulation | X |
| **Hydrolysis rates or half-lives** | Hydrolysis | X |
| **$K_{AW}$, Henry's Law constant, and other volatilization information** | Volatilization | X |
| **$K_{OC}$ and other sorption information** | Sorption, Mobility | X |
| **Abiotic transformation products** | Hydrolysis, Photolysis | X |
| **Aerobic biotransformation products** | Aerobic biodegradation | X |
| **Anaerobic biotransformation products** | Anaerobic biodegradation | X |
| **Biomagnification and related information** | Trophic magnification | X |
| **Desorption information** | Sorption, Mobility | X |
| **Wastewater treatment removal information** | Wastewater treatment | X |

## F.2 Inclusion Criteria for Data Sources Reporting Release and Occupational Exposure Data

EPA/OPPT developed a generic RESO statement to guide the full text screening of release and occupational exposure literature (Table_Apx F-3). RESO stands for Receptors, Exposure, Setting or Scenario, and Outcomes. Subsequent versions of the RESO statement may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the inclusion criteria specified in the RESO statement will be eligible for inclusion, considered for evaluation, and possibly included in the environmental release and occupational exposure assessments, while those that do not meet these criteria will be excluded.

The RESO statement should be used along with the engineering and occupational exposure data needs table (Table_Apx F-4) when screening the literature.

**Table_Apx F-3. Inclusion Criteria for Data Sources Reporting Engineering and Occupational Exposure Data**

| RESO Element | Evidence |
|---|---|
| **Receptors** | • **Humans:**<br>Workers, including occupational non-users<br><br>• **Environment:**<br>Aquatic ecological receptors (relevant release estimates input to Exposure)<br><br>Please refer to the conceptual models for more information about the ecological and human receptors included in the TSCA risk evaluation. |
| **Exposure** | • Worker exposure to and relevant occupational environmental releases of the chemical substance of interest<br>o Dermal and inhalation exposure routes (as indicated in the conceptual model)<br>o Surface water (as indicated in the conceptual model)<br><br>Please refer to the conceptual models for more information about the routes and media/pathways included in the TSCA risk evaluation. |
| **Setting or Scenario** | • Any occupational setting or scenario resulting in worker exposure and relevant environmental releases (includes all manufacturing, processing, use, disposal indicated in Table_Apx F-4 below. |
| **Outcomes** | • Quantitative estimates* of worker exposures and of relevant environmental releases from occupational settings<br>• General information and data related and relevant to the occupational estimates* |

* Metrics (e.g., mg/kg/day or mg/m$^3$ for worker exposures, kg/site/day for releases) are determined by toxicologists for worker exposures and by exposure assessors for releases; also, the Engineering, Release and Occupational Exposure Data Needs (Table_Apx F-4) provides a list of related and relevant general information.

| Table_Apx F-4. Engineering, Environmental Release and Occupational Data Necessary to Develop the Environmental Release and Occupational Exposure Assessments | |
|---|---|
| **Objective Determined during Scoping** | **Type of Data** |
| General Engineering Assessment (may apply for either or both Occupational Exposures and / or Environmental Releases) | 1. Description of the life cycle of the chemical(s) of interest, from manufacture to end-of-life (e.g., each manufacturing, processing, or use step), and material flow between the industrial and commercial life cycle stages. {Tags: Life cycle description, Life cycle diagram}[a]<br>2. The total annual U.S. volume (lb/yr or kg/yr) of the chemical(s) of interest manufactured, imported, processed, and used; and the share of total annual manufacturing and import volume that is processed or used in each life cycle step. {Tags: Production volume (PV), Import volume, Use volume, Percent PV} [a]<br>3. Description of processes, equipment, unit operations, and material flows and frequencies (lb/site-day or kg/site-day and days/yr; lb/site-batch and batches/yr) of the chemical(s) of interest during each industrial/ commercial life cycle step. Note: if available, include weight fractions of the chemicals (s) of interest and material flows of all associated primary chemicals (especially water). {Tags: Process description, Process material flow rate, Annual operating days, Annual batches, Weight fractions (for each of above, manufacture, import, processing, use)} [a]<br>4. Basic chemical properties relevant for assessing exposures and releases, e.g., molecular weight, normal boiling point, melting point, physical forms, and room temperature vapor pressure. {Tags: Molecular weight, Boiling point, Melting point, Physical form, Vapor pressure, Water solubility} [a]<br>5. Number of sites that manufacture, process, or use the chemical(s) of interest for each industrial/ commercial life cycle step and site locations. {Tags: Numbers of sites (manufacture, import, processing, use), Site locations} [a] |
| Occupational Exposures | 6. Description of worker activities with exposure potential during the manufacture, processing, or use of the chemical(s) of interest in each industrial/commercial life cycle stage. {Tags: Worker activities (manufacture, import, processing, use)} [a]<br>7. Potential routes of exposure (e.g., inhalation, dermal). {Tags: Routes of exposure (manufacture, import, processing, use)} [a]<br>8. Physical form of the chemical(s) of interest for each exposure route (e.g., liquid, vapor, mist) and activity. {Tags: Physical form during worker activities (manufacture, import, processing, use)} [a]<br>9. Breathing zone (personal sample) measurements of occupational exposures to the chemical(s) of interest, measured as time-weighted averages (TWAs), short-term exposures, or peak exposures in each occupational life cycle stage (or in a workplace scenario similar to an occupational life cycle stage). {Tags: Personal Breathing Zone (PBZ) measurements (manufacture, import, processing, use)} [a]<br>10. Area or stationary measurements of airborne concentrations of the chemical(s) of interest in each occupational setting and life cycle stage (or in a workplace scenario similar to the life cycle stage of interest). {Tags: Area measurements (manufacture, import, processing, use)} [a]<br>11. For solids, bulk and dust particle size characterization data. {Tags: Particle Size Distribution (PSD) measurements (manufacture, import, processing, use)} [a]<br>12. Dermal exposure data. {Tags: Dermal measurements (manufacture, import, processing, use)}<br>13. Data needs associated with mathematical modeling (will be determined on a case-by-case basis). {Tags: Worker exposure modeling data needs (manufacture, import, processing, use)} [a]<br>14. Exposure duration (hr/day). {Tags: Worker exposure durations (manufacture, import, processing, use)} [a]<br>15. Exposure frequency (days/yr). {Tags: Worker exposure frequencies (manufacture, import, processing, use)} [a]<br>16. Number of workers who potentially handle or have exposure to the chemical(s) of interest in each occupational life cycle stage. {Tags: Numbers of workers exposed (manufacture, import, processing, use)} [a]<br>17. Personal protective equipment (PPE) types employed by the industries within scope. {Tags: Worker PPE (manufacture, import, processing, use)} [a]<br>18. Engineering controls employed to reduce occupational exposures in each occupational life cycle stage (or in a workplace scenario similar to the life cycle stage of interest), and associated data or estimates of exposure reductions. {Tags: Engineering controls (manufacture, import, processing, use), Engineering control effectiveness data} [a] |

| Table_Apx F-4. Engineering, Environmental Release and Occupational Data Necessary to Develop the Environmental Release and Occupational Exposure Assessments | |
|---|---|
| **Objective Determined during Scoping** | **Type of Data** |
| Environmental Releases (to relevant environmental media) | 19. Description of sources of potential environmental releases, including cleaning of residues from process equipment and transport containers, involved during the manufacture, processing, or use of the chemical(s) of interest in each life cycle stage. {Tags: Release sources (manufacture, import, processing, use)} [a]<br>20. Estimated mass (lb or kg) of the chemical(s) of interest released from industrial and commercial sites to each environmental medium (water) and treatment and disposal methods (POTW), including releases per site and aggregated over all sites (annual release rates, daily release rates) {Tags: Release rates (manufacture, import, processing, use)} [a]<br>21. Release or emission factors. {Tags: Emission factors (manufacture, import, processing, use)} [a]<br>22. Number of release days per year. {Tags: Release frequencies (manufacture, import, processing, use)} [a]<br>23. Data needs associated with mathematical modeling (will be determined on a case-by-case basis). {Tags: Release modeling data needs (manufacture, import, processing, use)} [a]<br>24. Waste treatment methods and pollution control devices employed by the industries within scope and associated data on release/emission reductions. {Tags: Treatment/ emission controls (manufacture, import, processing, use), Treatment/ emission controls removal/ effectiveness data} [a] |
| **Note:**<br>[a] These are the tags included in the full text screening form. The screener makes a selection from these specific tags, which describe more specific types of data or information. | |

## F.3 Inclusion Criteria for Data Sources Reporting Exposure Data on Consumers and Ecological Receptors

EPA/OPPT developed PECO statements to guide the full text screening of exposure data/information for human (i.e., consumers, potentially exposed or susceptible subpopulations) and ecological receptors. Subsequent versions of the PECO statements may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the inclusion criteria in the PECO statement are eligible for inclusion, considered for evaluation, and possibly included in the exposure assessment. On the other hand, data sources are excluded if they do not meet the criteria in the PECO statement. The methylene chloride-specific PECO is provided in Table_Apx F-5.

| Table_Apx F-5. Inclusion Criteria for the Data Sources Reporting Methylene Chloride Exposure Data on Consumers and Ecological Receptors | |
|---|---|
| **PECO Element** | **Evidence** |
| **P**opulation | **Human:** Consumers (i.e., receptors who use a product directly) and bystanders in the home (i.e., receptors who are non-product users that are incidentally exposed to the product or article); including PESS such as children; infants; pregnant women; lactating women, do it yourself (DIY) or consumers with high-end exposure. |
| | **Ecological:** Aquatic biota. |
| **E**xposure | **Expected Primary Exposure Sources, Pathways, Routes:**<br>• Sources: Consumer uses in the home producing releases to air and dermal contact; industrial and commercial activities involving non-closed systems producing releases to surface water<br>• Pathways: Indoor air and dermal contact in consumer products; surface water<br>• Routes of Exposure: Inhalation exposure via indoor air (consumer and bystander populations) and dermal exposure via direct contact with consumer products containing methylene chloride including occluded exposures; exposure to aquatic species via surface water |

| Table_Apx F-5. Inclusion Criteria for the Data Sources Reporting Methylene Chloride Exposure Data on Consumers and Ecological Receptors | |
|---|---|
| **PECO Element** | **Evidence** |
| **C**omparator (Scenario) | **Human:** Consumer and bystander exposure via use of methylene chloride containing consumer products in the home. |
| | **Ecological:** Aquatic species exposure via contact with surface water |
| **O**utcomes for Exposure Concentration or Dose | **Human:** Acute, subchronic, and/or chronic external dose estimates (mg/kg/day); acute, subchronic, and/or chronic air and water concentration estimates ($mg/m^3$ or mg/L). Both external potential dose and internal dose based on biomonitoring and reverse dosimetry mg/kg/day will be considered. |
| | **Ecological:** A range of ecological receptors will be considered (range dependent on available ecotoxicity data) using surface water concentrations. |

## F.4 Inclusion Criteria for Data Sources Reporting Human Health Hazards

EPA/OPPT developed a methylene chloride-specific PECO statement (Table_Apx F-6) to guide the full text screening of the human health hazard literature. Subsequent versions of the PECOs may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the criteria specified in the PECO statement will be eligible for inclusion, considered for evaluation, and possibly included in the human health hazard assessment, while those that do not meet these criteria will be excluded according to the exclusion criteria.

In general, the PECO statements were based on (1) information accompanying the TSCA Scope document, and (2) preliminary review of the health effects literature from authoritative sources cited in the TSCA Scope documents. When applicable, these authoritative sources (e.g., IRIS assessments, EPA/OPPT's Work Plan Problem Formulations or risk assessments) will serve as starting points to identify PECO-relevant studies.

| Table_Apx F-6. Inclusion Criteria for Data Sources Reporting Human Health Hazards Related to Methylene Chloride [a] | | | |
|---|---|---|---|
| **PECO Element** | **Evidence Stream** | **Papers/Features Included** | **Papers/Features Excluded** |
| Population [b] | *Human* | • Any population<br>• All lifestages<br>• Study designs:<br>o Controlled exposure, cohort, case-control, cross-sectional, case-crossover for all endpoints<br>o Case studies and case series only related to deaths and respiratory distress from acute exposure | • Case studies and case series for all endpoints ***other than*** death and respiratory distress from acute exposure |
| | *Animal* | • All non-human whole-organism mammalian species<br>• All lifestages | • Non-mammalian species |
| *Exposure* | *Human* | • Exposure based on administered dose or concentration of methylene chloride, biomonitoring data (e.g., urine, blood or other specimens), environmental or occupational-setting monitoring data (e.g., air, water levels), job title or residence<br>• Primary metabolites of interest (e.g., COHb) as identified in biomonitoring studies | |

| Table_Apx F-6. Inclusion Criteria for Data Sources Reporting Human Health Hazards Related to Methylene Chloride [a] | | | |
|---|---|---|---|
| | | • Exposure identified as ***or presumed to be*** from oral, dermal, inhalation routes<br>• Any number of exposure groups<br>• Quantitative, semi-quantitative or qualitative estimates of exposure<br>• Exposures to multiple chemicals/mixtures only if methylene chloride or related metabolites were independently measured and analyzed | • Route of exposure ***not*** by inhalation, oral or dermal type (e.g., intraperitoneal, injection)<br>• Multiple chemical/mixture exposures with no independent measurement of or exposure to methylene chloride (or related metabolite) |
| | *Animal* | • A minimum of 2 quantitative dose or concentration levels of methylene chloride plus a negative control group[a]<br>• Acute, subchronic, chronic exposure from oral, dermal, inhalation routes<br>• Exposure to methylene chloride only (no chemical mixtures) | • Only 1 quantitative dose or concentration level in addition to the control<br>• Route of exposure ***not*** by inhalation, oral or dermal type (e.g., intraperitoneal, injection)<br>• No duration of exposure stated<br>• Exposure to methylene chloride in a chemical mixture |
| Comparator | *Human* | • A comparison population [not exposed, exposed to lower levels, exposed below detection] for endpoints ***other than*** death or respiratory distress Any or no comparison for exposures associated with death or respiratory distress | • No comparison population for endpoints other than death or respiratory distress from acute exposure |
| | *Animal* | • Negative controls that are vehicle-only treatment and/or no treatment | • Negative controls ***other than*** vehicle-only treatment or no treatment |
| Outcome | *Human*<br>*Animal* | • Endpoints described in the methylene chloride scope document [c]:<br>o Acute toxicity (neurotoxicity and lethality)<br>o Liver toxicity<br>o Neurotoxicity<br>o Irritation<br>o Cancer<br>• Other endpoints (e.g., immunotoxicity, reproductive/developmental toxicity) [d] | |
| General Considerations | | **Papers/Features Included** | **Papers/Features Excluded** |
| | | • Written in English [e]<br>• Reports primary data<br>• Full text available<br>• Reports both methylene chloride exposure ***and*** a health outcome | • Not written in English<br>• Reports secondary data (e.g., review papers)<br>• No full text available (e.g., only a study description/abstract, out-of-print text)<br>• Reports a methylene chloride-related exposure ***or*** a health outcome, but not both (e.g. incidence, prevalence report) |

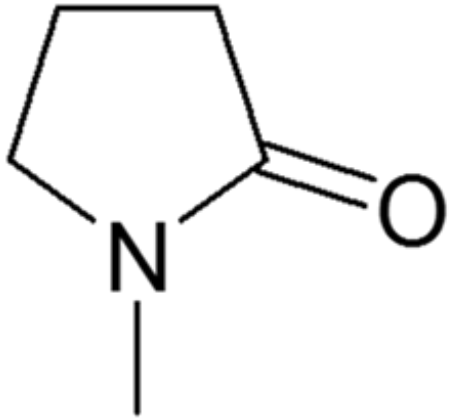
[a] Some of the studies that are excluded based on the PECO statement may be considered later during the systematic review process. For methylene chloride, EPA will evaluate studies related to susceptibility and may evaluate, toxicokinetics and physiologically based pharmacokinetic models after other data (e.g., human and animal data identifying adverse health outcomes) are reviewed. EPA may need to evaluate mechanistic data (especially related to immunotoxicity, CNS depression, lethality) depending on the review of health effects data. Finally, EPA may also review other data as needed (e.g., animal studies using one concentration, review papers) when analyzing evidence during the data integration phase of the systematic review process.
[b] Mechanistic data are excluded during the full text screening phase of the systematic review process but may be considered later (see footnote *a*).
[c] EPA will review key and supporting studies in the IRIS assessment (U.S. EPA, 2011b) that were considered in the dose-response assessment for non-cancer and cancer endpoints as well as studies published after the IRIS assessment (U.S. EPA, 2011b).
[d] EPA may screen for hazards other than those listed in the scope document if they were identified in the updated literature search that accompanied the scope document.
[e] EPA may translate studies as needed.

EPA Document# EPA-740-R1-7015
May 2018
Office of Chemical Safety and
Pollution Prevention

United States
Environmental Protection Agency

# Problem Formulation of the Risk Evaluation for N-Methylpyrrolidone (2-Pyrrolidinone, 1-Methyl-)

# CASRN: 872-50-4




*May 2018*

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**Docket**

Supporting information can be found in the public docket: EPA-HQ-OPPT-2016-0743

**Disclaimer**

Reference herein to any specific commercial products, process or service by trade name, trademark, manufacturer or otherwise does not constitute or imply its endorsement, recommendation or favoring by the United States Government.

# ABBREVIATIONS

| | |
|---|---|
| °C | Degrees Celsius |
| AIHA | American Industrial Hygiene Association |
| atm | Atmosphere(s) |
| ATSDR | Agency for Toxic Substances and Disease Registry |
| BAF | Bioaccumulation Factor |
| BCF | Bioconcentration Factor |
| CAA | Clean Air Act |
| CASRN | Chemical Abstracts Service Registry Number |
| CBI | Confidential Business Information |
| CCL | Contaminant Candidate List |
| CDR | Chemical Data Reporting |
| CEHD | Chemical Exposure Health Data |
| CEM | Consumer Exposure Model |
| CFR | Code of Federal Regulations |
| ChV | Chronic Value |
| $cm^3$ | Cubic Centimeter(s) |
| COC | Concentration of Concern |
| CSCL | Chemical Substances Control Law |
| DMR | Discharge Monitoring Report |
| DTSC | Department of Toxic Substances Control |
| EC | European Commission |
| $EC_{50}$ | Effective Concentration with 50% immobilized test organisms |
| ECHA | European Chemicals Agency |
| EPA | Environmental Protection Agency |
| EPCRA | Emergency Planning and Community Right-to-Know Act |
| ESD | Emission Scenario Document |
| EU | European Union |
| FDA | Food and Drug Administration |
| FFDCA | Federal Food, Drug and Cosmetic Act |
| GBL | Gamma-Butyrolactone |
| GS | Generic Scenarios |
| HESIS | Hazard Evaluation System and Information Service |
| HHE | Health Hazard Evaluation |
| HPV | High Production Volume |
| Hr | Hour |
| IMAP | Inventory Multi-Tiered Assessment and Prioritisation |
| IRIS | Integrated Risk Information System |
| kg | Kilogram(s) |
| L | Liter(s) |
| LOAEL | Lowest Observed Adverse Effect Level |
| LOEC | Lowest Observed Effect Concentration |
| lb | Pound(s) |
| LC50 | Lethal Concentration of 50% test organisms |
| LOEC | Lowest Observed Effect Concentration |
| Log $K_{oc}$ | Logarithmic Soil Organic Carbon:Water Partition Coefficient |
| Log $K_{ow}$ | Logarithmic Octanol:Water Partition Coefficient |
| $m^3$ | Cubic Meter(s) |
| MADL | Maximum Allowable Dose Level |

| | |
|---|---|
| mg | Milligram(s) |
| NOAEL | No Observed Adverse Effect Level |
| NOEC | No Observed Effect Concentration |
| ONU | Occupational Non-User |
| µg | Microgram(s) |
| MMA | Monomethylamine |
| mmHg | Millimeter(s) of Mercury |
| mPa·s | Millipascal(s)-Second |
| MITI | Ministry of International Trade and Industry |
| SDS | Safety Data Sheet |
| MSW | Municipal Solid Waste |
| NAICS | North American Industry Classification System |
| NESHAP | National Emission Standards for Hazardous Air Pollutants |
| NICNAS | National Industrial Chemicals Notification and Assessment Scheme |
| NIOSH | National Institute for Occupational Safety and Health |
| NITE | National Institute of Technology and Evaluation |
| NMP | N-Methylpyrrolidone |
| NSPS | New Source Performance Standards |
| NWQMC | National Water Quality Monitoring Council |
| OCSPP | Office of Chemical Safety and Pollution Prevention |
| OECD | Organisation for Economic Cooperation and Development |
| OEHHA | Office of Environmental Health Hazard Assessment |
| OEL | Occupational Exposure Limits |
| OPPT | Office of Pollution Prevention and Toxics |
| OSHA | Occupational Safety and Health Administration |
| PBZ | Personal Breathing Zone |
| PDE | Permissible Daily Exposure |
| PDM | Probabilistic Dilution Model |
| PECO | Populations, Exposures, Comparisons, Outcomes |
| PEL | Permissible Exposure Limit |
| POD | Point of Departure |
| POTW | Publicly Owned Treatment Works |
| PPE | Personal Protective Equipment |
| ppm | Part(s) per Million |
| PSD | Particle Size Distribution |
| RCRA | Resource Conservation and Recovery Act |
| REACH | Registration, Evaluation, Authorisation and Restriction of Chemicals |
| SDWA | Safe Drinking Water Act |
| SIDS | Screening Information Data Set |
| SNAP | Significant New Alternatives Policy |
| STORET | STOrage and RETrieval |
| SVHC | Substance of Very High Concern |
| TRI | Toxics Release Inventory |
| TSCA | Toxic Substances Control Act |
| TWA | Time-Weighted Average |
| USGS | United States Geological Survey |
| VOC | Volatile Organic Compound |
| WEEL | Workplace Environmental Exposure Level |
| Yr | Years(s) |

# EXECUTIVE SUMMARY

TSCA § 6(b)(4) requires the U.S. Environmental Protection Agency (EPA) to establish a risk evaluation process. In performing risk evaluations for existing chemicals, EPA is directed to "determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of costs or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator under the conditions of use." In December of 2016, EPA published a list of 10 chemical substances that are the subject of the Agency's initial chemical risk evaluations (81 FR 91927), as required by TSCA § 6(b)(2)(A). N-methylpyrrolidone (NMP) was one of these chemicals.

TSCA § 6(b)(4)(D) requires that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use and potentially exposed or susceptible subpopulations that the Administrator expects to consider. In June 2017, EPA published the Scope of the Risk Evaluation for NMP (EPA-HQ-OPPT-2016-0743) As explained in the scope document, because there was insufficient time for EPA to provide an opportunity for comment on a draft of the scope, as EPA intends to do for future scope documents, EPA is publishing and taking public comment on the problem formulation document to refine the current scope, as an additional interim step prior to publication of the draft risk evaluation for NMP. Comments received on this problem formulation document will inform development of the draft risk evaluation.

This problem formulation document refines the conditions of use and exposures presented in the scope of the risk evaluation for NMP and presents refinements to the conceptual models and analysis plan that describe how EPA expects to evaluate risks.

N-methylpyrrolidone, also called N-methyl-2-pyrrolidone, or 1-methyl-2-pyrrolidone, is a high production volume (HPV) chemical that is widely used during the manufacture and production of polymers, pharmaceuticals, agrichemicals and petroleum products (U.S. EPA, 2015). For the purposes of this problem formulation, "NMP" refers to N-methylpyrrolidone (CASRN 872-50-4). NMP is subject to federal and state regulations and reporting requirements. In terms of federal regulation, NMP has been a reportable Toxics Release Inventory (TRI) chemical under Section 313 of the Emergency Planning and Community Right-to-Know Act (EPCRA) since 1995. NMP is also reported under the Toxic Substances Control Act's Chemical Data Reporting (CDR) Rule. NMP is subject to Clean Air Act (CAA) Section 111 Performance Standards for New Stationary Sources of Air Pollution for volatile organic carbon (VOC) emissions from synthetic organic chemical manufacturing industry distillation operations and reactor processes. NMP also is listed under the CAA's National Volatile Organic Compound Emission Standards for Aerosol Coatings. NMP is identified on both the Third (2009) and Fourth (2016) Contaminant Candidate Lists under the Safe Drinking Water Act (SDWA).

Information on domestic manufacture, processing and use of NMP is available to EPA through its Chemical Data Reporting (CDR) Rule, issued under TSCA. In 2015, more than 160 million pounds of NMP was reported to be manufactured (including imported) in the U.S. According to a recent EPA market report, the primary uses for NMP include petrochemical processing, engineering plastic coatings, electronics, pharmaceutical and agrichemical manufacturing and solvent cleaning (EPA-HQ-OPPT-2016-0743).

This document presents the potential exposures that may result from NMP conditions of use considered under the scope of the risk evaluation. Exposures may occur to workers and occupational non-users (i.e., workers who do not directly handle NMP but perform work in an area where it is used), consumers and bystanders (i.e., non-users who are incidentally exposed to NMP as a result of consumer product use)

and members of the general population. Workers and occupational non-users may be exposed to NMP during various conditions of use (e.g., manufacturing, processing and industrial/commercial uses). General population exposures may result from industrial and/or commercial uses; industrial releases to air, water or land and other conditions of use. EPA expects the highest exposures to NMP will generally involve workers in industrial and commercial settings; however, NMP occurs in numerous consumer products and can therefore, result in exposures outside the occupational setting. For NMP, EPA considers workers, occupational non-users, consumers, bystanders, and certain other groups of individuals who may experience greater exposures than the general population to be potentially exposed or susceptible subpopulations. During risk evaluation, EPA expects to further analyze inhalation exposures to NMP vapor and mist (for workers, occupational non-users, consumers and bystanders). EPA also expects to analyze dermal exposures from direct contact with NMP-containing liquids (for workers and consumers) and indirect exposure from vapor-through-skin contact (for workers, occupational non-users, consumers and bystanders).

NMP has been the subject of numerous assessments with various hazards identified following oral, dermal and inhalation exposure. Reproductive/developmental effects were identified as sensitive endpoints for evaluating human health risks in the previous assessment of NMP use in paint and coating removal (U.S. EPA, 2015). EPA expects to evaluate all potential hazards for NMP, using the previous analysis as a starting point for identifying key and supporting studies and including any information found in recent literature. The relevant studies will be evaluated using the data quality criteria provided in the *Application of Systematic Review in TSCA Risk Evaluations* document (U.S. EPA, 2018). Previously identified human health hazards include irritation and adverse effects on hepatic, renal, immune, reproductive/developmental and central nervous systems. If additional hazard concerns are identified during systematic review of the literature, these effects will also be considered. Risks will be evaluated based on the specific hazards and exposure scenarios identified.

The revised conceptual models presented in this problem formulation identify conditions of use; exposure pathways (e.g., media); exposure routes (e.g., inhalation, dermal, oral); potentially exposed or susceptible subpopulations; and hazards EPA expects to consider during risk evaluation. The initial conceptual models provided in the scope document were revised during problem formulation based on evaluation of reasonably available information for physical and chemical properties, fate, exposures, hazards, and conditions of use and based upon consideration of other statutory and regulatory authorities. In each problem formulation document for the first 10 chemical substances, EPA also refined the activities, hazards, and exposure pathways that will be included in and excluded from the risk evaluation.

EPA's overall objectives are to conduct timely, relevant, high-quality and scientifically credible risk evaluations within the statutory deadlines and to evaluate the conditions of use that raise the greatest potential for risk 82 FR 33726, 33728 (July 20, 2017).

# 1 INTRODUCTION

This document presents for comment the problem formulation of the risk evaluation to be conducted for NMP under the Frank R. Lautenberg Chemical Safety for the 21st Century Act. The Frank R. Lautenberg Chemical Safety for the 21st Century Act amended the Toxic Substances Control Act (TSCA), the Nation's primary chemicals management law, on June 22, 2016. The new law includes statutory requirements and deadlines for actions related to conducting risk evaluations of existing chemicals.

In December of 2016, EPA published a list of 10 chemical substances that are the subject of the Agency's initial chemical risk evaluations (81 FR 91927), as required by TSCA § 6(b)(2)(A). These 10 chemical substances were drawn from the 2014 update of EPA's TSCA Work Plan for Chemical Assessments, a list of chemicals that EPA identified in 2012 and updated in 2014 (currently totaling 90 chemicals) for further assessment under TSCA. EPA's designation of the first 10 chemical substances constituted the initiation of the risk evaluation process for each of these chemical substances, pursuant to the requirements of TSCA § 6(b)(4).

TSCA § 6(b)(4)(D) requires that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use and potentially exposed or susceptible subpopulations that the Administrator expects to consider, within 6 months after the initiation of a risk evaluation. The scope documents for all first 10 chemical substances were issued on June 22, 2017. The first 10 problem formulation documents are a refinement of what was presented in the first 10 scope documents. TSCA § 6(b)(4)(D) does not distinguish between scoping and problem formulation, and requires EPA to issue scope documents that include information about the chemical substance, including the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations that the Administrator expects to consider in the risk evaluation. In the future, EPA expects scoping and problem formulation to be completed prior to the issuance of scope documents and intends to issue scope documents that include problem formulation.

As explained in the scope document, because there was insufficient time for EPA to provide an opportunity for comment on a draft of the scope, as EPA intends to do for future scope documents, EPA is publishing and taking public comment on a problem formulation document to refine the current scope, as an additional interim step prior to publication of the draft risk evaluation for NMP. Comments received on this problem formulation document will inform development of the draft risk evaluation.

The Agency defines problem formulation as the analytical phase of the risk assessment in which "the purpose for the assessment is articulated, the problem is defined and a plan for analyzing and characterizing risk is determined" [see Section 2.2 of the *Framework for Human Health Risk Assessment to Inform Decision Making*; (U.S. EPA, 2014)]. The outcome of problem formulation includes the conceptual model(s) and an analysis plan. The conceptual model describes the linkages between stressors and adverse human health effects, including the stressor(s), exposure pathway(s), exposed life stage(s) and population(s) and endpoint(s) that will be addressed during risk evaluation (U.S. EPA, 2014). The analysis plan follows the development of the conceptual model(s) and is intended to describe the approach for conducting the risk evaluation, including its design, methods, key inputs and intended outputs as described in EPA's *Human Health Risk Assessment Fram*ework (U.S. EPA, 2014). The problem formulation documents refine the initial conceptual models and analysis plans that were provided in the scope documents.

EPA identified exposure pathways that are covered under the jurisdiction of regulatory programs and associated analytical processes carried out under other EPA-administered environmental statutes –

namely, the Safe Drinking Water Act (SDWA), and the Resource Conservation and Recovery Act (RCRA) – which EPA does not expect to include in the risk evaluation. As a general matter, EPA believes certain programs under other Federal environmental laws adequately assess and effectively manage the risks for those covered exposure pathways. To use Agency resources efficiently under the TSCA program, to avoid duplicating efforts taken pursuant to other Agency programs, to maximize scientific and analytical efforts and to meet the three-year statutory deadline, EPA is planning to exercise its discretion under TSCA 6(b)(4)(D) to focus its analytical efforts on exposures that are likely to present the greatest concern and consequently merit a risk evaluation under TSCA, by excluding, on a case-by-case basis, certain exposure pathways that fall under the jurisdiction of other EPA-administered statutes.[1] EPA does not expect to include any such excluded pathways in the risk evaluation. The provisions of various EPA environmental statutes and their implementing regulations represent the judgement of Congress and the Administrator, respectively, as to the degree of health and environmental risk reduction that is sufficient under various environmental statutes.

EPA also identified any conditions of use, hazards, or exposure pathways which were included in the scope document and that EPA expects to include in the risk evaluation but which EPA does not expect to further analyze during risk evaluation. EPA expects to be able to reach conclusions about specific conditions of use, hazards or exposure pathways without further analysis and therefore expects to conduct no further analysis on those conditions of use, hazards or exposure pathways in order to focus the Agency's resources on more extensive or quantitative analyses. Each risk evaluation will be "fit-for-purpose," meaning not all conditions of use will warrant the same level of evaluation and the Agency may be able to reach some conclusions without comprehensive or quantitative risk evaluations. 82 FR 33726, 33734, 33739 (July 20, 2017).

EPA received comments on the published scope document for NMP and has considered the comments specific to NMP in this problem formulation document. EPA is soliciting public comment on this problem formulation document and when the draft risk evaluation is issued, the Agency intends to respond to comments that are submitted. In its draft risk evaluation, EPA may revise the conclusions and approaches contained in this problem formulation, including the conditions of use and pathways covered and the conceptual models and analysis plan, based on comments received.

## 1.1 Regulatory History

EPA conducted a search of existing laws and regulations and assessments pertaining to NMP. EPA compiled information available from federal, state, international and other government sources, as cited in Appendix A. EPA evaluated and considered the impact of existing laws and regulations (e.g., regulations on landfill disposal, design, and operations) during problem formulation to determine what, if any further analysis might be necessary as part of the risk evaluation. Additional consideration of the nexus between these existing regulations and TSCA conditions of use may be necessary as specific exposure scenarios are developed during the analysis phase of the risk evaluation.

***Federal Laws and Regulations***

NMP is subject to federal statutes or regulations other than TSCA, that are implemented by other offices within EPA and/or other federal agencies/departments. A summary of federal laws, regulations and implementing authorities is provided in Appendix A.1.

[1] As explained in the final rule for chemical risk evaluation procedures, "EPA may, on a case-by case basis, exclude certain activities that EPA has determined to be conditions of use in order to focus its analytical efforts on those exposures that are likely to present the greatest concern, and consequently merit an unreasonable risk determination." 82 FR 33726, 33728 (July 20, 2017).

***State Laws and Regulations***
NMP is subject to state statutes or regulations implemented by state agencies or departments. A summary of state laws, regulations and implementing authorities is provided in Appendix A.2.

***Laws and Regulations in Other Countries and International Treaties or Agreements***
NMP is subject to statutes or regulations in countries other than the United States and/or international treaties and/or agreements. A summary of these laws, regulations, treaties and/or agreements is provided in Appendix A.3.

## 1.2 Assessment History

EPA has identified assessments conducted by other EPA Programs and other organizations (see Table 1-1). Depending on the source, these assessments may include information on conditions of use, hazards, exposures and potentially exposed or susceptible subpopulations. Table 1-1 shows the assessments that have been conducted. EPA found no additional assessments beyond those listed.

In addition to using this information, EPA intends to conduct a full review of the relevant data/information collected in the initial comprehensive search [see *NMP (CASRN 872-50-4) Bibliography: Supplemental File for the TSCA Scope Document*, (EPA-HQ-OPPT-2016-0743)] following the literature search and screening strategies documented in the *Strategy for Conducting Literature Searches for NMP: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0743). This will ensure that EPA considers all data/information that has been made available since these assessments were conducted.

**Table 1-1. Assessment History of NMP**

| Authoring Organization | Assessment |
|---|---|
| **EPA Assessments** | |
| U.S. EPA, Office of Pollution Prevention and Toxics (OPPT) | TSCA Work Plan Chemical Risk Assessment N-Methylpyrrolidone: Paint Stripping Use CASRN 872-50-4 U.S. EPA (2015) |
| U.S. EPA, OPPT | Re-assessment of Pesticide Inert Ingredient Exemption under the Food Quality Protection Act U.S. EPA (2006a) |
| **Other U.S.-Based Organizations** | |
| California Office of Environmental Health Hazard Assessment (OEHHA) | Proposition 65 Maximum Allowable Dose Level for Reproductive Toxicity OEHHA (2003) |
| **International** | |
| National Industrial Chemicals Notification and Assessment Scheme (NICNAS), Australian Government | Human Health Tier III assessment NICNAS (2013) |
| Government of Canada, Environment Canada, Health Canada | Draft Screening Assessment of Risks to Human and Ecological Receptors EC/HC (2017) |
| European Commission (EC), Scientific Committee on Occupational Exposure Limits (OELs) | Evaluation of Occupational Exposure Limits for NMP EC (2016) |

| Authoring Organization | Assessment |
|---|---|
| Organisation for Economic Co-operation and Development (OECD), Cooperative Chemicals Assessment Program | NMP: SIDS Initial Assessment Profile OECD (2007) |
| World Health Organization (WHO) International Programme on Chemical Safety (IPCS) | Concise International Chemical Assessment Document 35 N-METHYLPYRROLIDONE WHO (2001) |
| Danish Ministry of the Environment Environmental Protection Agency | Survey of NMP - Miljøstyrelsen (Danish EPA, 2015) |

## 1.3 Data and Information Collection

EPA/OPPT generally applies a systematic review process and workflow that includes: (1) data collection; (2) data evaluation; and (3) integration of the scientific data used in risk evaluations developed under TSCA. Scientific analysis is often iterative in nature as new knowledge is obtained. Hence, EPA/OPPT expects multiple refinements regarding data collection will occur during the process of risk evaluation. Additional information that may be considered, and was not part of the initial comprehensive bibliographies will be documented in the Draft Risk Evaluation for NMP.

***Data Collection: Data Search***

EPA/OPPT conducted chemical-specific searches for information on: physical-chemical properties; environmental fate and transport; conditions of use; environmental and human exposures; and ecological and human health hazards, including potentially exposed or susceptible subpopulations.

EPA/OPPT designed its initial data search to be broad enough to capture a comprehensive set of sources containing data and/or information potentially relevant to the risk evaluation. For most disciplines, the search was not limited by date and was conducted on a wide range of data sources, including but not limited to: peer-reviewed and gray literature (e.g., publicly-available industry reports, trade association resources, government reports). When available, EPA/OPPT relied on the search strategies from recent assessments to identify relevant references and supplemented these searches to identify relevant information published after the end date of the previous search to capture more recent literature. *Strategy for Conducting Literature Searches for NMP: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0743) provides details about the data sources and search terms used in the literature search.

***Data Collection: Data Screening***

Following the data search, references were screened and categorized using selection criteria outlined in the *Strategy for Conducting Literature Searches for NMP: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0743). Titles and abstracts were screened against the criteria as a first step with the goal of identifying a smaller subset of the relevant data to move forward into the subsequent data extraction and data evaluation steps. Prior to full-text review, EPA/OPPT anticipates refinements to the screening strategies, as informed by an evaluation of the performance of the initial title/abstract screening and categorization process.

The categorization scheme (or tagging structure) used for data screening varies by scientific discipline (i.e., physical-chemical properties; environmental fate and transport; chemical use/conditions of use information; environmental and human exposures, including potentially exposed or susceptible

subpopulations identified by virtue of greater exposure; human health hazards, including potentially exposed or susceptible subpopulations identified by virtue of greater susceptibility; and ecological hazards). However, within each data set, there are two broad categories or data tags: (1) *on-topic* references or (2) *off-topic* references. *On-topic* references are those that may contain data and/or information relevant to the risk evaluation. *Off-topic* references are those that do not appear to contain data or information relevant to the risk evaluation. The *Strategy for Conducting Literature Searches for NMP: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0743) discusses the inclusion and exclusion criteria that EPA/OPPT used to categorize references as *on-topic* or *off-topic*.

Additional data screening using sub-categories (or sub-tags) was also performed to facilitate further sorting of data/information. For example, identifying references by source type (e.g., published peer-reviewed journal article, government report); data type (e.g., primary data, review article); human health hazard (e.g., liver toxicity, reproductive toxicity); or chemical-specific and use-specific data or information. These sub-categories are described in the *Strategy for Conducting Literature Searches for NMP: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0743) and will be used to organize the different streams of data during the stages of data evaluation and data integration steps of systematic review.

Results of the initial search and categorization results can be found in the *NMP (CASRN 872-50-4) Bibliography: Supplemental File for the TSCA Scope Document*, (EPA-HQ-OPPT-2016-0743). This document provides a comprehensive list (bibliography) of the sources of data identified by the initial search and categorization for *on-topic* and *off-topic* references. Because systematic review is an iterative process, EPA/OPPT expects that some references may move from *on-topic* to *off-topic* categories, and vice versa. Moreover, targeted supplemental searches may also be conducted to address specific needs for the analysis phase (e.g., to locate specific data needed for modeling); hence, additional *on-topic* references not initially identified in the initial search may be identified as the systematic review process proceeds.

## 1.4 Data Screening During Problem Formulation

EPA/OPPT is in the process of completing the full text screening of the on-topic references identified in the *NMP (CASRN 872-50-4) Bibliography: Supplemental File for the TSCA Scope Document*, (EPA-HQ-OPPT-2016-0743). The screening process and criteria at the full-text level is described in the *Application of Systematic Review in TSCA Risk Evaluations* document (U.S. EPA, 2018). Appendix G provides the inclusion and exclusion criteria applied at the full text screening. The eligibility criteria are guided by the analytical considerations in the revised conceptual models and analysis plan, as discussed in the problem formulation document. Thus, it is expected that the number of data/information sources entering evaluation is reduced to those that are relevant to address the technical approach and issues described in the analysis plan of this document.

Following the screening process, the quality of the included data/information sources will be assessed using the evaluation strategies described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018).

# 2 PROBLEM FORMULATION

As required by TSCA, the scope of the risk evaluation identifies the conditions of use, hazards, exposures and potentially exposed or susceptible subpopulations the Administrator expects to consider. To communicate and visually convey the relationships between these components, EPA included in the scope document a life cycle diagram and conceptual models that describe the potential relationships between NMP and human and ecological receptors. During problem formulation, EPA revised the conceptual models based on further data gathering and analysis as presented in this document. An updated analysis plan is also included which identifies, to the extent feasible, the approaches and methods that EPA may use to assess exposures, effects (hazards) and risks associated with the conditions of use identified for NMP.

## 2.1 Physical-Chemical Properties

Physical-chemical properties influence the environmental behavior and the toxic properties of a chemical, thereby informing the potential conditions of use, exposure pathways, routes and hazards that EPA intends to consider. During problem formulation, EPA considered the measured or estimated physical-chemical properties set forth in Table 2-1. The value reported for vapor pressure was updated (0.345 mmHg) to reflect information obtained from a primary source, which is considered more defensible than the original value (0.19 mmHg) taken from a secondary source.

**Table 2-1. Physical-Chemical Properties of NMP**

| Property | Value [a] | Reference |
|---|---|---|
| Molecular formula | $C_5H_9ON$ | |
| Molecular weight | 99.1 g/mole | O'Neil et al. (2006) |
| Physical form | Colorless to yellow liquid; amine odor | O'Neil et al. (2006) |
| Melting point | -25°C | Ashford (1994) |
| Boiling point | 202°C | O'Neil et al. (2006) |
| Density | 1.03 at 25°C | O'Neil et al. (2006) |
| Vapor pressure | 0.345 mmHg at 25°C | Daubert and Danner (1989) |
| Vapor density | 3.4 (air = 1) | NFPA (1997) |
| Water solubility | 1,000 g/L at 25°C | O'Neil et al. (2006) |
| Octanol:water partition coefficient (log $K_{ow}$) | - 0.38 at 25°C | Sasaki et al. (1988) |
| Henry's Law constant | $3.2 \times 10^{-9}$ atm $m^3$/mole | U.S. EPA (2012b) |
| Flash point | 95°C (open cup) | Riddick et al. (1986) |
| Autoflammability | Not available | |
| Viscosity | 1.65 mPa·s at 25°C | O'Neil et al. (2006) |
| Refractive index | Not applicable | |
| Dielectric constant | Not applicable | |

[a] Measured unless otherwise noted.

## 2.2 Conditions of Use

TSCA § 3(4) defines the conditions of use as ‘‘the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of.’’

### 2.2.1 Data and Information Sources

In the scope documents, EPA identified, based on reasonably available information, the conditions of use for the subject chemicals. EPA searched available data sources (e.g., *Use and Market Profile for NMP*, EPA-HQ-OPPT-2016-0743). Based on this search, EPA published a preliminary list of information and sources related to chemical conditions of use (see *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: NMP*, EPA-HQ-OPPT-2016-0743-0003) prior to a February 2017 public meeting on scoping efforts convened to solicit comment and input from the public. EPA also convened meetings with companies, industry groups, chemical users and other stakeholders to aid in identifying conditions of use and verifying conditions of use identified by EPA. The information and input received from the public and stakeholder meetings was incorporated into this problem formulation document to the extent appropriate, as indicated in Table 2-3. Thus, EPA believes the identified manufacturing, processing, distribution, use and disposal activities constitute the intended, known, and reasonably foreseen activities associated with the subject chemical, based on reasonably available information.

### 2.2.2 Identification of Conditions of Use

To determine the current conditions of use of NMP and conversely, activities that do not qualify as conditions of use, EPA conducted extensive research and outreach. This included EPA’s review of published literature and online databases including the most recent data available from EPA’s Chemical Data Reporting program (CDR) and Safety Data Sheets (SDSs). EPA also conducted online research by reviewing company websites of potential manufacturers, importers, distributors, retailers, or other users of NMP and queried government and commercial trade databases. EPA also received comments on the *Scope of the Risk Evaluation for NMP* (EPA-HQ-OPPT-2016-0743) that were used to determine the conditions of use. In addition, EPA convened meetings with companies, industry groups, chemical users, states, environmental groups, and other stakeholders to aid in identifying and verifying the conditions of use identified by EPA. Those meetings included a February 14, 2017 public meeting with such entities (EPA-HQ-OPPT-2016-0743).

EPA has removed from the problem formulation any conditions of use that EPA does not plan to include in the risk evaluation – for example because EPA has insufficient information to find certain activities are circumstances under which the chemical is actually “intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used or disposed of.” EPA has also identified any conditions of use that EPA does not expect to include in the risk evaluation. As explained in the final rule for Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act, TSCA section 6(b)(4)(D) requires EPA to identify "the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations that the Administrator expects to consider” in a risk evaluation, suggesting that EPA may exclude specific activities that EPA has determined to be conditions of use on a case-by-case basis. (82 FR 33736, 33729; July 20, 2017). For example, EPA may exclude conditions of use that the Agency has sufficient basis to conclude would present only *de minimis* exposures or otherwise insignificant risks (such as use in a closed system that effectively precludes exposure, or use as an intermediate).

The activities that EPA no longer believes are conditions of use or that were otherwise excluded during problem formulation are described in Section 2.2.2.1. The conditions of use included in the scope of the risk evaluation are summarized in Section 2.2.2.2

#### 2.2.2.1 Categories and Subcategories Determined Not to be Conditions of Use or Otherwise Excluded During Problem Formulation

Based on the foregoing research and outreach, EPA does not have reason to believe that any conditions of use identified in the NMP Scope document should be excluded from the risk evaluation.

**Table 2-2. Categories and Subcategories Determined Not to be Conditions of Use or Otherwise Excluded During Problem Formulation**

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| No activities were excluded from risk evaluation. | | | |

#### 2.2.2.2 Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation

For NMP, EPA has conducted public outreach and literature searches to collect information about NMP's conditions of use and has reviewed reasonably available information obtained by EPA concerning activities associated with NMP. Based on this research and outreach, EPA does not have reason to believe that any conditions of use identified in the NMP scope should be excluded from risk evaluation. Therefore, all NMP conditions of use will be included in the risk evaluation.

NMP is widely used in the manufacture and production of electronics, petroleum products, pharmaceuticals, polymers and other specialty chemicals. It also has numerous applications in paints, coatings, and adhesives as well as products that facilitate their removal.

Table 2-3 summarizes each life cycle stage and the corresponding categories and subcategories of conditions of use for NMP that EPA expects to consider during risk evaluation. Using the 2016 CDR (U.S. EPA, 2016b), EPA identified industrial processing or use activities, industrial function categories and commercial and consumer use product categories. EPA identified the subcategories by supplementing CDR data with other published literature and information obtained through stakeholder consultations. For risk evaluations, EPA intends to consider each life cycle stage (with corresponding use categories and subcategories) and assess the potential sources of release and related exposures associated with that life cycle stage.

Beyond the uses identified in the *Scope of the Risk Evaluation for NMP* ( EPA-HQ-OPPT-2016-0743), EPA has received no additional information identifying additional current conditions of use for NMP from public comment and stakeholder meetings.

**Table 2-3. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation**

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| Manufacture | Domestic Manufacture | Domestic Manufacture | U.S. EPA (2016b) |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| | Import | Import | U.S. EPA (2016b) |
| Processing | Processing as a reactant or intermediate | Intermediate in Plastic Material and Resin Manufacturing and in Pharmaceutical and Medicine Manufacturing | U.S. EPA (2016b), Public comments EPA-HQ-OPPT-2016-0743-0010, EPA-HQ-OPPT-2016-0743-0015, EPA-HQ-OPPT-2016-0743-0017 |
| | | Other | U.S. EPA (2016b) |
| | Incorporated into formulation, mixture or reaction product | Adhesives and sealant chemicals in Adhesive Manufacturing | U.S. EPA (2016b), Market profile EPA-HQ-OPPT-2016-0743, Public comments EPA-HQ-OPPT-2016-0743-0007, EPA-HQ-OPPT-2016-0743-0009, EPA-HQ-OPPT-2016-0743-0011 |
| | | Anti-adhesive agents in Printing and Related Support Activities | U.S. EPA (2016b), Market profile EPA-HQ-OPPT-2016-0743 |
| | | Paint additives and coating additives not described by other codes in Paint and Coating Manufacturing; and Print Ink Manufacturing | U.S. EPA (2016b), Market profile EPA-HQ-OPPT-2016-0743, Public comments EPA-HQ-OPPT-2016-0743-0007, EPA-HQ-OPPT-2016-0743-0009, EPA-HQ-OPPT-2016-0743-0013 |
| | | Plating agents and surface treating agents in Fabricated Metal Product Manufacturing | U.S. EPA (2016b) |
| Processing | Incorporated into formulation, mixture or reaction product | Processing aids, not otherwise listed in Plastic Material and Resin Manufacturing | U.S. EPA (2016b), Public comments EPA-HQ-OPPT-2016-0743-0015, EPA-HQ-OPPT-2016-0743-0017, EPA-HQ-OPPT-2016-0743-0035, EPA-HQ-OPPT-2016-0743-0038 |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| | | Solvents (for cleaning or degreasing) in Non-Metallic Mineral Product Manufacturing; Machinery Manufacturing; Plastic Material and Resin Manufacturing; Primary Metal Manufacturing; Soap, Cleaning Compound and Toilet Preparation Manufacturing; Transportation Equipment Manufacturing; All Other Chemical Product and Preparation Manufacturing; Printing and Related Support Activities; Services; Wholesale and Retail Trade | U.S. EPA (2016b), Market profile EPA-HQ-OPPT-2016-0743, Public comments EPA-HQ-OPPT-2016-0743-0010, EPA-HQ-OPPT-2016-0743-0011, EPA-HQ-OPPT-2016-0743-0027, EPA-HQ-OPPT-2016-0743-0028 |
| | | Solvents (which become part of product formulation or mixture) in Electrical Equipment, Appliance and Component Manufacturing; Other Manufacturing; Paint and Coating Manufacturing; Print Ink Manufacturing; Soap, Cleaning Compound and Toilet Preparation Manufacturing; Transportation Equipment Manufacturing; All Other Chemical Product and Preparation Manufacturing; Printing and Related Support Activities; Wholesale and Retail Trade | U.S. EPA (2016b), Market profile EPA-HQ-OPPT-2016-0743, Public comments EPA-HQ-OPPT-2016-0743-0007, EPA-HQ-OPPT-2016-0743-0009, EPA-HQ-OPPT-2016-0743-0010, EPA-HQ-OPPT-2016-0743-0011, EPA-HQ-OPPT-2016-0743-0019, EPA-HQ-OPPT-2016-0743-0024, EPA-HQ-OPPT-2016-0743-0031, EPA-HQ-OPPT-2016-0743-0034 |
| Processing | Incorporated into formulation, mixture or reaction product | Surface active agents in Soap, Cleaning Compound and Toilet Preparation Manufacturing | U.S. EPA (2016b), Market profile EPA-HQ-OPPT-2016-0743 |
| | | Other uses in Oil and Gas Drilling, Extraction and Support Activities; Plastic Material and Resin Manufacturing; Services | U.S. EPA (2016b), Market profile EPA-HQ-OPPT-2016-0743, Public comment EPA-HQ-OPPT-2016-0743-0016 |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| | Incorporated into article | Lubricants and lubricant additives in Machinery Manufacturing | U.S. EPA (2016b), Market profile EPA-HQ-OPPT-2016-0743 |
| | | Paint additives and coating additives not described by other codes in Transportation Equipment Manufacturing | U.S. EPA (2016b) |
| | | Solvents (which become part of product formulation or mixture), including in Textiles, Apparel and Leather Manufacturing | U.S. EPA (2016b), Market profile EPA-HQ-OPPT-2016-0743, Public comment EPA-HQ-OPPT-2016-0743-0027 |
| | | Other, including in Plastic Product Manufacturing | U.S. EPA (2016b), Market profile EPA-HQ-OPPT-2016-0743; EPA-HQ-OPPT-2016-0743-0067 |
| | Repackaging | Wholesale and Retail Trade | U.S. EPA (2016b) |
| | Recycling | Recycling | U.S. EPA (2017b), U.S. EPA (2016b), Public comments EPA-HQ-OPPT-2016-0743-0017, EPA-HQ-OPPT-2016-0743-0031 |
| Distribution in commerce | Distribution | Distribution in Commerce | U.S. EPA (2017b), U.S. EPA (2016b); Use document EPA-HQ-OPPT-2016-0743-0003 |
| Industrial commercial and consumer use | Paints and coatings | Paint and coating removers | U.S. EPA (2016b), Market profile EPA-HQ-OPPT-2016-0743, Public comments EPA-HQ-OPPT-2016-0743-0008, EPA-HQ-OPPT-2016-0743-0010, EPA-HQ-OPPT-2016-0743-0011, EPA-HQ-OPPT-2016-0743-0018, EPA-HQ-OPPT-2016-0743-0023, EPA-HQ-OPPT-2016-0743-0025, EPA-HQ-OPPT-2016-0743-0035 |
| | | Adhesive removers | Market profile EPA-HQ-OPPT-2016-0743, Public comments EPA-HQ-OPPT-2016-0743- |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| | | | 0011, EPA-HQ-OPPT-2016-0743-0018 |
| | | Lacquers, stains, varnishes, primers and floor finishes | Market profile EPA-HQ-OPPT-2016-0743, Public comments EPA-HQ-OPPT-2016-0743-0018, EPA-HQ-OPPT-2016-0743-0032, EPA-HQ-OPPT-2016-0743-0035 |
| | | Powder coatings (surface preparation) | Market profile EPA-HQ-OPPT-2016-0743, Public comments EPA-HQ-OPPT-2016-0743-0016 |
| | Paint additives and coating additives not described by other codes<br>Paint additives and coating additives not described by other codes | Use in Computer and Electronic Product Manufacturing, Construction, Fabricated Metal Product Manufacturing, Machinery Manufacturing, Other Manufacturing, Paint and Coating Manufacturing, Primary Metal Manufacturing, Transportation Equipment Manufacturing, Wholesale and Retail Trade | U.S. EPA (2016b), Public comments EPA-HQ-OPPT-2016-0743-0006, EPA-HQ-OPPT-2016-0743-0007, EPA-HQ-OPPT-2016-0743-0009, EPA-HQ-OPPT-2016-0743-0011, EPA-HQ-OPPT-2016-0743-0013, EPA-HQ-OPPT-2016-0743-0018, EPA-HQ-OPPT-2016-0743-0019, EPA-HQ-OPPT-2016-0743-0023, EPA-HQ-OPPT-2016-0743-0024, EPA-HQ-OPPT-2016-0743-0027, EPA-HQ-OPPT-2016-0743-0031, EPA-HQ-OPPT-2016-0743-0032, EPA-HQ-OPPT-2016-0743-0035, EPA-HQ-OPPT-2016-0743-0036, EPA-HQ-OPPT-2016-0743-0063; EPA-HQ-OPPT-2016-0743-0064 |
| Industrial commercial and consumer use | Solvents (for cleaning or degreasing) | Use in Electrical Equipment, Appliance and Component Manufacturing. | U.S. EPA (2016b), Public comments EPA-HQ-OPPT-2016-0743-0006, EPA-HQ-OPPT-2016-0743-0007, EPA-HQ-OPPT-2016-0743-0009, EPA-HQ-OPPT-2016-0743-0023, EPA-HQ-OPPT-2016-0743-0024, EPA-HQ-OPPT-2016-0743-0027 |
| | Ink, toner and colorant products | Printer ink | U.S. EPA (2016b), Use document, EPA-HQ-OPPT- |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| | Processing aids, specific to petroleum production<br>Processing aids, specific to petroleum production | | 2016-0743-0003, Public comments EPA-HQ-OPPT-2016-0743-0006, EPA-HQ-OPPT-2016-0743-0016, EPA-HQ-OPPT-2016-0743-0018 |
| | | Inks in writing equipment | U.S. EPA (2016b), Market profile EPA-HQ-OPPT-2016-0743, Public comment EPA-HQ-OPPT-2016-0743-0018 |
| | | Petrochemical Manufacturing | U.S. EPA (2016b), Public comment, EPA-HQ-OPPT-2016-0743-0031 |
| | Adhesives and sealants | Adhesives and sealant chemicals including binding agents | U.S. EPA (2016b), Market profile EPA-HQ-OPPT-2016-0743, Public comments EPA-HQ-OPPT-2016-0743-0006, EPA-HQ-OPPT-2016-0743-0007EPA-HQ-OPPT-2016-0743-0007, EPA-HQ-OPPT-2016-0743-0011EPA-HQ-OPPT-2016-0743-0011, EPA-HQ-OPPT-2016-0743-0016EPA-HQ-OPPT-2016-0743-0016, EPA-HQ-OPPT-2016-0743-0018EPA-HQ-OPPT-2016-0743-0018, EPA-HQ-OPPT-2016-0743-0023 |
| Industrial commercial and consumer use | Adhesives and sealants | Single component glues and adhesives, including lubricant adhesives | U.S. EPA (2016b), Market profile EPA-HQ-OPPT-2016-0743, Public comments EPA-HQ-OPPT-2016-0743-0011, EPA-HQ-OPPT-2016-0743-0018, EPA-HQ-OPPT-2016-0743-0035, EPA-HQ-OPPT-2016-0743-0036 |
| | | Two-component glues and adhesives, including some resins | U.S. EPA (2016b), Market profile EPA-HQ-OPPT-2016-0743, Public comments EPA-HQ-OPPT-2016-0743-0011, EPA-HQ-OPPT-2016-0743-0016, EPA-HQ-OPPT-2016-0743-0018, |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| | | Soldering materials | Market profile EPA-HQ-OPPT-2016-0743, Public comments EPA-HQ-OPPT-2016-0743-0023 |
| | Other uses | Anti-freeze and de-icing products | U.S. EPA (2016b) |
| | | Automotive care products | U.S. EPA (2016b), Public comment, EPA-HQ-OPPT-2016-0743-0035 |
| | | Lubricants and greases | U.S. EPA (2016b) |
| | | Metal products not covered elsewhere | U.S. EPA (2016b), Public comment, EPA-HQ-OPPT-2016-0743-0027, EPA-HQ-OPPT-2016-0743-0028 Public comment, EPA-HQ-OPPT-2016-0743-0027, EPA-HQ-OPPT-2016-0743-0028 |
| | | Laboratory chemicals | U.S. EPA (2016b), Public comments EPA-HQ-OPPT-2016-0743-0007, EPA-HQ-OPPT-2016-0743-0009 |
| Industrial commercial and consumer use | Other uses | Lithium ion batteries | Market profile EPA-HQ-OPPT-2016-0743, Public comment EPA-HQ-OPPT-2016-0743-0005 |
| | | Cleaning and furniture care products, including wood cleaners, gasket removers | Market profile EPA-HQ-OPPT-2016-0743, Public comment EPA-HQ-OPPT-2016-0743-0025, EPA-HQ-OPPT-2016-0743-0035 |
| | | Other uses in Oil and Gas Drilling, Extraction and Support Activities [c] | U.S. EPA (2016b), |
| | | Lubricant and lubricant additives, including hydrophilic coatings | Market profile EPA-HQ-OPPT-2016-0743 |
| | | Fertilizer and other agricultural chemical manufacturing - processing aids and solvents | U.S. EPA (2016b), Public comment EPA-HQ-OPPT-2016-0743-0010, EPA-HQ-OPPT-2016-0743-0036 |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| | | Pharmaceutical and Medicine Manufacturing - functional fluids (closed systems) | U.S. EPA (2016b), Public comment EPA-HQ-OPPT-2016-0743-0031 |
| | | Wood preservatives | Market profile EPA-HQ-OPPT-2016-0743, Public comment EPA-HQ-OPPT-2016-0743-0023 |
| Disposal | Disposal | Industrial pre-treatment | U.S. EPA (2017b) |
| | | Industrial wastewater treatment | |
| | | Publicly owned treatment works (POTW) | U.S. EPA (2017b) |
| | | Underground injection | U.S. EPA (2017b), Public comment EPA-HQ-OPPT-2016-0743-0031 |
| | | Landfill (municipal, hazardous or other land disposal) | |
| | | Emissions to air | |
| | | Incinerators (municipal and hazardous waste) | |

[a] These categories of conditions of use appear in the life cycle diagram, reflect CDR codes and broadly represent NMP conditions of use in industrial and/or commercial settings.
[b] These subcategories reflect more specific uses of NMP.
[c] Industrial use added to reflect the use of NMP in products in the Oil and Gas Drilling, Extraction This addition to the risk evaluation will help ensure that EPA determines whether NMP presents an unreasonable risk "under the conditions of use," TSCA 6(b)(4)(A).

Although the NMP Scope Document indicated that uses assessed in the 2015 risk assessment would not be re-evaluated (EPA-HQ-OPPT-2016-0743), EPA has decided to include these conditions of use in the risk evaluation as described in this problem formulation. EPA is including these conditions of use so that they are part of EPA's determination of whether NMP may present an unreasonable risk "under the conditions of use," TSCA 6(b)(4)(A). EPA has concluded that the Agency's assessment of the potential risks from this widely used chemical will be more robust if the risks from these conditions of use are evaluated by applying the standards and guidance provided under amended TSCA. This includes ensuring the evaluation is consistent with the scientific standards in Section 26 of TSCA, the Procedures for Chemical Risk Evaluation under the Amended Toxic Substances Control Act (40 CFR Part 702) and EPA's supplemental document, *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018). EPA also expects to consider other available hazard and exposure data to ensure that all reasonably available information is taken into consideration. It is important to note that conducting these evaluations does not preclude EPA from finalizing the proposed NMP regulation (82 FR 7464).

### 2.2.2.3 Overview of Conditions of Use and Life Cycle Diagram

The life cycle diagram provided in Figure 2-1 depicts the conditions of use that are considered within the scope of the risk evaluation during various life cycle stages including manufacturing, processing, distribution, use (industrial, commercial, and consumer) and disposal. Additions or changes to conditions of use based on additional information gathered or analyzed during problem formulation are described further in Sections 2.2.2.1 and 2.2.2.2. The information is grouped according to Chemical Data Reporting (CDR) processing codes and use categories (including functional use codes for industrial uses and product categories for industrial, commercial and consumer uses), in combination with other data sources (e.g., published literature and consultation with stakeholders), to provide an overview of conditions of use. EPA notes that some subcategories of use may be grouped under multiple CDR categories.

Use categories include the following: "industrial use" means use at a site at which one or more chemicals or mixtures are manufactured (including imported) or processed. "Commercial use" means the use of a chemical or a mixture containing a chemical (including as part of an article) in a commercial enterprise providing saleable goods or services. "Consumer use" means the use of a chemical or a mixture containing a chemical (including as part of an article, such as furniture or clothing) when sold to or made available to consumers for their use (U.S. EPA, 2016b).

To understand conditions of use relative to one another and the associated exposure potential under those conditions of use, the life cycle diagram includes the production volume associated with each stage of the life cycle, as reported during the 2016 CDR reporting period (U.S. EPA, 2016b), when the volume was not claimed confidential business information (CBI).

The 2016 CDR reporting data for NMP are provided in Table 2-4 from EPA's CDR database. This information has not changed from that provided in the scope document.

**Table 2-4. Production Volume of NMP in CDR Reporting Period (2012 to 2015) [a]**

| Reporting Year | 2012 | 2013 | 2014 | 2015 |
|---|---|---|---|---|
| Total Aggregate Production Volume (lbs) | 164,311,844 | 168,187,596 | 171,095,221 | 160,818,058 |

[a] The CDR data for the 2016 reporting period is available via ChemView (https://java.epa.gov/chemview) (U.S. EPA, 2016b). Because of an ongoing CBI substantiation process required by amended TSCA, the CDR data available in the scope document is more specific than currently in ChemView.

Descriptions of the industrial, commercial and consumer use categories identified from the 2016 CDR (U.S. EPA, 2016b) and included in the life cycle diagram are summarized below. The descriptions provide a brief overview of the use category; Appendix B contains more detailed descriptions (e.g., process descriptions, worker activities, process flow diagrams, equipment illustrations) for each manufacture, processing, use and disposal category. The descriptions provided below are primarily based on the corresponding industrial function category and/or commercial and consumer product category descriptions from the 2016 CDR and can be found in EPA's *Instructions for Reporting 2016 TSCA Chemical Data Reporting* (U.S. EPA, 2016a).

The "**Paints and Coatings**" category encompasses chemical substances contained in products that are used in a variety of coatings including paints, glazes, grouts, hydrophilic coatings, stains and wood preservatives. Removers of paints and coatings also fall into this category. Products in this category

have applications in industrial, commercial and consumer settings and are available in both liquid and aerosol formulations.

The "**Solvents for Cleaning and Degreasing**" category encompasses various chemical substances used to dissolve oil, grease and similar materials from a variety of substrates including metal surfaces, glassware and textiles. This category includes industrial, commercial and consumer uses of NMP for cleaning electrical equipment, gaskets, leather and other textiles, as well as a variety of other substrates. This category also includes chemical substances used as solvents during the production of electronic products and lithium ion batteries. Most NMP formulations in this category are liquid, but aerosol cleaning formulations are also available.

The "**Ink, Toner and Colorant Products**" category encompasses chemical substances that are contained in products used for printer inks and toners. Specifically, NMP can be found as a component of ink thinners, weather resistant markers for polyurethane tags and inks used in 3D printers. NMP is also found in inks used within industrial, commercial and consumer settings, and is typically formulated as a liquid.

The "**Processing Aids, Specific to Petroleum Production**" category encompasses chemical substances which are used to aid in the production of petrochemical, plastic and rubber products. This category is primarily industrial, and formulations are liquid.

The "**Adhesives and Sealants**" category encompasses chemical substances contained in adhesive and sealant products used to fasten other materials together. NMP is used as an adhesive or sealant for a wide variety of products including: pressure-sensitive adhesives, polyurethane curatives, floor sealants and sealants for automotive parts. These products have industrial, commercial and consumer applications and can be found in liquid, solid and aerosol formulations.

The **"Other uses"** category covers a wide variety of products containing NMP, including automotive care products, deicers as well as NMP use in laboratory settings. EPA notes that some of the uses identified for NMP may be considered critical to national security. These uses and their importance to national security will be considered during the risk evaluation, and as part of any resulting regulatory actions the Agency may deem necessary to protect human health and the environment.

Figure 2-1 depicts the life cycle diagram of NMP, from manufacturing to the point of disposal. Activities related to distribution (e.g., loading, unloading) will be considered throughout the NMP life cycle, rather than using a single distribution scenario.

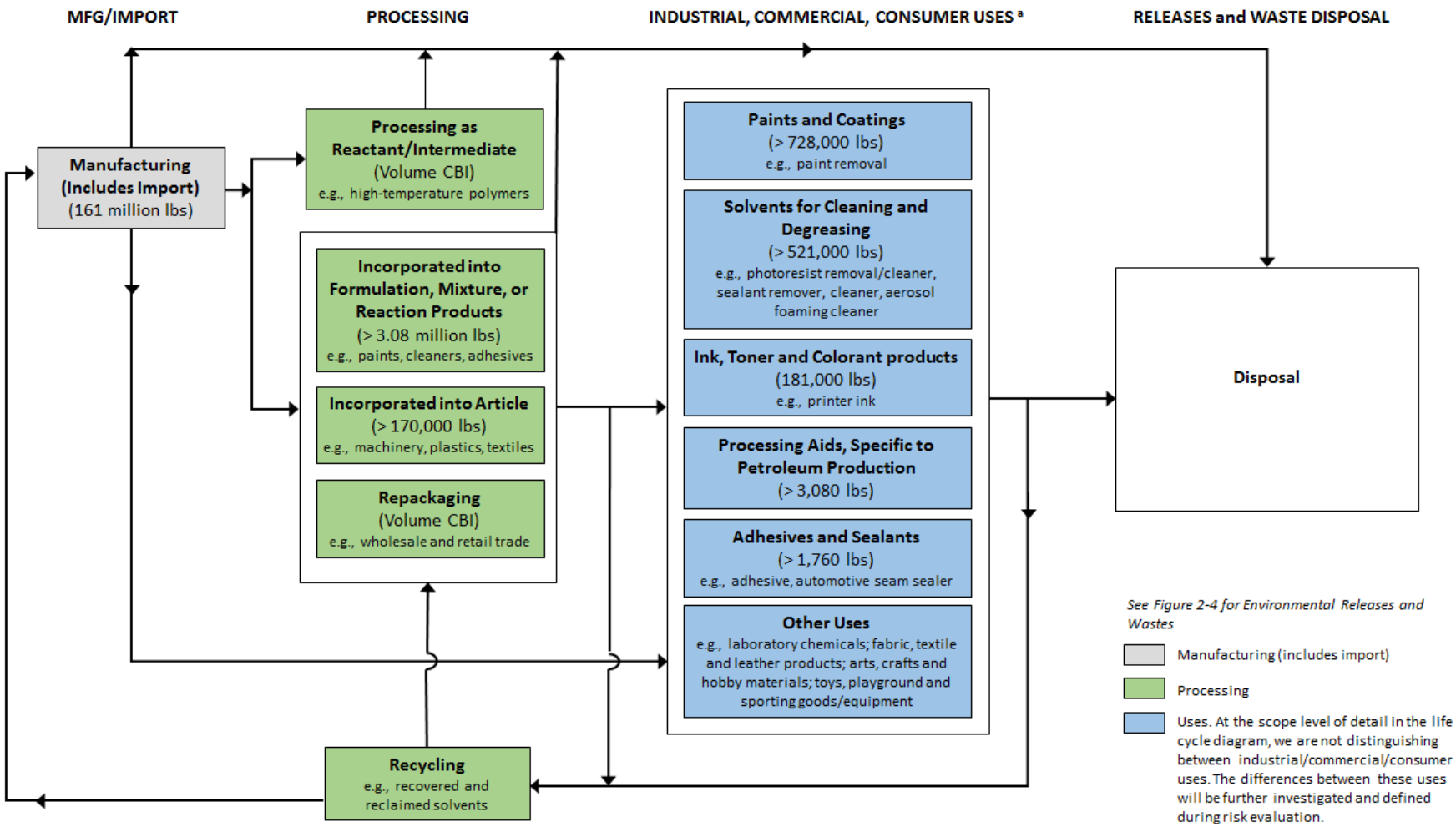


**Figure 2-1. NMP Life Cycle Diagram**

The life cycle diagram depicts the conditions of use that are within the scope of the risk evaluation during various life cycle stages including manufacturing, processing, distribution, use and disposal. The production volumes shown are for reporting year 2015 from the 2016 CDR reporting period (U.S. EPA, 2016b). Activities related to distribution (e.g., loading, unloading) will be considered throughout the NMP life cycle, rather than using a single distribution scenario.

[a] See Table 2-3 for additional uses not mentioned specifically in this diagram.

## 2.3 Exposures

For TSCA exposure assessments, EPA expects to evaluate exposures and releases to the environment resulting from the conditions of use applicable to NMP. Post-release pathways and routes will be described to characterize the relationship or connection between the conditions of use for NMP and the exposure to receptors, including potentially exposed or susceptible subpopulations and ecological receptors. EPA will take into account, where relevant, the duration, intensity (concentration), and frequency of exposures in characterizing exposures to NMP.

### 2.3.1 Fate and Transport

Environmental fate includes both transport and transformation processes. Environmental transport is the movement of the chemical within and between environmental media. Transformation occurs through the degradation or reaction of the chemical with other species in the environment. Hence, knowledge of the environmental fate of the chemical informs the determination of the specific exposure pathways and potential human and ecological receptors EPA expects to consider during risk evaluation. Table 2-5 provides environmental fate data that EPA identified and considered in developing the scope for NMP. This information has not changed from that provided in the scope document.

During problem formulation, fate data including information pertaining to volatilization during wastewater treatment, volatilization from lakes and rivers, biodegradation rates and the organic carbon:water partition coefficient (log $K_{OC}$) were used when considering changes to the conceptual models. Model results and basic principles were used to support the fate data while relevant literature is evaluated via the systematic review process.

EPI Suite™ modules were used to predict volatilization of NMP from wastewater treatment plants, lakes, and rivers (U.S. EPA, 2012b). The EPI Suite™ module that estimates chemical removal in sewage treatment plants ("STP" module) was run using default settings to evaluate the potential for NMP to biodegrade, volatilize to air or adsorb to sludge during wastewater treatment. The STP module, using BIOWIN predictions for biodegradation rates, estimates that most (> 90%) of the NMP releases to wastewater will be removed by biodegradation. BIOWIN model predictions further indicate negligible (< 1%) removal of NMP via adsorption to sludge or volatilization to air.

The EPI Suite™ module that estimates volatilization from lakes and rivers ("Volatilization" module) was run using default settings to evaluate the potential for NMP to volatilize from surface water. The input parameters required for estimating the volatilization (evaporation) rate of an organic chemical from a water body are water depth, wind speed and current velocity of a river or lake. The model results indicate that volatilization from surface water is unlikely to be a significant removal pathway for NMP (U.S. EPA, 2012b). Aerobic biodegradation is expected to be the primary removal pathway for NMP in many surface water environments based on measured data (see Table 2-5).

Experimental data and EPISuite™ model predictions indicate that NMP will degrade in aerobic environments (U.S. EPA, 2012b); however, the BIOWIN module within EPISuite™ that estimates anaerobic biodegradation potential (BIOWIN 7) predicts that NMP will not rapidly biodegrade under anaerobic conditions. These model predictions are consistent with previous NMP assessments (OECD, 2007; WHO, 2001; U.S. EPA, 1998b).

**Table 2-5. Environmental Fate Characteristics of NMP**

| Property or Endpoint | Value [a] | Reference |
|---|---|---|
| Direct photo-degradation | Not available | |
| Indirect photo-degradation | 5.8 hours (estimated for atmospheric degradation) | U.S. EPA (2015) |
| Hydrolysis half-life | Does not undergo hydrolysis | U.S. EPA (2015) |
| Biodegradation | 99% (duration not indicated) (aerobic in water, coupled-units)<br>50% in < 12 days (aerobic in soil)<br>95% removal in 2 weeks (aerobic in static die-away system test, sewage sludge inoculum, OECD 301A)<br>95% in 7 days (SCAS, OECD 303A) | U.S. EPA (1998b) |
| | 73% in 28 days (aerobic in water, Modified Ministry of International Trade and Industry (MITI), OECD 301C)<br>91-97% in 28 days (aerobic, Sturm, OECD 301B)<br>98% in 4 days (aerobic in water and sludge, Zahn-Wellens, OECD 302B)<br>88% in 30 days (closed-bottle test, OECD 301D)<br>99% in 19 days (modified screening, OECD 301E) | U.S. EPA (2015) |
| Bioconcentration factor (BCF) | 3.16 (estimated) | U.S. EPA (2015) |
| Bioaccumulation factor (BAF) | 0.9 (estimated) | U.S. EPA (2012b) |
| Soil organic carbon/water partition coefficient (log $K_{oc}$) | 0.9 (estimated) | U.S. EPA (2012b) |

[a] Measured unless otherwise noted.

NMP does not persist in the environment. Upon release into the atmosphere, it is expected to biodegrade via reaction with photo-chemically produced hydroxyl radicals in ambient air. The half-life for this reaction is approximately 5.8 hours, assuming a hydroxyl radical concentration of $1.5 \times 10^6$ hydroxyl radicals/$cm^3$ air and a 12-hour day (U.S. EPA, 2015). NMP is hygroscopic and can dissolve in water droplets. Atmospheric releases may be removed via condensation, wet deposition or further reaction with hydroxyl radicals.

Although neat (pure) NMP is slightly volatile, volatilization from water and moist soils is not likely based on its Henry's Law constant ($3.2 \times 10^{-9}$ atm $m^3$/mole). NMP is not expected to adsorb to suspended solids or sediment upon release to water due to its estimated soil organic carbon/water partition coefficient (log $K_{oc}$ = 0.9). NMP exhibits high mobility in soil; hence, environmental releases are expected to migrate from soil to ground water (U.S. EPA, 2012b).

NMP exhibits low potential for bioaccumulation in the environment. Measured bioconcentration studies for NMP were not presented in EPA's previous evaluation of risks associated with NMP use in paint and coating removal (U.S. EPA, 2015); however, based on the estimated BAF and BCF values (0.9 and 3.16,

respectively), NMP is not expected to bioaccumulate or bioconcentrate in aquatic organisms (U.S. EPA, 2012b, 1999); OECD, 2007, 3809443}.

### 2.3.2 Releases to the Environment

Releases to the environment from conditions of use (e.g., industrial and commercial processes, commercial or consumer uses resulting in down-the-drain releases) are one component of potential exposure and may be derived from reported data that are obtained through direct measurement, calculations based on empirical data and/or assumptions and models.

A source of information EPA expects to consider for evaluating exposures are data reported under the Toxics Release Inventory (TRI) program. Under the Emergency Planning and Community Right-to-Know Act (EPCRA) Section 313, NMP is a TRI-reportable substance effective January 1, 1995. During problem formulation EPA further analyzed the TRI data and examined the definitions of elements in the TRI data to determine the level of confidence that a release would result from specific types of disposal to land (e.g., RCRA Subtitle C hazardous landfill and Class I underground Injection wells) and incineration. EPA also examined how NMP is treated at industrial facilities.

Table 2-6 provides production-related waste management data (also referred to as waste managed) for NMP reported by industrial facilities to the TRI program for 2015. Table 2-7 provides more detailed information on the actual quantities of NMP released to air and water or disposed of on land.

**Table 2-6. Summary of NMP TRI Production-Related Waste Managed in 2015 (lbs)**

| Number of Facilities | Recycling | Energy Recovery | Treatment | Releases [a, b, c] | Total Production Related Waste |
|---|---|---|---|---|---|
| 386 | 47,453,751 | 7,603,919 | 14,944,336 | 8,807,902 | 78,819,909 |

Data source: 2015 TRI Data (updated March 2017) (U.S. EPA, 2017b).
[a] Terminology used in these columns may not match the more detailed data element names used in the TRI public data and analysis access points.
[b] Does not include releases due to a one-time event not associated with production such as remedial actions or earthquakes.
[c] Counts all releases including release quantities transferred and those disposed of by a receiving facility reporting to TRI.

In 2015, 386 facilities reported a total of 78.8 million pounds of NMP waste managed. Of this total, over 47.5 million pounds of NMP were recycled; 34 TRI facilities reported recycling NMP on-site and 85 facilities reported distribution of NMP off-site for recycling, representing approximately 60% of the total waste managed. In addition, approximately 7.6 million pounds of NMP was used for energy recovery; 14.9 million pounds were treated and 8.8 million pounds were released to the environment.

**Table 2-7. Summary of NMP TRI Releases to the Environment in 2015 (lbs)**

| | | Air Releases | | | Land Disposal | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Number of Facilities | Stack Air Releases | Fugitive Air Releases | Water Releases | Class I Under-ground Injection | RCRA [a] Subtitle C Landfills | All other Land Disposal [b] | Other Releases [b] | Total Releases [c] |
| Subtotal | | 884,851 | 542,101 | | 3,625,939 | 93,217 | 2,719,441 | | |
| Total | 386 | 1,426,952 | | 14,092 | 6,438,597 | | | 28,099 | 8,108,070 |

Data source: 2015 TRI Data (updated March 2017) (U.S. EPA, 2017b).
[a] RCRA (Resource Conservation and Recovery Act)

| | Number of Facilities | Air Releases | | Water Releases | Land Disposal | | | Other Releases [b] | Total Releases [c] |
|---|---|---|---|---|---|---|---|---|---|
| | | Stack Air Releases | Fugitive Air Releases | | Class I Under-ground Injection | RCRA [a] Subtitle C Landfills | All other Land Disposal [b] | | |

[b] Terminology used in these columns may not match the more detailed data element names used in the TRI public data and analysis access points.
[c] These release quantities do include releases due to one-time events not associated with production such as remedial actions or earthquakes.

Roughly 79% (~ 6.4 million pounds) of the environmental releases reported for NMP in 2015 were to land, 18% (~ 1.4 million pounds) were to air (stack and fugitive emissions), and 0.2% (~14,000 pounds) were discharged to water (Table 2-7). The stack releases reported to TRI represent the total amount of NMP air releases from stacks, confined vents, ducts, pipes or other confined air streams. Many facilities reported stack air releases from NMP destruction via incineration, including hazardous waste facilities and facilities that perform other industrial activities (i.e., federal, state or municipal). These estimates likely represent decomposition products, as NMP destruction via incineration is highly efficient.

Most of the on-site land disposal reported for NMP in 2015 was to Class I underground injection wells (~ 3.6 million pounds). Only 13 pounds went to on-site landfills other than RCRA Subtitle C Landfills and other land disposal. No NMP was reported as disposed on-site in Class II-V underground injection wells, on-site land treatment, or on-site surface impoundments. Most off-site releases (~ 2.7 million pounds) went to landfills other than RCRA Subtitle C Landfills. Other release amounts were reported as transfers to RCRA Subtitle C Landfills (~ 93,217 pounds), other land disposal types (~ 25,648 pounds) and off-site land treatment (~ 330 pounds).

While the production-related waste managed shown in Table 2-6 excludes any quantities reported as catastrophic or one-time releases (TRI Section 8 data), release quantities shown in Table 2-7 include both production-related and non-routine quantities (TRI Section 5 and 6 data). As a result, release quantities may differ slightly and may further reflect differences in TRI calculation methods for reported release range estimates (U.S. EPA, 2016c).

EPA is aware of additional sources of information for NMP release data, such as assessments from other countries. and the Discharge Monitoring Report (DMR) Pollutant Loading Tool, which provides additional information on releases to surface water. For example, the 2011 European Chemicals Agency (ECHA) Dossier on the identification of NMP as a substance of very high concern includes a compilation of the conditions of use for NMP, along with some discussion of potential sources of environmental release information. The DMR loading tool calculates pollutant loadings from permit and DMR data from EPA's Integrated Compliance Information System for the National Pollutant Discharge Elimination System. The limited DMR data available for NMP will be further analyzed during risk evaluation.

### 2.3.3 Presence in the Environment and Biota

Monitoring studies or a collection of relevant and reliable monitoring studies provide(s) information that can be used in an exposure assessment. Monitoring studies that measure environmental concentrations or concentrations of chemical substances in biota provide evidence of exposure. Limited environmental monitoring data were identified in EPA's data search for NMP.

EPA has developed an electronic STOrage and RETrieval system for water quality monitoring data known as STORET, which maps monitoring sites and allows for download of sampling data of surface water monitoring sites (U.S. EPA, 2012c). In addition, the Water Quality Portal, a cooperative service sponsored by the U.S. Geological Survey (USGS), EPA and the National Water Quality Monitoring Council (NWQMC, 2017) provide both STORET data and surface water and ground water monitoring data from USGS. An initial search within the STORET system listed NMP as a sampled parameter, but did not include any site-specific information for NMP (NWQMC, 2017).

NMP has been detected in industrial landfill leachate (Danish EPA, 2015). Although it is not currently subject to any proposed or promulgated water regulations, NMP has been detected in wastewater (WHO, 2001) and is included on EPA's Drinking Water Contaminant Candidate Lists (CCL) 3 and 4 because it is a suspected contaminant in public water systems that may require regulation under the Safe Drinking Water Act (SDWA) (74 FR 51850, October 8, 2009 and 81 FR 81099 November 16, 2016).

The Air Quality System contains air pollution monitoring data collected by EPA, as well as state, local and tribal agencies. A preliminary search of this database revealed that NMP is not a pollutant included in national, state or tribal ambient air monitoring programs.

According to the Environment Canada and Health Canada Draft Screening Assessment, NMP has been monitored in indoor air samples in Canada. NMP air concentrations associated with carpet and rubber-based flooring were reported in a Canadian study on indoor air releases from building materials and furnishings. NMP also was detected in air and dust samples collected from homes during a field study in Quebec (EC/HC, 2017).

### 2.3.4 Environmental Exposures

The manufacturing, processing, distribution, use and disposal of NMP can result in releases to the environment. In this section, EPA presents exposures to aquatic and terrestrial organisms.

***Aquatic Exposures***

EPA did not identify water monitoring data for NMP during its review of the national surface water monitoring database. The 2015 TRI data on direct and indirect environmental releases were used to estimate NMP concentrations in surface water. Direct releases represent environmental releases of NMP that are discharged directly from a facility into a receiving water body (after treatment), whereas indirect releases represent discharges to surface water that occur following treatment at a municipal wastewater facility.

To capture "high-end" surface water concentrations, EPA compiled the release data for six facilities that reported the largest NMP direct water releases. This represented > 99% of the total volume of NMP reported as a direct discharge to surface water during the 2015 TRI reporting period. Since there were many more facilities reporting indirect releases of NMP to surface water, seven of the facilities reporting the largest indirect water releases (representing ~ 11% of the total number of facilities reporting indirect discharges) were compiled. The volume of NMP released from these facilities encompassed more than 68% of the total volume of NMP reported as an indirect discharge to surface water (see Appendix C).

For problem formulation, EPA used release data reported in the 2015 TRI to predict surface water concentrations near the associated reporting facilities. To examine whether (near-facility) surface water concentrations may present a risk concern for aquatic organisms, EPA employed a first-tier screening approach, utilizing readily-available data, modeling tools and conservative assumptions.

EPA's Probabilistic Dilution Model (PDM) was used to estimate site-specific surface water concentrations based on the 2015 TRI data for "on-site" NMP releases to surface waters (U.S. EPA, 2007). The reported TRI releases were based on available information including monitoring data, emission factors, mass balance and/or other engineering calculations. The PDM also incorporates wastewater treatment removal efficiency. For this analysis, wastewater treatment removal efficiency was conservatively assumed to be 0%, as the reported NMP water releases were assumed to account for wastewater treatment *a priori*. Further, as the total days of release were not reported in these sources, EPA assumed a range of possible release days (i.e., 12 and 250 days/year) for facilities directly discharging NMP to surface water and 250 days/year for indirect discharges from wastewater treatment plants or Publicly Owned Treatment Works (POTWs) receiving indirect discharges of NMP).

The "high-end" surface water concentrations (i.e., those obtained assuming a low stream flow for the receiving water body) from all PDM runs ranged from 224 µg/L to 0.00005 µg/L, for the acute (i.e., assumed fewer than 20 days of environmental releases per year) and chronic exposure scenario (i.e., more than 20 days of environmental releases per year assumed), respectively. The maximum acute scenario concentration was 224 µg/L and the maximum chronic scenario concentration was 11 µg/L. For a full table of results, see Table_Apx C-1 in Appendix C.

***Terrestrial Exposures***

Terrestrial populations living near industrial and commercial facilities that use NMP may be exposed via multiple routes. EPA did not identify monitoring data for NMP releases to the environment; however, the 2015 TRI data indicate that most of the reported releases were landfilled or injected underground.

### 2.3.5 Human Exposures

In this section EPA presents information on occupational, consumer and general population exposures. Subpopulations within these exposed groups, including potentially exposed or susceptible subpopulations, are also presented.

#### 2.3.5.1 Occupational Exposures

Exposure pathways and exposure routes are listed below for worker activities under the various conditions of use (industrial or commercial) described in Section 2.2. In addition, exposures to occupational non-users (i.e., individuals who do not directly handle NMP, but perform work in an area where it is present) are also listed. Engineering controls and/or personal protective equipment may impact occupational exposure levels.

In the previous risk assessment (U.S. EPA, 2015), EPA assessed dermal and inhalation exposures associated with occupational use of NMP in paint and coating removal. These uses and exposure pathways will be further considered during risk evaluation.

Workers and occupational non-users may be exposed to NMP when performing activities associated with the conditions of use described in Section 2.2 including, but not limited to:

- Unloading and transferring NMP to and from storage containers to process vessels;
- Using NMP in process equipment (e.g., applying photoresists during silicon wafer production);
- Applying formulations and products containing NMP onto substrates (e.g., applying adhesives, sealants and NMP-containing products that facilitate their removal);
- Cleaning and maintaining equipment;
- Sampling chemical formulations or products containing NMP for quality control
- Repackaging chemical formulations or products containing NMP

- Handling, transporting and disposing wastes containing NMP;
- Performing other work activities in or near areas where NMP is used.

***Key Data***
Key data that inform occupational exposure assessment include the Occupational Safety and Health Administration (OSHA) Chemical Exposure Health Data (CEHD) and National Institute for Occupational Safety and Health (NIOSH) Health Hazard Evaluation (HHE) program data. OSHA data are workplace monitoring data from OSHA inspections. OSHA data can be obtained through CEHD https://www.osha.gov/opengov/healthsamples.html. Table_Apx B-1and Table_Apx B-2 in Appendix B provide a summary of the monitoring data available for NMP (air samples obtained from OSHA inspections conducted between 2011 and 2016). NIOSH HHEs are conducted at the request of employees, union officials, or employers and help inform potential hazards at the workplace. HHEs can be downloaded at https://www.cdc.gov/niosh/hhe/. Table_Apx B-3 provides a summary of the NMP air monitoring data obtained from NIOSH HHEs. EPA will review these data and evaluate their utility during risk evaluation.

There is a potential for dermal and inhalation exposures to NMP in the workplace (including contact with liquid, aerosol mist and vapor forms of NMP)**.** OSHA has not established regulatory exposure limits for NMP. The only recommended exposure limit identified for NMP is a non-regulatory limit established by the American Industrial Hygiene Association (AIHA): a workplace environmental exposure level (WEEL) of 10 ppm as an 8-hour (hr) time weighted average (TWA), with the addition of a cautionary note addressing concerns for skin contact. Additional information can be obtained at https://www.tera.org/OARS/WEEL.html.

***Dermal***
Based on the occupational exposure scenarios identified in Table 2-3, EPA expects a potential for worker exposure via skin contact with NMP (liquid, vapor, mist or dust). Because NMP is readily absorbed through the skin, dermal exposures can significantly impact body burden. Dermal exposure is therefore expected to be an important pathway for workers and occupational non-users (i.e., vapor-through-skin exposure).

***Inhalation***
Although NMP has a relatively low vapor pressure, some conditions of use identified in Table 2-3 may present a concern for inhalation exposure to workers and occupational non-users, particularly those that involve vaporization or spray application. Exposures can also occur from NMP (i.e., vapor, mist, dust) that deposits in the upper respiratory tract. Because NMP is expected to be rapidly absorbed at the point of contact, materials deposited in the upper airway will be considered as an inhalation exposure.

#### 2.3.5.2 Consumer Exposures

NMP can be found in consumer products and/or commercial products that are readily available for purchase at common retailers (EPA-HQ-OPPT-2016-0743-0003, Sections 3 and 4 and Table 2-3) and can therefore result in exposures to consumers and bystanders (non-users who are incidentally exposed to NMP as a result of consumer product use).

In the previous risk assessment (U.S. EPA, 2015), EPA investigated dermal and inhalation exposures from consumer use of NMP-containing products during paint and coating removal. EPA modeled exposures to consumers and bystanders using a variety of indoor exposure scenarios that varied specific input parameters including (but not limited to) the product formulation (NMP weight fraction), method

of application (i.e., brush vs. spray), and duration of use (U.S. EPA, 2015). The conditions of use assessed in the previous NMP assessment will be further considered during risk evaluation.

***Dermal***
EPA expects dermal exposure to be a significant route of exposure for consumers and bystanders. Dermal exposure to consumers may occur from direct contact with NMP-containing liquids or from deposition onto skin (e.g., vapor, mist or dust). Direct skin contact with NMP-containing liquids could be concurrent with vapor-through-skin exposures for some conditions of use, particularly those that involve heating or spray application. The frequency/duration and extent of exposure (i.e., surface area of exposed skin) are expected to significantly impact body burden. Bystanders are not expected to have direct contact with NMP-containing liquids, but may be exposed via skin deposition.

***Inhalation***
Although NMP has a low vapor pressure, there is potential for inhalation exposure to consumers and bystanders during heating or spray application of products that contain NMP. Exposures to consumers and bystanders may also occur through ingestion of airborne materials that deposit in the upper respiratory tract. EPA assumes these exposures are absorbed via inhalation.

***Oral***
There is potential for oral exposure to consumers from contact with NMP-containing products via hand-to-mouth activity. Mouthing behaviors may also be an important consideration, especially for children. The frequency and duration of these activities and the NMP content in related products can significantly impact exposure potential. During risk evaluation. EPA expects to further analyze oral exposures to consumers that may result from incidental ingestion of NMP during use of formulations, products or other articles that contain NMP (e.g., children's toys, arts and crafts kits, games, bedding, textiles, and kitchenware).

EPA's previous assessment of NMP use in paint and coating removal did not include an evaluation of oral exposure to consumers, which may have resulted in an underestimation of the total exposure potential for this population. During problem formulation, EPA reviewed publicly available consumer product data (e.g., the Centers for Disease Control Household Database and the Chemical and Product Categories database). Based on the use categories listed in Table 2-3, a table of preliminary exposure scenarios was developed to map the associated conditions of use and exposure pathways identified for NMP (see Appendix Table_Apx E-1. Supporting Table for Consumer Activities and Uses Conceptual Model).

#### 2.3.5.3 General Population Exposures

Wastewater/liquid wastes, solid wastes or air emissions of NMP could result in potential pathways for oral, dermal or inhalation exposure to the general population

***Oral***
Oral exposure to NMP is expected to be a relevant route of exposure for the general population. Individuals may be exposed to NMP levels that occur in drinking water and/or well water. EPA was unable to locate monitoring data for NMP levels in the ambient environment; however, wet deposition from air could be a significant (air-to-ground) removal pathway. NMP exhibits high mobility in soil; environmental releases are ultimately expected to migrate to water.

***Dermal***
General population exposure to NMP may occur through dermal contact with NMP concentrations in drinking water and/or well water during bathing, or from public recreation in impacted waterways.

***Inhalation***
Inhalation is expected to be a relevant route of exposure for the general population due to the propensity for NMP air releases from ongoing commercial and industrial activities. Limited information was identified for air emissions resulting from NMP use in industrial operations.

#### 2.3.5.4 Potentially Exposed or Susceptible Subpopulations

TSCA requires the determination of whether a chemical substance presents an unreasonable risk to "a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation" by EPA. TSCA § 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." General population is "the total of individuals inhabiting an area or making up a whole group" and refers here to the U.S. general population (U.S. EPA, 2011).

As part of problem formulation, EPA identified potentially exposed or susceptible subpopulations for further analysis during the development and refinement of the conceptual models, exposure scenarios and analysis plan. In this section, EPA addresses the potentially exposed or susceptible subpopulations identified as relevant based on greater exposure. EPA will address the subpopulations identified as relevant based on greater susceptibility in the hazard section.

EPA identifies the following as potentially exposed or susceptible subpopulations that EPA expects to consider in the risk evaluation due to their *greater exposure*:

- Workers and occupational non-users;
- Consumers and bystanders associated with consumer use. NMP has been identified in products available to consumers; however, only some individuals within the general population may use these products. Therefore, those who do use these products represent a potentially exposed or susceptible subpopulation due to greater exposure.
- Other groups of individuals within the general population who may experience greater exposures due to their proximity to conditions of use identified in Section 2.2 that result in releases to the environment and subsequent exposures (e.g., individuals who live or work near manufacturing, processing, use or disposal sites).

In developing exposure scenarios, EPA will analyze available data to ascertain whether some human receptor groups may be exposed via pathways that may be distinct to a particular subpopulation or life stage and whether some human receptor groups may have higher exposure via identified pathways of exposure due to unique characteristics (e.g., activities, duration or location of exposure) when compared with the general population (U.S. EPA, 2006b).

In summary, in the risk evaluation for NMP, EPA expects to analyze the following potentially exposed groups of human receptors: workers, occupational non-users, consumers, bystanders associated with consumer use and other groups of individuals within the general population who may experience greater

exposure. EPA may also identify additional potentially exposed or susceptible subpopulations that will be considered based on greater exposure.

## 2.4 Hazards (Effects)

For scoping, EPA conducted comprehensive searches for data on hazards of NMP, as described in the *Strategy for Conducting Literature Searches for NMP: Supplemental File for the TSCA Scope Document* EPA-HQ-OPPT-2016-0743). Based on initial screening, EPA expects to analyze the hazards of NMP identified in this problem formulation document. However, when conducting the risk evaluation, the relevance of each hazard within the context of a specific exposure scenario will be judged for appropriateness. For example, hazards that occur only as a result of chronic exposures may not be applicable to acute exposure scenarios. Thus it is unlikely that all identified hazards will be considered for every exposure scenario.

### 2.4.1 Environmental Hazards

EPA identified the following sources of environmental hazard data for NMP: U.S. EPA (2006a), OECD (2007), (U.S. EPA, 2015), (Danish EPA, 2015), EC/HC (2017) and Ecological Hazard Literature Search Results in the *NMP (CASRN 872-50-4) Bibliography: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0743). Only the *on-topic* references listed in the Ecological Hazard Literature Search Results were considered as potentially relevant data/information sources for the risk evaluation. Inclusion criteria were used to screen the results of the ECOTOX literature search (as explained in the *Strategy for Conducting Literature Searches for NMP: Supplemental Document to the TSCA Scope* document, *CASRN 872-50-4*). Data from the screened literature are summarized below (**Table 2-8**) as ranges (min-max). EPA expects to review these data/information sources during risk evaluation using the data quality review evaluation metrics and the rating criteria described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018).

***Acute Toxicity to Aquatic Organisms***

The acute 96-hour $LC_{50}$ values reported for fish range from >500 mg/L Rainbow trout (*Oncorhynchus* mykiss) to 4,030 mg/L for Orfe (*Leuciscus idus*). Four acute toxicity studies with aquatic invertebrates have been identified; two used the water flea and two studies used grass shrimp as the test species. The 48-hr $EC_{50}$ for water fleas ranged from 1.23 to 4,897 mg/L, whereas the reported 48-hr $EC_{50}$ for grass shrimp ranged from > 299 to 1,107 mg/L. For green algae, the 72-hr $EC_{50}$ values ranged from > 500 to 600.5 mg/L.

***Chronic Toxicity to Aquatic Invertebrates***

Chronic aquatic toxicity data are available for NMP. From a 21-day study with *Daphnia magna*, the chronic toxicity value was calculated as 17.68 mg/L based on reproduction (using the NOEC value of 12.5 mg/L and the LOEC value of 25 mg/L).

***Toxicity to Sediment and Terrestrial Organisms***

EPA did not identify data on NMP hazards to sediment invertebrates, or terrestrial organisms including soil invertebrates; however, based on the physical-chemical and fate properties of NMP, accumulation in these environmental compartments is unlikely (see Section 2.3.1). NMP exposure to soil- or sediment-dwelling organisms is not expected to be significant; therefore, hazards to these organisms will not be analyzed further during risk evaluation (see Section 2.3.4).

**Table 2-8. Ecological Hazard Characterization of NMP**

| Duration | Test organism | Endpoint | Hazard value* | Units | Effect Endpoint | Reference |
|---|---|---|---|---|---|---|
| **Aquatic Organisms** | | | | | | |
| **Acute** | Fish | $LC_{50}$ | >500-4030 | mg/L | Mortality | (BASF, 1983) as cited in OECD (2009b); (BASF, 1986) as cited in OECD (2009b) |
| | Aquatic invertebrates | $EC_{50}$ | 1.23 - 4897 | mg/L | Immobilization | Lan et al. (2004); GAF (1979) as cited in OECD (2009b) |
| | Algae | $EC_{50}$ | > 500-600.5 | mg/L | Growth | (ECHA, 2014b) |
| | Acute COC | 0.246 mg/L | | | | |
| **Chronic** | Fish | ChV | - | mg/L | | |
| | Aquatic invertebrates | NOEC<br>LOEC<br>ChV | 12.5<br>25<br>17.68 | mg/L | Reproduction | BASF AG (2001) as cited in OECD (2009b) |
| | Algae | ChV | 125 (NOEC) | mg/L | | (ECHA, 2014b) |
| | Chronic COC | 1.768 mg/L | | | | |
| **Terrestrial Organisms** | | | | | | |
| Acute | Avian | LD50 | 2500-5000 | mg/kg-bw | Mortality | Hazelton Lab (1980) as cited in OECD (2009b) |

* Values in the tables are presented as reported by the study authors; - = endpoint not addressed

***Concentrations of Concern***

The screening-level acute and chronic concentrations of concern (COCs) for NMP were derived based on the lowest or most toxic ecological toxicity values (e.g., L/EC50). The information below describes how the acute and chronic COC's were calculated for environmental toxicity of NMP using assessment factors.

The application of assessment factors is based on established EPA/OPPT methods (U.S. EPA, 2013, 2012d) and were used in this hazard assessment to calculate lower bound effect levels (referred to as the concentration of concern; COC) that would likely encompass more sensitive species not specifically represented by the available experimental data. Also, assessment factors are included in the COC calculation to account for differences in inter- and intraspecies variability, as well as laboratory-to-field variability. It should be noted that these assessment factors are dependent upon the availability of datasets that can be used to characterize relative sensitivities across multiple species within a given taxa or species group, but are often standardized in risk assessments conducted under TSCA, since the data available for most industrial chemicals is limited.

The concentrations of concern for each endpoint were derived based on the ecological hazard data for NMP. The information below describes how the acute and chronic COCs were calculated for aquatic toxicity.

The acute COC is derived by dividing the aquatic invertebrates 48-hr EC50 of 1.23 mg/L (the lowest acute value in the dataset) by an assessment factor of 5:

- Lowest acute value for 48-hr aquatic invertebrates EC50 (1.23 mg/L)/5 = 0.246 mg/L (246 µg/L)

The acute COC of 246 µg/L, derived from the experimental aquatic invertebrate endpoint, is used as a conservative hazard level for NMP in this problem formulation.

The chronic COC was determined based on the lowest chronic toxicity value divided by an assessment factor of 10:

- Lowest chronic value for (21-day) Daphnia = 17.68 mg/L/10 = 1.768 mg/L (1,768 µg/L)

The chronic COC of 1,768 µg/L, derived from the experimental aquatic invertebrate endpoint, is used as the lower bound hazard level for NMP in this problem formulation.

### 2.4.2 Human Health Hazards

EPA recently published a risk assessment on NMP use in paint and coating removal, hence many of the hazards of NMP exposure have been compiled and reviewed (U.S. EPA, 2015). EPA relied heavily on this comprehensive review in preparing the current problem formulation document. Numerous human health hazards have been identified for NMP including adverse effects on hepatic, renal, immune, reproductive/developmental and central nervous systems (RIVM, 2013; OECD, 2007; WHO, 2001). EPA expects to use the previous review as a starting point for identifying both key and supporting studies that will be used to inform hazard characterization, including dose-response analysis. The relevant studies will be evaluated using the data quality criteria in the *Application of Systematic Review in TSCA Risk Evaluations* document (U.S. EPA, 2018). EPA also expects to consider studies that have been published since this review, as identified in the literature search conducted by the Agency (*NMP (CASRN 872-50-4) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0743). Based on reasonably available information, the following sections briefly describe the potential hazards that may be associated with NMP exposure.

#### 2.4.2.1 Non-Cancer Hazards

***Irritation and Sensitization***

NMP is a skin, eye and possible respiratory irritant. Although the available sensitization data have significant limitations, there are multiple studies of NMP in humans with no reports of sensitization following NMP exposure (RIVM, 2013).

***Acute Toxicity***

The acute toxicity of NMP is expected to be low based on results from laboratory animal studies including oral, dermal, inhalation, intraperitoneal and intravenous routes of exposure in rats and mice (RIVM, 2013; OECD, 2007; WHO, 2001).

***Systemic Effects***

Systemic effects observed following oral repeated-dose toxicity testing include body weight reductions, alterations in hematology and clinical chemistry parameters, liver and kidney toxicity, neurotoxicity and thymic atrophy. More severe effects have been noted following whole-body inhalation exposure (which includes dermal and oral uptake), including bone marrow hypoplasia, testicular effects, necrosis of lymphoid tissue (observed in the thymus, spleen and lymph nodes) and mortality (RIVM, 2013; OECD, 2007; WHO, 2001).

***Reproductive/Developmental Toxicity***

A continuum of biologically relevant reproductive/developmental effects have been reported following NMP exposure (e.g., decreased fetal and pup body weight, delayed ossification, skeletal malformations

and increased fetal and pup mortality). EPA previously identified reproductive/developmental effects as sensitive endpoints for evaluating the human health risks associated with NMP exposure U.S. EPA (2015).

#### 2.4.2.2 Genotoxicity and Cancer Hazards

NMP is not mutagenic, based on results from bacterial and mammalian *in vitro* tests and *in vivo* systems and is not considered to be carcinogenic (RIVM, 2013; OECD, 2007; WHO, 2001).

Unless new information indicates otherwise, EPA does not expect to conduct additional in-depth analysis of genotoxicity and cancer hazards during risk evaluation.

#### 2.4.2.3 Potentially Exposed or Susceptible Subpopulations

TSCA requires that the determination of whether a chemical substance presents an unreasonable risk include consideration of unreasonable risk to "a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation" by EPA. TSCA § 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." In developing the hazard assessment, EPA will analyze available data to ascertain whether some human receptor groups may have greater susceptibility than the general population to the chemical's hazard(s). In the previous risk assessment (U.S. EPA, 2015), EPA identified young children and pregnant women as potentially susceptible subpopulations.

## 2.5 Conceptual Models

EPA risk assessment guidance (U.S. EPA, 2014, 1998c), defines problem formulation as the part of the risk assessment framework that identifies the major factors to be considered in the assessment. It draws from the regulatory, decision-making and policy context of the assessment and informs the assessment's technical approach.

A conceptual model describes the actual or predicted relationships between the chemical substance and receptors, either human or environmental. These conceptual models are integrated depictions of the conditions of use, exposures (pathways and routes), hazards and receptors. The initial conceptual models describing the scope of the assessment for NMP, have been refined during problem formulation. The changes to the conceptual models in this problem formulation are described along with the rationales.

In this section EPA outlines those pathways that will be included and further analyzed in the risk evaluation; will be included but will not be further analyzed in risk evaluation; and will not be included in the TSCA risk evaluation; and the underlying rationale for these decisions.

EPA determined as part of problem formulation that it is not necessary to conduct further analysis on certain exposure pathways that were identified in the NMP Scope Document (EPA-HQ-OPPT-2016-0743) and that remain in the risk evaluation. Each risk evaluation will be "fit-for-purpose," meaning not all conditions of use will warrant the same level of evaluation and the Agency may be able to reach some conclusions without extensive or quantitative risk evaluations 82 FR 33726, 33734, 33739 (July 20, 2017).

As part of this problem formulation, EPA identified exposure pathways under regulatory programs of other environmental statutes, administered by EPA, which adequately assess and effectively manage

exposures and for which long-standing regulatory and analytical processes already exist, i.e., the Safe Drinking Water Act (SDWA) and the Resource Conservation and Recovery Act (RCRA). OPPT worked closely with the offices within EPA that administer and implement the regulatory programs under these statutes. In some cases, EPA has determined that chemicals present in various media pathways (i.e., air, water, land) fall under the jurisdiction of existing regulatory programs and associated analytical processes carried out under other EPA-administered statutes and have been assessed and effectively managed under those programs. EPA believes the TSCA risk evaluation should generally focus on those exposure pathways associated with TSCA conditions of use that are not adequately assessed and effectively managed under the regulatory regimes discussed above because these pathways are likely to represent the greatest areas of risk concern. As a result, EPA does not expect to include in the risk evaluation certain exposure pathways identified in the NMP scope document.

### 2.5.1 Conceptual Model for Industrial and Commercial Activities and Uses: Potential Exposures and Hazards

The revised conceptual model (Figure 2-2) describes the pathways of exposure from industrial and commercial activities and uses of NMP that EPA expects to include in the risk evaluation. There is a potential for inhalation and dermal exposure to workers during manufacturing, processing, use and disposal of NMP. Inhalation and vapor-through-skin exposures are also possible for occupational non-users, particularly with conditions of use that involve heating or spray application.

Dermal exposure is expected to be a major route of concern in occupational settings; however, there is a potential for inhalation exposure with some conditions of use that involve heating or spray application. EPA expects to evaluate dermal and inhalation risks to workers and occupational non-users exposed during manufacturing, processing, distribution, use and disposal of NMP.

***Inhalation***

EPA's previous assessment of NMP use in paint and coating removal identified inhalation as a route of concern for occupational exposure U.S. EPA (2015). NMP is well absorbed from the respiratory tract (Akesson and Paulsson, 1997), but has a low vapor pressure which effectively limits inhalation potential. Lung uptake is directly related to the NMP air concentration and duration of exposure. EPA expects that inhalation exposure may be significant for some conditions of use identified in Table 2-3, particularly those that involve heating or spray application. Incidental ingestion of inhaled NMP (vapor/mist/dust) will be considered as an inhalation exposure. EPA expects to further analyze inhalation exposures to workers and occupational non-users during risk evaluation.

***Dermal***

EPA's previous assessment identified dermal contact as a major route of concern for NMP U.S. EPA (2015). For workers, dermal exposures would be concurrent with inhalation exposures and NMP is well absorbed; therefore, dermal contact (e.g., liquid, vapor, mist, dust) is expected to significantly impact body burden (Bader et al., 2008; Keener et al., 2007). Because occupational non-users would not handle NMP directly, EPA does not expect to further analyze dermal exposure via liquid contact. During risk evaluation, EPA expects to further analyze dermal exposures to workers from skin contact with NMP (e.g., liquid, vapor, mist, dust) and vapor-through-skin contact in occupational non-users.

The Occupational Safety and Health Administration (OSHA) has not established regulatory exposure limits for NMP. The only recommended exposure limit identified is a non-regulatory limit established by the AIHA: a workplace environmental exposure level (WEEL) of 10 ppm as an 8-hr time weighted average (TWA), with the addition of a cautionary note addressing concerns for skin contact (AIHA,

2011). EPA expects to further analyze dermal exposure to workers and occupational non-users during risk evaluation.

***Waste Handling, Treatment and Disposal***

Figure 2-2 shows that waste handling, treatment and disposal is expected to lead to the same exposure pathways as other industrial and commercial activities and uses. The path leading from "Waste Handling, Treatment and Disposal" to "Hazards Potentially Associated with Acute and/or Chronic Exposures" was re-routed to accurately reflect the expected exposure pathway, route and receptors associated with the conditions of use identified for NMP.

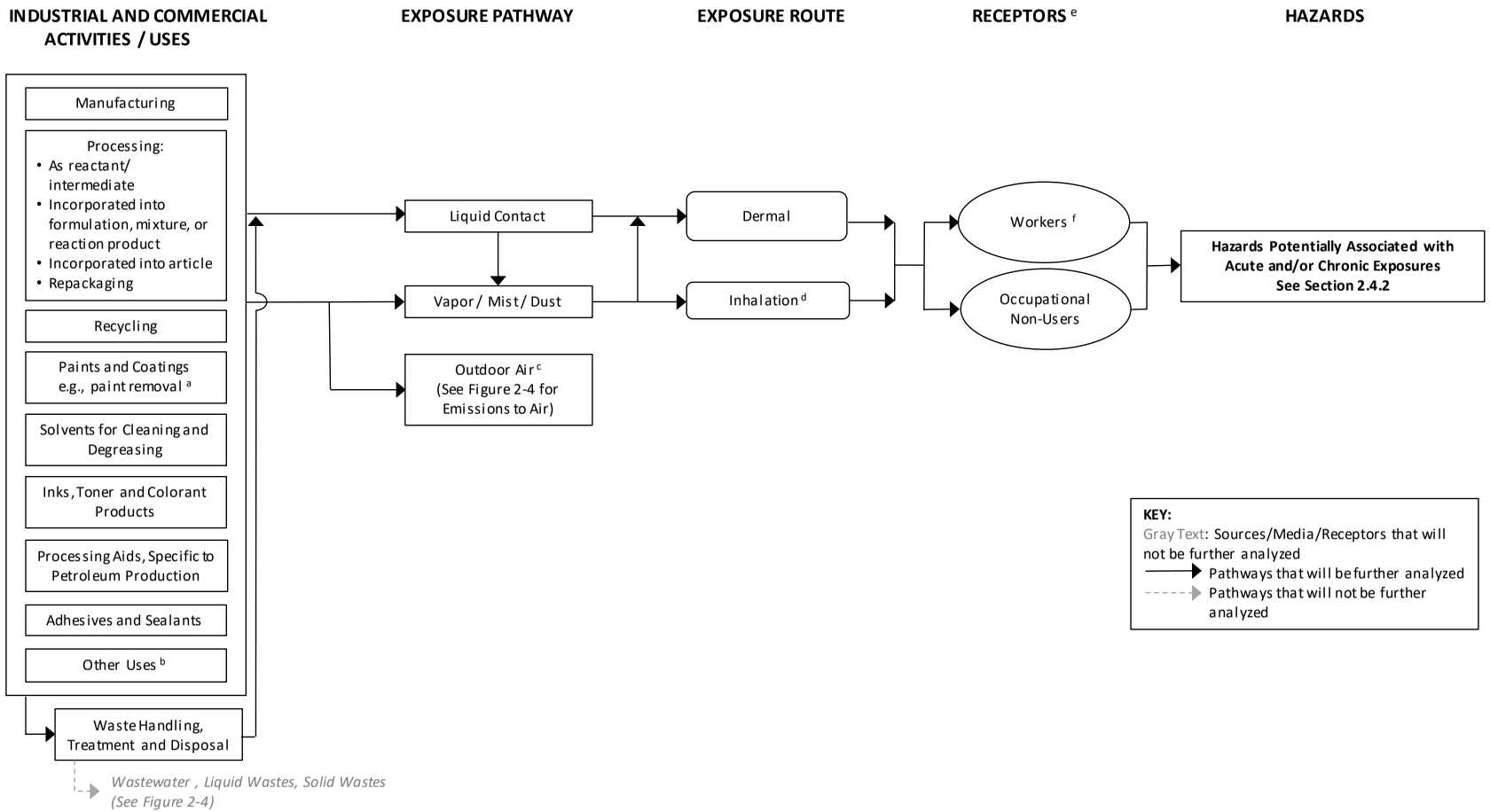


**Figure 2-2. NMP Conceptual Model for Industrial and Commercial Activities and Uses: Potential Exposures and Hazards**

The exposure pathways, exposure routes and hazards to human receptors from industrial and commercial activities and uses of NMP.

[a] U.S. EPA (2015) assessed NMP use in paint removal; these uses will be considered during risk evaluation to ensure previous assessments are in alignment with the Procedures for Chemical Risk Evaluation under the Amended Toxic Substances Control Act (40 CFR Part 702).

[b] Some products are used in both commercial and consumer applications. Additional uses of NMP are included in Table 2-3.

[c] Emissions to outdoor air include stack emissions and fugitive emissions such as fugitive equipment leaks from valves, pump seals, flanges, compressors, sampling connections and open-ended lines; evaporative losses from surface impoundment and spills; and releases from building ventilation systems.

[d] Oral exposure via incidental ingestion of inhaled vapor/mist/dust will be considered as an inhalation exposure.

[e] Receptors include potentially exposed or susceptible subpopulations.

[f] When data and information are available to support the analysis, EPA expects to consider the effect that engineering controls and/or personal protective equipment have on occupational exposure levels.

### 2.5.2 Conceptual Model for Consumer Activities and Uses: Potential Exposures and Hazards

The revised conceptual model (Figure 2-3) illustrates the pathways of exposure resulting from NMP consumer uses that EPA expects to evaluate. In the (U.S. EPA, 2015) risk assessment, dermal and inhalation exposures were assessed as the most likely exposure routes; however, there is a potential for oral exposure under some conditions of use. It should be noted that consumers may purchase and use products primarily intended for commercial use.

***Inhalation***

As mentioned above, EPA/OPPT's 2015 assessment of NMP use in paint stripping identified inhalation as a route of concern U.S. EPA (2015). EPA expects inhalation exposure to be significant for some conditions of use identified in Table 2-3, particularly those that involve heating or spray application. Incidental ingestion of inhaled NMP (vapor/mist/dust) will be considered as an inhalation exposure. EPA expects to further analyze inhalation exposures to consumers and bystanders during risk evaluation.

***Dermal***

There is a potential for dermal exposure from use of consumer products that contain NMP. Dermal exposure may occur from vapor or mist deposition onto skin, or from direct contact with NMP liquid during use. Dermal exposure to liquid NMP could be concurrent with vapor-through-skin exposures for some conditions of use, particularly those that involve heating or spray application of products with a high NMP weight fraction. Bystanders will not have dermal contact with liquid NMP, but could have vapor-through-skin uptake.

Consumers and bystanders can have skin contact with NMP vapor concurrently with inhalation exposures. As noted for workers (see Section 2.5.1), lung uptake is impacted by the NMP weight fraction in liquid, the NMP vapor concentration in air and the duration and extent of dermal contact (i.e., surface area of exposed skin) with liquid and vapor forms of NMP. EPA expects to further analyze dermal exposure to consumers via direct contact with NMP-containing liquids and vapor-through-skin exposure to consumers and bystanders.

***Oral***

There is a potential for oral exposure to consumers from contact with NMP-containing products via hand-to-mouth activity. Mouthing behaviors may also be an important consideration, especially for children. The frequency and duration of these activities, as well as the NMP content in related products can impact exposure potential. EPA expects to further analyze consumer oral exposures that may result from hand-to-mouth activity and mouthing behaviors during use of formulations, products or other articles that contain NMP (e.g., toys, textiles).

***Disposal***

There is a potential for consumer exposure via oral, dermal and inhalation routes during disposal of NMP-containing products. Individuals may be exposed via contact with liquid or vapor forms of NMP when products are discarded. During risk evaluation, EPA expects to further analyze consumer exposures associated with the disposal of consumer products that contain NMP.

For each condition of use identified in Table 2-3, a determination was made as to whether each unique combination of exposure pathway, route, and receptor would be further analyzed during risk evaluation. The results of that analysis along with the supporting rationale are presented in Appendix C and Appendix E.

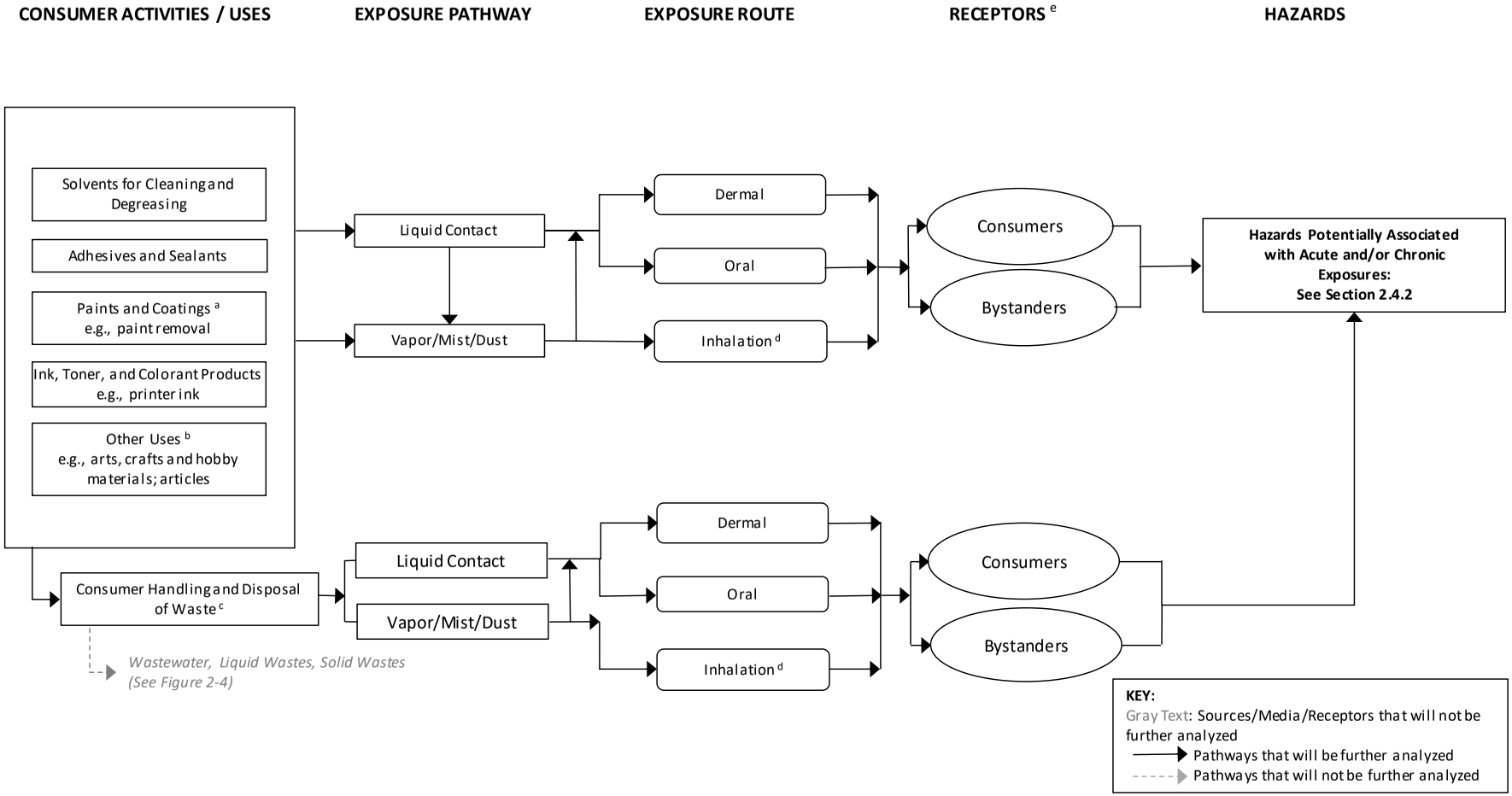


**Figure 2-3. NMP Conceptual Model for Consumer Activities and Uses: Potential Exposures and Hazards**

The conceptual model presents the exposure pathways, exposure routes and hazards to human receptors from consumer activities and uses of NMP.

[a] U.S. EPA (2015) assessed NMP use in paint and coating removal; these uses will be considered during risk evaluation to ensure previous assessments are in alignment with the Procedures for Chemical Risk Evaluation under the Amended Toxic Substances Control Act (40 CFR Part 702).

[b] Some products are used in both commercial and consumer applications; additional uses of NMP are included in Table 2-3.

[c] Consumers may also be exposed while handling municipal wastes; however, the pathway is uncertain.

[d] Oral exposure via incidental ingestion of inhaled vapor/mist/dust will be considered as an inhalation exposure.

[e] Receptors include potentially exposed or susceptible subpopulations.

### 2.5.3 Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards

The revised conceptual model (Figure 2-4) illustrates the exposure pathways anticipated for humans and other ecological receptors from environmental releases and waste streams associated with industrial and commercial use of NMP that EPA expects to include in the risk evaluation. The exposure pathways that EPA expects to include but not further analyze in the risk evaluation are described in Section 2.5.3.1 and shown in the conceptual model.

#### 2.5.3.1 Pathways That EPA Expects to Include in Risk Evaluation but Not Further Analyze

EPA does not expect to further analyze environmental exposures to NMP.

***Ambient Water Pathways***

EPA does not plan to further analyze exposures to humans or ecological receptors including fish, aquatic invertebrates and algae from NMP releases to ambient surface water. Based on 2015 TRI reporting, an estimated 14,092 pounds of NMP was released to surface water from industrial and commercial sources (U.S. EPA, 2017b). Although NMP exhibits high water solubility, it is not expected to persist in surface waters because it readily biodegrades under aerobic conditions.

Environmental monitoring data were not identified for NMP; however, based on the estimated exposure concentrations (described in Section 2.3.4), and available ecological hazard information (summarized in Section 2.4.1), EPA does not plan to further analyze risks to aquatic organisms from NMP releases to surface water. A first-tier exposure analysis predicted surface water concentrations as high as 224 µg/L and 11 µg/L for the acute and chronic exposure scenarios, respectively based on reported TRI releases (summarized in Section 2.4.1). These values do not exceed the acute and chronic COCs for aquatic organisms (246 µg/L and 1,768 µg/L, respectively) indicating a low risk concern. This finding is supported by a recent ecological risk classification completed by Environment and Climate Change Canada which identified a low risk concern for NMP (ECCC, 2016).

EPA does not plan to further analyze exposures to humans that may result from NMP releases to ambient surface water. A first-tier analysis used to estimate NMP surface water concentrations based on the highest water releases reported in the 2015 TRI database showed that NMP levels in well water could be as high as 0.07 mg/kg/day. In the previous NMP risk assessment (U.S. EPA (2015), EPA identified a point of departure (POD) for chronic exposure in humans (48 mg/kg/day), which when compared to the estimated exposure concentration, resulted in a margin of exposure (MOE) that exceeded the benchmark MOE (675 versus 30, respectively). EPA also estimated oral and dermal exposure to NMP during showering/bathing. The calculated MOE, based on aggregate estimates of oral, inhalation and dermal exposure (338), exceeded the benchmark MOE (30), indicating a low risk concern.

***Sediment Pathway***

EPA does not plan to further analyze exposures to sediment-dwelling organisms during risk evaluation, as NMP is unlikely to accumulate in sediment. NMP is not expected to adsorb to sediment due to its water solubility (> 1000 g/L) and low partitioning to organic matter (log $K_{oc}$ = 0.9). This is supported by EPISUITE fugacity model predictions which indicate limited partitioning to sediment (< 1%). No ecotoxicity studies were identified for sediment-dwelling organisms; however, the available hazard data indicate a low concern for NMP toxicity to plants and aquatic organisms. Because NMP toxicity to sediment-dwelling invertebrates is expected to be comparable to that of aquatic invertebrates and NMP

is unlikely to accumulate in sediment, a low risk concern is expected for this environmental compartment.

***Land-Applied Biosolids Pathway***

EPA does not plan to further analyze other land releases during risk evaluation, including those that may result from land application of biosolids. NMP exhibits high water solubility (1000 g/L) and limited potential for adsorption to organic matter (estimated log Koc = 0.9); therefore, land releases will ultimately partition to the aqueous phase (i.e., biosolids associated waste water and soil pore water) upon release into the environment. Because NMP readily biodegrades in environments with active microbial populations, NMP residues that remain following waste water treatment are not expected to persist. NMP concentrations in biosolids-associated water are expected to decrease, primarily via aerobic degradation, during transport, processing (including dewatering), handling, and land application of biosolids (which may include spraying).

Migration of NMP between ground water and surface water has not been documented, but may be mitigated by abiotic and biotic degradation in the water column. Overall, the NMP concentrations in surface water resulting from land application of biosolids are expected to be much less than those associated with direct release of wastewater treatment plant effluents to surface water. EPA's conservative assessment of this exposure scenario predicted NMP surface water concentrations that are well below the hazard benchmarks identified for humans and aquatic organisms (see Appendix C); therefore, this exposure pathway is not expected to present a risk concern.

***Ambient Air Pathways***

EPA does not plan to further analyze NMP air releases or associated exposures to terrestrial wildlife, as inhalation exposure and bioaccumulation potential are expected to be low (BCF = 3.16, BAF = 0.9; see Section 2.4). Negligible volatilization of NMP is expected from moist soil and wastewater. Because NMP exhibits low volatility and readily biodegrades under aerobic conditions (U.S. EPA (2015), the concentrations in ambient air are unlikely to reach levels that would present a risk concern for terrestrial organisms. This conclusion is supported by the ecological risk classification derived for NMP by Environment and Climate Change Canada, which identified a low ecological risk concern for NMP (ECCC, 2016).

EPA does not plan to further analyze human exposures that may result from inhalation of outdoor air containing NMP released from industrial and commercial facilities. A first-tier screening analysis was used to estimate the potential (near field) exposure to populations located downwind of facilities reporting the highest NMP air releases based on 2015 TRI data. Using EPA's SCREEN3 Model and the highest reported stack emissions, the estimated NMP concentration in ambient air was approximately 0.41 $mg/m^3$.

In the previous NMP assessment, EPA used data on NMP-induced decreases in fetal body weight as the basis for risk estimation. Benchmark dose modeling of internal dose estimates based on physiologically-based pharmacokinetic modelling was used to determine a POD (48 mg/kg/day) for estimating risks associated with chronic exposure in humans (U.S. EPA (2015). This POD was converted to an inhalation dose (based on a total dose of 3,840 mg/day, and 80 kg bodyweight). EPA's EFAST model uses a default breathing rate of 0.61 $m^3$/hour over a 24-hour period (14.6 $m^3$/day). Hence the inhalation POD is: (3,840 mg/day)/(14.6 $m^3$/day) = 263 $mg/m^3$ (24-hour TWA). EPA also expects to consider studies that have been published since this assessment, as identified in the literature search conducted by

the Agency (*NMP (CASRN 872-50-4) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0743).

During problem formulation, EPA assessed the risks associated with chronic NMP exposure by comparing the estimated concentration of NMP in ambient air (0.41 mg/m$^3$) to the POD for inhalation exposure (263 mg/m$^3$). This resulted in a margin of exposure (MOE) that exceeded the benchmark MOE (641 versus 30, respectively) indicating a low risk concern.

EPA acknowledges the possibility that NMP releases to ambient air may be wet deposited to soil and surface water; however, aerobic degradation and atmospheric dispersion are expected to limit the NMP air concentrations available to organisms that inhabit these compartments. As such, NMP air removal via wet deposition (from air to water or soil) is not expected to result in significant accumulation in these environmental compartments. This conclusion is supported by EPA's conservative assessment of NMP concentrations in air and surface water; the Tier 1 exposure estimates for these media do not indicate a concern for humans or other ecological receptors. The exposure pathways associated with NMP releases to ambient air will not be further analyzed during risk evaluation.

#### 2.5.3.2 Pathways that EPA Does Not Plan to Include in the Risk Evaluation

Exposures to receptors (i.e., general population, terrestrial species) may occur from industrial and/or commercial uses, industrial releases to air, water or land, and other conditions of use. As described in Section 2.5, EPA does not expect to include in the risk evaluation pathways under programs of other environmental statutes, administered by EPA, which adequately assess and effectively manage exposures and for which long-standing regulatory and analytical processes already exist. These pathways are described below.

***Drinking Water Pathway***

EPA has regular analytical processes to identify and evaluate drinking water contaminants of potential regulatory concern for public water systems under the Safe Drinking Water Act (SDWA).

The Contaminant Candidate List (CCL) is a list of unregulated contaminants that are known or anticipated to occur in public water systems and that may require regulation. EPA must publish a CCL and make Regulatory Determinations to regulate at least five CCL contaminants every 5 years. To regulate a contaminant, EPA must conclude the contaminant may have adverse health effects, occurs or is substantially likely to occur in public water systems at a level of concern and that regulation, in the sole judgement of the Administrator, presents a meaningful opportunity for health risk reduction.

NMP is listed on EPA's fourth CCL. NMP is on the CCL because EPA's Office of Water concluded that based on occurrence and health information the chemical is known or anticipated to occur in public water systems and may require regulation. Based on TRI information, the Agency concluded that NMP may occur in public water systems. Once contaminants have been placed on the CCL, EPA identifies if there are any additional data needs, including gaps in occurrence data for evaluation under Regulatory Determination; if sufficient occurrence data is lacking, the contaminant may be considered for monitoring under the Unregulated Contaminant Monitoring Rule. Hence, because the drinking water exposure pathway for NMP is being addressed under the regular analytical processes used to identify and evaluate drinking water contaminants of potential regulatory concern for public water systems under SDWA, EPA does not expect to include this pathway in the risk evaluation for NMP under TSCA. EPA's Office of Water and Office of Pollution Prevention and Toxics will continue to work together providing understanding and analysis of the SDWA regulatory analytical processes for public water

systems and to exchange information related to toxicity and occurrence data on chemicals undergoing risk evaluation under TSCA.

***Disposal Pathways***

The general standard in RCRA section 3004(a) for the technical criteria that govern the management (treatment, storage, and disposal) of hazardous waste (i.e., Subtitle C) are those "necessary to protect human health and the environment," RCRA 3004(a). The regulatory criteria for identifying "characteristic" hazardous wastes and for "listing" a waste as hazardous also relate solely to the potential risks to human health or the environment. 40 C.F.R. §§ 261.11, 261.21-261.24. RCRA statutory criteria for identifying hazardous wastes require EPA to "tak[e] into account toxicity, persistence, and degradability in nature, potential for accumulation in tissue, and other related factors such as flammability, corrosiveness, and other hazardous characteristics." Subtitle C controls cover not only hazardous wastes that are landfilled, but also hazardous wastes that are incinerated (subject to joint control under RCRA Subtitle C and the Clean Air Act (CAA) hazardous waste combustion maximum achievable control technology) or injected underground into Class I hazardous waste wells (subject to joint control under Subtitle C and SDWA).

EPA does not expect to include emissions to ambient air from municipal and industrial waste incineration and energy recovery units in the risk evaluation, as they are regulated under section 129 of the Clean Air Act. CAA section 129 requires EPA to review and, if necessary, add provisions to ensure the standards adequately protect public health and the environment. Thus, combustion by-products from incineration treatment of NMP wastes (approximately 6 million lbs) would be subject to these regulations, as would NMP burned for energy recovery (7.6 million lbs).

EPA does not expect to consider on-site NMP land releases that are disposed via underground injection in the risk evaluation. Most of the on-site land disposal reported for NMP in the 2015 TRI was to Class I underground injection wells (approximately 3.6 million pounds), with no reported environmental releases via underground injection to Class II-VI wells (U.S. EPA, 2017b). Environmental disposal of NMP via injection into Class I wells is managed and prevented from further environmental releases by RCRA and SDWA regulations. Therefore, disposal of NMP via underground injection is not likely to result in environmental and general population exposures.

EPA does not plan to consider on-site land releases that go to RCRA Subtitle C hazardous waste landfills during risk evaluation. Based on the 2015 TRI data, approximately 93,217 pounds of NMP were transferred to RCRA Subtitle C landfills; smaller amounts (approximately 25,648 pounds) were characterized as "other" land disposal and off-site land treatment (approximately 330 pounds) (U.S. EPA, 2017b). Design standards for Subtitle C landfills require double liner, double leachate collection and removal systems, leak detection system, run on, runoff, and wind dispersal controls, and a construction quality assurance program. They are also subject to closure and post-closure care requirements including installing and maintaining a final cover, continuing operation of the leachate collection and removal system until leachate is no longer detected, maintaining and monitoring the leak detection and groundwater monitoring system. Bulk liquids may not be disposed in Subtitle C landfills. Subtitle C landfill operators are required to implement an analysis and testing program to ensure adequate knowledge of waste being managed and to train personnel on routine and emergency operations at the facility. Hazardous waste being disposed in Subtitle C landfills must also meet RCRA waste treatment standards before disposal. Given these controls, general population exposure to NMP from Subtitle C landfill leachate is not expected to be a significant exposure pathway.

EPA does not expect to include releases to land from RCRA Subtitle D municipal solid waste (MSW) landfills or exposures to the general population or terrestrial species from such releases in the risk evaluation. While permitted and managed by individual states, MSW landfills are required by federal regulations to implement some of the same requirements as Subtitle C landfills. MSW landfills must have a liner system with leachate collection and conduct groundwater monitoring and corrective action when releases are detected. MSW landfills are also subject to closure and post-closure care requirements, as well as providing financial assurance for funding of any needed corrective actions. MSW landfills have been designed to allow for the small amounts of hazardous waste generated by households and very small quantity waste generators (< 220 pounds per month). Bulk liquids, such as free solvent, may not be disposed of in MSW landfills.

EPA does not expect to consider on-site releases to land from industrial non-hazardous waste and construction/demolition waste landfills in the NMP risk evaluation. Industrial non-hazardous and construction/demolition waste landfills are primarily regulated under state regulatory programs. States must also implement limited federal regulatory requirements for siting, groundwater monitoring and corrective action and a prohibition on open dumping and disposal of bulk liquids. States may also establish additional requirements such as for liners, post-closure and financial assurance, but are not required to do so. Therefore, EPA does not expect to include this exposure pathway in the risk evaluation.

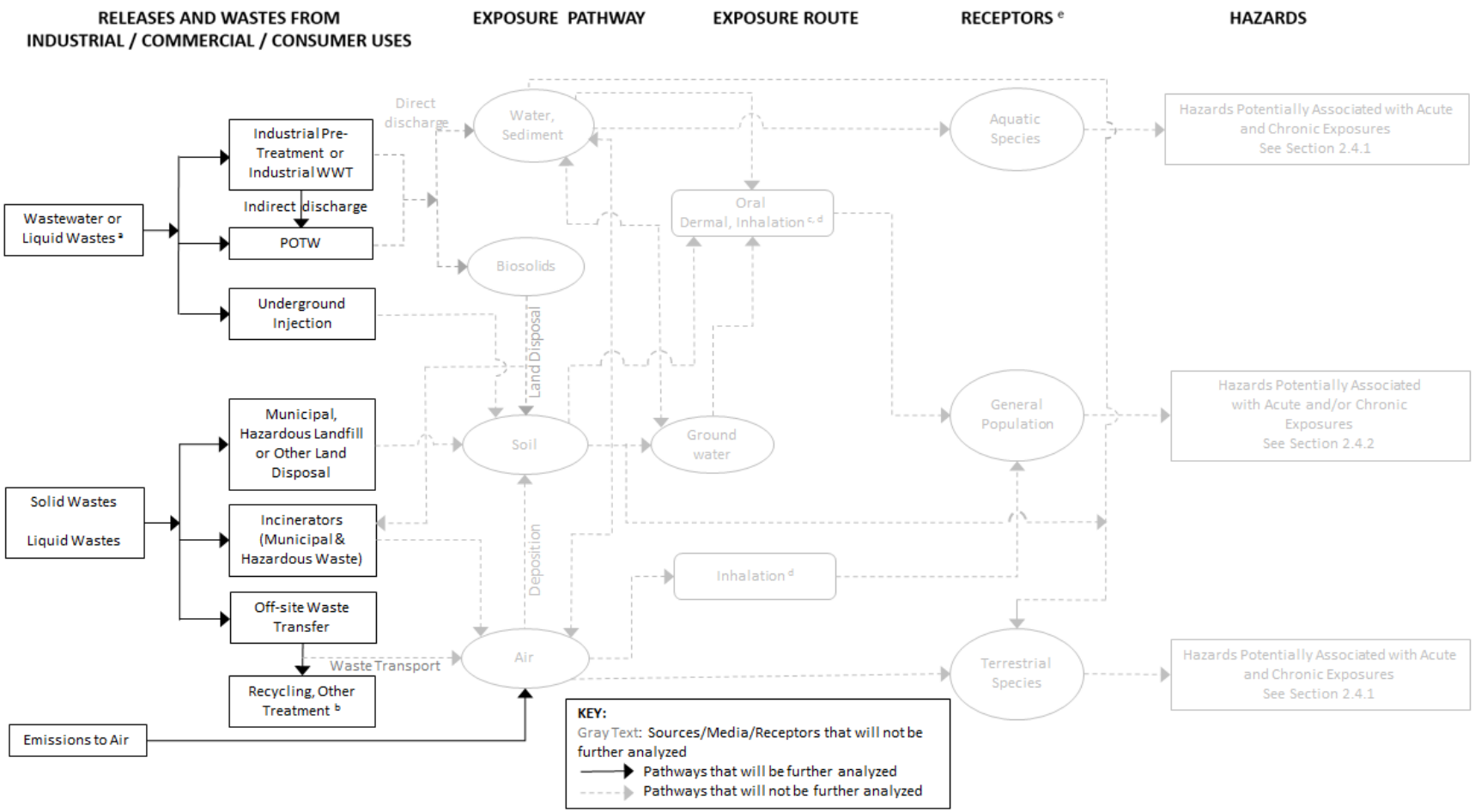


**Figure 2-4. NMP Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards**

The conceptual model presents the exposure pathways, exposure routes and hazards to human and environmental receptors from environmental releases and wastes of NMP.

[a] Industrial wastewater or liquid wastes may be treated on-site and then released to surface water (direct discharge), or pre-treated and released to POTW (indirect discharge). For consumer uses, such wastes may be released directly to POTW (i.e., down the drain). Drinking water will undergo further treatment in drinking water treatment plant. Ground water may also be a source of drinking water.

[b] Additional releases may occur from recycling and other waste treatment.

[c] Volatilization from or liquid contact with drinking/tap water in the home during showering, bathing and washing represents another potential exposure pathway.

[d] Presence of mist is unlikely; inhalation and oral exposure are expected to be negligible.

[e] Receptors include potentially exposed or susceptible subpopulations.

## 2.6 Analysis Plan

The analysis plan presented in this problem formulation is a refinement of the initial analysis plan published in the *Scope of the Risk Evaluation for NMP* (U.S. EPA, 2017a).

The analysis plan outlined here is based on the conditions of use identified for NMP, as described in Section 2.2 of this problem formulation. EPA is implementing systematic review approaches to identify, select, assess, integrate and summarize the findings of studies supporting the TSCA risk evaluation. The analytical approaches and considerations in the analysis plan are used to frame the scope of the systematic review activities for this assessment. The supplemental document, *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018), provides additional information about criteria and methods that have been and will be applied to the first 10 chemical risk evaluations.

While EPA has conducted a search for reasonably available information from public sources as described in the *Scope of the Risk Evaluation for NMP* (U.S. EPA, 2017a), EPA encourages submission of additional existing data, such as full study reports or workplace monitoring from industry sources, that may be relevant for refining conditions of use, exposures, hazards and potentially exposed or susceptible subpopulations during the risk evaluation. EPA will continue to consider new information submitted by the public.

During risk evaluation, EPA will rely on the comprehensive literature results [*NMP (CASRN 872-50-4) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0743], or supplemental literature searches to address specific questions. Further, EPA may consider any relevant CBI in the risk evaluation in a manner that protects the confidentiality of the information from public disclosure. The analysis plan is based on EPA's knowledge of NMP to date, which includes partial, but not complete review of identified literature. If additional data or approaches become available, EPA may refine its analysis plan based on this information.

### 2.6.1 Exposure

Based on their physical-chemical properties, expected sources, and transport and transformation within the outdoor and indoor environment chemical substances are more likely to be present in some media and less likely to be present in others. Media-specific levels will vary based on the chemical substance of interest. For most chemical substances, level(s) can be characterized through a combination of available monitoring data and modeling approaches.

#### 2.6.1.1 Environmental Releases

EPA expects to consider and analyze releases to relevant environmental media as follows:

1) Review reasonably available published literature or information on processes and activities associated with NMP conditions of use to evaluate the types of releases and wastes generated. EPA has reviewed some key data sources containing information on processes and activities resulting in releases. EPA will continue to review potentially relevant data sources identified in Appendix B during risk evaluation.
2) Review reasonably available chemical-specific release data, including measured or estimated release data (e.g., data collected under the TRI program). EPA has reviewed key data sources including TRI; this data is summarized in Section 2.3.2 above. EPA will continue to review relevant data sources during risk evaluation. EPA will match identified data to applicable conditions of use and identify data gaps where no data are found for specific conditions of use.

EPA will attempt to address data gaps identified as described in steps 3 and 4 below by considering potential surrogate data and models.

3) Review measured or estimated release data for surrogate chemicals that have similar uses, volatility, and physical-chemical properties. Data for solvents that are used in the same types of applications may be considered as surrogate data for NMP. Perchloroethylene, dimethylformamide and NMP are used in paints, coatings, adhesives, sealants, and cleaning formulations. In addition, NMP is sometimes used as a replacement for methylene chloride in some paint removal use applications. EPA will review the literature sources identified and if surrogate data are found, EPA will match these data to applicable conditions of use to determine their suitability for filling data gaps. EPA will evaluate the utility of surrogate data to fill data gaps where uses of NMP and other solvents align. If surrogate data are used, EPA normally converts air concentrations using the ratio of the vapor pressures of the two chemicals.

4) Understand and consider regulatory limits that may inform estimation of environmental releases. EPA has identified information from various EPA statutes (including, for example, regulatory limits, reporting thresholds or disposal requirements) that may be relevant to release estimation. EPA will further consider relevant regulatory requirements in estimating releases during risk evaluation. While NMP is not a hazardous air pollutant regulated under the Clean Air Act, some related rules may provide relevant information on sectors that use NMP. For example, the National Emission Standards for Hazardous Air Pollutants (NESHAP) for Paint Stripping and Miscellaneous Surface Coating Operations (40 CFR Part 63, Subpart HHHHHH) may provide useful information on industry sectors that use solvents (including NMP) for paint removal and surface coating applications.

5) Review and determine the applicability of the Organisation for Economic Cooperation and Development (OECD) Emission Scenario Documents (ESD) and EPA Generic Scenarios to estimation of environmental releases. Potentially relevant OECD ESDs and EPA Generic Scenarios (GS) have been identified that correspond to some conditions of use. For example, the ESD on Industrial Use of Adhesives for Substrate Bonding, the ESD on the Coating Industry (paints, lacquers and varnishes), and the GS on Application of Agricultural Pesticides are some of the ESDs and GSs that EPA may use to assess potential releases. EPA will need to critically review the GSs and ESDs to determine their applicability to the conditions of use assessed. EPA was not able to identify ESDs or GSs corresponding to several conditions of use, including the manufacture and import of NMP, use of NMP in soldering materials and use of NMP in petrochemical purifications. EPA will perform additional targeted research to understand those conditions of use which may inform identification of release scenarios. EPA may also need to perform targeted research for applicable models and associated parameters that EPA may use to estimate releases for specific conditions of use. If ESDs and GSs are not available to fill data gaps, other methods may be considered, including existing emission factors, such as those from EPA AP-42, to estimate environmental releases of NMP to air from various conditions of use.

6) Map or group condition(s) of use to release assessment scenario(s). EPA has identified release scenarios and mapped them to some conditions of use. For example, some scenario groupings include Contractor Adhesive Removal and Industrial Spray Application of Lacquers, Paints, and Coatings. EPA grouped similar conditions of use (based on factors including process equipment and handling, release sources and usage rates of NMP and formulations containing NMP, or professional judgement) into scenario groupings but may further refine these groupings as

additional information becomes available during risk evaluation. EPA was not able to identify release scenarios corresponding to several conditions of use due to a lack of general knowledge of those conditions of use. EPA will perform additional targeted research to understand those uses which may inform identification of release scenarios.

Evaluate the weight of evidence for environmental release data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

#### 2.6.1.2 Environmental Fate

EPA expects to consider and analyze fate and transport in environmental media as follows:

1) Review reasonably available measured or estimated environmental fate endpoint data collected through the literature search.

   A general overview of persistence and bioaccumulation was presented in the TSCA Work Plan Chemical Risk Assessment of N-Methylpyrrolidone: Paint Removal Use CASRN 872-50-4 (U.S. EPA, 2015). Key environmental fate characteristics were included in the *Scope of the Risk Evaluation for N-Methylpyrrolidone* (U.S. EPA, 2017a) and in previous assessments of NMP, including those conducted by EPA's Office of Pesticide Programs (U.S. EPA, 2015), US California Office of Environmental Health Hazard Assessment (OEHHA, 2003), Australia Department of Health, National Industrial Chemicals Notification and Assessment Scheme (Australian Government Department of Health, 2016), Environment Canada, Health Canada (EC/HC, 2017), and European Commission, Scientific Committee on Occupational Exposure Limits (EC, 2016). These information sources will be used as a starting point for the environmental fate assessment. Other sources that will be consulted include those that are identified through the systematic review process. Studies will be evaluated using the evaluation strategies laid out in the supplemental document, *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018).

   If measured values are not available (this will be determined during systematic review), chemical properties will be estimated using EPI Suite, SPARC and other chemical parameter estimation models. Estimated fate properties will be reviewed for applicability and quality.

2) Using measured environmental fate data and/or environmental fate modeling, determine the influence of environmental fate endpoints (e.g., persistence, bioaccumulation, partitioning, transport) on pathways and routes of exposure for human and environmental receptors.

   Measured fate data including atmospheric photolysis rates, hydrolysis, and aerobic and anaerobic biodegradation rates, along with physical-chemical properties and models such as the EPI Suite™ STP model (which estimates removal during wastewater treatment due to adsorption to sludge and volatilization to air), will be used to characterize the movement of NMP within and among environmental media and the persistence of NMP within specific media.

3) Evaluate the weight of the evidence of environmental fate data.

#### 2.6.1.3 Environmental Exposures

EPA does not plan to further analyze environmental exposures to NMP, based on the rationale described in Section 2.3.4.

#### 2.6.1.4 Occupational Exposures

EPA expects to consider and analyze exposures to workers and occupational non-users as follows:

1) Review reasonably available exposure monitoring data for specific condition(s) of use. Exposure data to be reviewed may include workplace monitoring data collected by government agencies such as OSHA and the National Institute of Occupational Safety and Health (NIOSH), and monitoring data found in published literature. These workplace monitoring data may include personal exposure monitoring data and area monitoring data (e.g., stationary sampling). Data, information, and studies will be evaluated using the evaluation strategies laid out in the *Application of Systematic Review in TSCA Risk Evaluations* document (U.S. EPA, 2018). EPA has reviewed available monitoring data collected by OSHA (see the summary in Appendix 2.6.3B.2) and will match these data to applicable conditions of use. EPA has also identified additional data sources that may contain relevant monitoring data for the various conditions of use. EPA will review the sources identified in Appendix B and extract relevant data for consideration and analysis during risk evaluation. Data gaps will be identified where no data are found for specific conditions of use. EPA will attempt to address data gaps identified as described in steps 2 and 3 below. Where possible, job descriptions may be useful in distinguishing exposures to different subpopulations within a specific condition of use.

2) Review reasonably available exposure data for surrogate chemicals that have uses, volatility and physical-chemical properties that are comparable to NMP. EPA will review literature sources identified and if surrogate data are found, these data will be matched to applicable conditions of use for potentially filling data gaps. For several uses (e.g., use as solvent), EPA believes that dimethylformamide may share the same or similar conditions of use and may be considered as a surrogate for NMP.

3) For conditions of use where data are limited or not available, review existing exposure models that may be applicable in estimating exposure levels. Models may be generic, broadly applicable models or may be specific to conditions of use (e.g., some OECD Emission Scenario Documents (ESDs) and U.S. EPA Generic Scenarios (GSs) may be identified as potentially mapping to some conditions of use). EPA has identified potentially relevant OECD ESDs and EPA GSs that correspond to some conditions of use. For example, the ESD on Industrial Use of Adhesives for Substrate Bonding, the ESD on Metal Finishing and the GS on the Manufacture and Use of Printing Inks are some of the ESDs and GSs that EPA may use to estimate occupational exposures. EPA will need to critically review these scenarios to determine their applicability to the conditions of use identified for NMP. EPA was not able to identify ESDs or GSs corresponding to several conditions of use, including recycling of NMP and solvent mixtures containing NMP, processing and formulation of NMP into industrial, commercial and consumer products, use of NMP in paints and coatings, and use of NMP in petrochemical purifications. EPA will perform additional targeted research to understand those conditions of use, which may inform identification of exposure scenarios. EPA may also need to perform targeted research to identify applicable models that EPA may use to estimate exposures for specific conditions of use. If any models are identified as applicable, EPA will search for appropriate model parameter data (as described in step 4 below). If parameter data can be located or assumed, exposure estimates generated from these models may be used for potentially filling data gaps.

4) Review reasonably available information that may be used in developing, adapting or applying exposure models to the risk evaluation. This step will be performed after Steps 2 and 3 above. Based on information developed from Steps 2 and 3, EPA will evaluate relevant data to determine whether the data can be used to develop, adapt, or apply models for specific conditions of use (and corresponding exposure scenarios). EPA previously assessed dermal and inhalation exposure to workers and occupational non-users during NMP use in paint and graffiti removal (U.S. EPA, 2015). Inputs to the PBPK model were developed from air monitoring data and dermal parameter data and assumptions for workers. EPA will utilize results from the previous assessment during risk evaluation. EPA may develop models for other conditions of use, where appropriate.

5) Consider and incorporate applicable engineering controls and/or personal protective equipment into exposure scenarios. EPA will review potentially relevant data sources on engineering controls and personal protective equipment as identified in Table_Apx B-7 and determine their applicability for incorporation into specific exposure scenarios during risk evaluation. OSHA has not established any occupational exposure limits for NMP; however, AIHA has adopted a recommended workplace environmental exposure level (WEEL) of 10 ppm based on a time-weighted average (TWA) over an 8-hour workday. EPA will consider the influence of the recommended exposure guidelines in its occupational exposure assessment.

6) Map or group each condition of use to occupational exposure assessment scenario(s). EPA has identified occupational exposure scenarios and mapped them to conditions of use. For example, one scenario grouping is the Industrial Spray Application of Lacquers, Paints, and Coatings, where products containing NMP are applied to substrates via spraying methods in an industrial setting. EPA grouped similar conditions of use (e.g., based on factors including process equipment and handling, usage rates and NMP content of product formulations, exposure/release sources, or professional judgement) into scenario groupings but may further refine these groupings as additional information is identified during risk evaluation. EPA was not able to identify occupational exposure scenarios corresponding to several conditions of use due to a lack of general understanding of those conditions of use. For example, EPA has not identified information related to exposure during the use of NMP in petrochemical purifications. EPA will perform targeted research to understand those uses which may inform identification and refinement of occupational exposure scenarios.

7) Evaluate the weight of evidence of occupational exposure data. The data integration strategy will be designed to be “fit-for-purpose”. EPA will use systematic review methods to assemble the relevant data and evaluate data quality, including strengths and limitations, followed by synthesis and integration of the evidence.

#### 2.6.1.5 Consumer Exposures

EPA expects to consider and analyze exposures to consumers as follows:

1) Refine and finalize exposure scenarios for consumers by considering unique combinations of sources (consumer uses), exposure pathways, exposure settings, exposed populations and exposure routes. For NMP, the following are noteworthy considerations in constructing exposure scenarios for consumers:
   - reasonably available data sources, including those that provide information on NMP content in manufactured, processed, used, or recycled consumer products and articles, including

temporal trends associated with such data; an example of an information source with product information (e.g., NMP content) is the CDC Household Products Database.

- information characterizing use patterns for consumer products that contain NMP including how the product is used, the amount of product used, the frequency and duration of use and specific characteristics regarding the room in which the product is used;
- the exposure setting and route of exposure for potentially exposed populations, including susceptible subpopulations that may be exposed via consumer product use, including those who use commercial products that contain higher concentrations of NMP, or those who may use NMP-containing products more frequently;
- information characterizing the potential for NMP release from products and articles into the indoor environment through diffusion from materials to air, physical abrasion, or direct transfer to dust;
- EPA will map products according to their NMP content, use patterns and exposure routes, including potentially exposed or susceptible subpopulations to develop exposure scenarios.

2) Evaluate consumer exposures to products and articles containing NMP. The 2015 NMP Risk Assessment for Paint Removal Use provides an in-depth characterization of paint removal products, including the NMP content, use patterns and associated exposures that may occur via their use. During risk evaluation, EPA will consider these paint removal uses along with other consumer uses to conduct a first-tier exposure analysis. The results of this analysis will then be used to determine which consumer use scenarios may need a more refined exposure assessment. In addition to the comparison of consumer exposure scenarios to each other, the associated exposure estimates for each scenario will also be compared to the hazard benchmarks identified for dermal and inhalation exposure. Based on the results of this evaluation, EPA may consider a subset of consumer use scenarios for a more extensive analysis.

3) Evaluate the indoor exposure pathways based on available data. Indoor exposures are likely to be higher than outdoor exposures and may include a potential for oral, dermal and inhalation contact. Data sources associated with these pathways have not been comprehensively evaluated; however, quantitative comparisons across exposure pathways will be considered during risk evaluation.

4) Review existing consumer exposure models that may be applicable in estimating indoor air concentrations (near field and far field) for the user and in estimating dermal exposure to consumer users. Determine the applicability of the identified models for use in a quantitative exposure assessment.

5) Review reasonably available consumer product-specific sources to determine how exposure estimates compare with each other and with indoor monitoring data on NMP levels in dust or indoor air. EPA will review the available empirical data for use in developing, adapting or applying exposure models such as the Consumer Exposure Model (CEM) to the risk evaluation. The CEM parameters used in EPA's 2015 assessment of NMP use in paint removal and will be reviewed to determine if they can be used to evaluate other NMP use scenarios.

6) Review reasonably available population- or subpopulation-specific exposure factors and activity patterns to determine if EPA's identification of potentially exposed or susceptible subpopulations need to be further refined. Possible considerations include:

- the characteristics of the user of the consumer product and the bystander(s) in the room, including for example, women of child bearing age and children.
- subpopulations who may have greater exposure due to the magnitude, frequency or duration of exposure as applicable to specific consumer products.

7) Evaluate the weight of evidence available for consumer exposure estimates based on different approaches.

#### 2.6.1.6 General Population Exposures

EPA does not expect to include general population exposures in the risk evaluation for NMP. EPA has determined that the existing regulatory programs and associated analytical processes adequately assess and effectively manage the risks of NMP that may be present in various media pathways (e.g., air, water, land) for the general population. For these cases, EPA believes that the TSCA risk evaluation should focus not on those exposure pathways, but rather on exposure pathways associated with TSCA conditions of use that are not subject to those regulatory processes, because the latter pathways are likely to represent the greatest areas of concern to EPA.

### 2.6.2 Hazards (Effects)

#### 2.6.2.1 Environmental Hazards

EPA's conservative screening analysis demonstrated a low risk concern for NMP based on currently available information (e.g., physical-chemical properties, fate characteristics and TRI-reported environmental releases). EPA does not expect to further analyze environmental hazards.

#### 2.6.2.2 Human Health Hazards

EPA expects to consider and analyze human health hazards as follows:

1) Review reasonably available human health hazard data, including data from alternative test methods as needed (e.g., computational toxicology and bioinformatics; high-throughput screening methods; data on categories and read-across; in vitro studies; systems biology).

   Human health studies will be evaluated using the evaluation strategies laid out in the supplemental document, *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018). Human and animal data will be identified and included as described in the inclusion and exclusion criteria in Appendix G. EPA expects to prioritize the evaluation of mechanistic evidence. Specifically, EPA does not plan to evaluate mechanistic studies unless needed to clarify questions about associations between NMP and health effects and its relevance to humans. The *Applications of Systematic Review in TSCA Risk Evaluations* document describes the process of how studies will be evaluated using specific data evaluation criteria and a predetermined approach. Study results will be extracted and presented in evidence tables by hazard endpoint. EPA expects to evaluate relevant studies identified in the *TSCA Work Plan Chemical Risk Assessment on NMP use in Paint Stripping* U.S. EPA (2015). In addition, EPA intends to review studies that were captured in the comprehensive literature search conducted by the Agency for NMP [*NMP (CASRN 872-50-4) Bibliography: Supplemental File for the TSCA Scope Document,* (EPA-HQ-OPPT-2016-0743)], and supplemental literature searches to address specific questions. Further, EPA will consider any relevant CBI in a manner that protects the confidentiality of the information from public disclosure.

2) When evaluating available data, determine whether specific individual groups may have greater susceptibility to NMP hazard(s) than the general population.

3) Conduct hazard identification (the qualitative process of identifying human health hazard endpoints) and dose-response assessment (the quantitative relationship between hazard and exposure) for all identified human health hazard endpoints.

   Human health hazards from acute and chronic exposures will be identified by evaluating the human and animal data that meet the data quality criteria described in *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018). Studies meeting data quality criteria will be grouped by routes of exposure relevant to humans.

4) Dose-response assessment will be performed in accordance with EPA guidance (U.S. EPA, 2012a). Dose-response analyses performed to support the *TSCA Work Plan Chemical Risk Assessment on NMP use in Paint Stripping* U.S. EPA (2015) may be used if the data meet data quality criteria and if additional information on the identified hazard endpoints or additional hazard endpoints would not alter this analysis.

5) Derive POD and conduct benchmark dose modeling when feasible based on the available data.

   Hazard data will be evaluated to determine the type of dose-response modeling that is applicable, if updates are needed. When modeling is feasible, a set of dose-response models that are consistent with a variety of underlying biological processes will be applied to empirically model the dose-response relationships within the range of the observed data consistent with EPA's *Benchmark Dose Technical Guidance Document*. When dose-response modeling is not feasible, NOAEL or LOAEL values will be identified.

6) Consider the route(s) of exposure (oral, inhalation, dermal), available exposure data and modeling approaches to integrate exposure and hazard assessment.

7) Evaluate the weight of evidence based on human health hazard data.

   EPA will rely on the weight of scientific evidence when evaluating and integrating human health hazard data. The strategy will be designed to be "fit-for-purpose". EPA will use systematic review methods to assemble the relevant data, evaluate for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

### 2.6.3 Risk Characterization

Risk characterization is an integral component of the risk assessment process for both ecological and human health risks. EPA will derive the risk characterization in accordance with EPA's *Risk Characterization Handbook* (U.S. EPA, 2000). As defined in EPA's Risk Characterization Policy, "the risk characterization integrates information from the preceding components of the risk evaluation and synthesizes an overall conclusion about risk that is complete, informative and useful for decision makers." Risk characterization is considered to be a conscious and deliberate process to bring all important considerations about risk, not only the likelihood of risk but also the strengths and limitations of the assessment and a description of how others have assessed the risk into an integrated picture.

Risk characterization at EPA assumes different levels of complexity depending on the nature of the risk being characterized. The level of information contained in each risk characterization varies according to the type of assessment for which the characterization is written. Regardless of the level of complexity or

information, the risk characterization for TSCA risk evaluations will be prepared in a manner that is transparent, clear, consistent and reasonable (U.S. EPA, 2000). EPA will also present information in this section consistent with approaches described in the *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act* (82 FR 33726). For instance, in the risk characterization summary, EPA will further carry out the obligations under TSCA section 26; for example, by identifying and assessing uncertainty and variability in each step of the risk evaluation, discussing considerations of data quality such as the reliability, relevance and whether the methods utilized were reasonable and consistent, explaining any assumptions used, and discussing information generated from independent peer review. EPA will also be guided by EPA's *Information Quality Guidelines* (U.S. EPA, 2002) which provide guidance for presenting risk information. Consistent with those guidelines, in the risk characterization, EPA will identify: (1) Each population addressed by an estimate of applicable risk effects; (2) the expected risk or central estimate of risk for the potentially exposed or susceptible subpopulations affected; (3) each appropriate upper-bound or lower-bound estimate of risk; (4) each significant uncertainty identified in the process of the assessment of risk effects and the studies that would assist in resolving the uncertainty; and (5) peer reviewed studies known to the Agency that support, are directly relevant to, or fail to support any estimate of risk effects and the methodology used to reconcile inconsistencies in the scientific information.

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# APPENDICES

# Appendix A REGULATORY HISTORY

## A.1 Federal Laws and Regulations

**Table_Apx A-1. Federal Laws and Regulations**

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| **EPA Regulations** | | |
| Toxic Substances Control Act (TSCA) – Section 6(a) | Provides EPA with the authority to prohibit or limit the manufacture (including import), processing, distribution in commerce, use or disposal of a chemical if EPA evaluates the risk and concludes that the chemical presents an unreasonable risk to human health or the environment. | Proposed rule (82 FR 7464) regulating NMP uses in paint and coating removal |
| Toxic Substances Control Act (TSCA) – Section 6(b) | Directs EPA to promulgate regulations to establish processes for prioritizing chemicals and conducting risk evaluations on priority chemicals. In the meantime, EPA is directed to identify and begin risk evaluations on 10 chemical substances drawn from the 2014 update of the TSCA Work Plan for Chemical Assessments. | NMP is on the initial list of chemicals to be evaluated for unreasonable risk under TSCA (81 FR 91927, December 19, 2016) |
| Toxic Substances Control Act (TSCA) – Section8(a) | The TSCA section 8(a) Chemical Data Reporting (CDR) Rule requires manufacturers (including importers) to give EPA basic exposure-related information on the types, quantities and uses of chemical substances produced domestically and imported into the US. | NMP manufacturing, importing, processing and use information is reported under the Chemical Data Reporting (CDR) rule (76 FR 50816, August 16, 2011). |
| Toxic Substances Control Act (TSCA) – Section8(b) | EPA must compile, keep current and publish a list (the TSCA Inventory) of each chemical substance manufactured, processed, or imported in the United States. | NMP was on the initial TSCA Inventory and therefore was not subject to EPA's new chemicals review process (60 FR 16309, March 29, 1995). |
| Toxic Substances Control Act (TSCA) – Section 8(e) | Manufacturers (including importers), processors and distributors must immediately notify EPA if they obtain information that supports the conclusion that a chemical substance or mixture presents a substantial risk of injury to health or the environment. | Seven notifications of substantial risk (Section 8(e)) received (2007 – 2010) (US EPA, ChemView. Accessed April 13, 2017). |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| Toxic Substances Control Act (TSCA) – Section 4 | Provides EPA with authority to issue rules and orders requiring manufacturers (including importers) and processors to test chemical substances and mixtures. | Six submissions from a test rule (Section 4) received in the mid-1990s. (US EPA, ChemView. Accessed April 13, 2017). |
| Emergency Planning and Community Right-To-Know Act (EPCRA) – Section 313 | Requires annual reporting from facilities in specific industry sectors that employ 10 or more full time equivalent employees and that manufacture, process, or otherwise use a TRI-listed chemical in quantities above threshold levels. A facility that meets reporting requirements must submit a reporting form for each chemical for which it triggered reporting, providing data across a variety of categories, including activities and uses of the chemical, releases and other waste management (e.g., quantities recycled, treated, combusted) and pollution prevention activities (under section 6607 of the Pollution Prevention Act). This data includes on-site and off-site data as well as multimedia data (i.e., air, land and water). | NMP is a listed substance subject to reporting requirements under 40 CFR 372.65 effective as of January 1, 1995. |
| Federal Food, Drug and Cosmetic Act (FFDCA) – Section 408 | FFDCA governs the allowable residues of pesticides in food. Section 408 of the FFDCA provides EPA with the authority to set tolerances (rules that establish maximum allowable residue limits), or exemptions from the requirement of a tolerance, for all residues of a pesticide (including both active and inert ingredients) that are in or on food. Prior to issuing a tolerance or exemption from tolerance, EPA must determine that the tolerance or exemption is "safe." Sections 408(b) and (c) of the FFDCA define "safe" to mean the Agency has a reasonable certainty that no harm will result from aggregate exposures to the pesticide residue, including all dietary exposure and all other exposure (e.g., non-occupational exposures) for which there is reliable information. Pesticide tolerances or exemptions from tolerance that do not meet the FFDCA safety standard are subject to revocation. In the absence of a tolerance or an exemption from tolerance, a food containing a pesticide residue is considered adulterated and may not be distributed in interstate commerce. | NMP is currently approved for use as a solvent and co-solvent inert ingredient in pesticide formulations for both food and non-food uses and is exempt from the requirements of a tolerance limit (40 CFR Part 180.920). |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | | |
| Clean Air Act (CAA) – Section 111 (b) | Requires EPA to establish new source performance standards (NSPS) for any category of new or modified stationary sources that EPA determines causes, or contributes significantly to, air pollution which may reasonably be anticipated to endanger public health or welfare. The standards are based on the degree of emission limitation achievable through the application of the best system of emission reduction which (considering the cost of achieving reductions and non-air quality health and environmental impacts and energy requirements) EPA determines has been adequately demonstrated. | NMP is subject to Clean Air Act Section 111 Standards of Performance for New Stationary Sources of Air Pollutants for VOC emissions from synthetic organic chemical manufacturing industry distillation operations (40 CFR Part 60, subpart NNN) and reactor processes (40 CFR Part 60, Subpart RRR). |
| Clean Air Act (CAA) – Section 183(e) | Section 183(e) requires EPA to list the categories of consumer and commercial products that account for at least 80 percent of all VOC emissions in areas that violate the National Ambient Air Quality Standards for ozone and to issue standards for these categories that require "best available controls." In lieu of regulations, EPA may issue control techniques guidelines if the guidelines are determined to be substantially as effective as regulations. | NMP is listed under the National Volatile Organic Compound Emission Standards for Aerosol Coatings (40 CFR part 59, subpart E). |
| Clean Air Act (CAA) – Section 612 | Under Section 612 of the Clean Air Act (CAA), EPA's Significant New Alternatives Policy (SNAP) program reviews substitutes for ozone depleting substances within a comparative risk framework. EPA publishes lists of acceptable and unacceptable alternatives. A determination that an alternative is unacceptable, or acceptable only with conditions, is made through rulemaking. | Under EPA's SNAP program, EPA listed NMP as an acceptable substitute for "straight organic solvent cleaning (with terpenes, C620 petroleum hydrocarbons, oxygenated organic solvents such as ketones, esters, alcohols, etc.)" for metals, electronics and precision cleaning and "Oxygenated organic solvents (esters, ethers, alcohols, ketones)" for aerosol solvents (59 FR, March 18, 1994). |
| Safe Drinking Water Act (SDWA) – Section 1412 (b) | Every 5 years, EPA must publish a list of contaminants (1) that are currently unregulated, (2) that are known or anticipated to occur in public water systems, | NMP was identified on both the Third (2009) and Fourth (2016) Contaminant Candidate Lists (74 |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | and (3) which might require regulations under SDWA. EPA must also determine whether to regulate at least five contaminants from the list every 5 years. | FR 51850, October 8, 2009) (81 FR 81099 November 17, 2016). |
| **Other Federal Regulations** | | |
| Occupational Safety and Health Act (OSHA) | Requires employers to provide their workers with a place of employment free from recognized hazards to safety and health, such as exposure to toxic chemicals, excessive noise levels, mechanical dangers, heat or cold stress, or unsanitary conditions.<br><br>Under the Act, OSHA can issue occupational safety and health standards including such provisions as Permissible Exposure Limits (PELs), exposure monitoring, engineering and administrative control measures and respiratory protection. | OSHA has not established a PEL for NMP, though OSHA identifies potential symptoms and health effects associated with NMP including eye irritation, severe skin irritation with chronic exposure and reproductive hazards including possible fetal toxicity. |
| Federal Food, Drug and Cosmetic Act (FFDCA) | Provides the U.S Food and Drug Administration (FDA) with authority to oversee the safety of food, drugs and cosmetics. | Food and Drug Administration identifies NMP as an "Indirect Additive Used in Food Contact Substances" specifically as:<br>1) an adjuvant substance in the preparation of slimicides (21 CFR 176.300),<br>2) an adjuvant substance in the production of polysulfone resin authorized for use as articles intended for use in contact with food (21 CFR 177.1655) and<br>3) a residual solvent in polyetherone sulfone resins authorized as articles for repeated use in contact with food (21 CFR 177.2440).<br>FDA also identifies NMP as a Class 2 solvent, namely a solvent that "should be limited in pharmaceutical products because of their inherent toxicity."<br>FDA established a Permissible Daily Exposure (PDE) for NMP of 5.3 mg/day with a concentration limit of 530 ppm.<br>FDA's Center for Veterinary Medicine developed a method in |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | | 2011 for detection of the residues of NMP in edible tissues of cattle (21 CFR 500.1410) |

## A.2 State Laws and Regulations

**Table_Apx A-2. State Laws and Regulations**

| State Actions | Description of Action |
|---|---|
| State Air Regulations | New Hampshire (Env-A 1400: Regulated Toxic Air Pollutants) lists NMP as a regulated toxic air pollutant.<br><br>Vermont (Vermont Air Pollution Control Regulations, 5261) lists NMP as a hazardous air contaminant. |
| Chemicals of Concern to Children | Several states have adopted reporting laws for chemicals in children's products that include NMP including Oregon (OAR 333-016-2000), Vermont (18 V.S.A. sections 1771 to 1779) and Washington state (WAC 173-334-130). Minnesota has listed NMP as a chemical of concern to children (Minnesota Statutes 116.9401 to 116.9407). |
| State Permissible Exposure Limits | California PEL is 1 ppm as an 8hr-time-weighted average (TWA), along with a skin notation (Cal Code Regs, title 8, section 5155). |
| State Right-to-Know Acts | Massachusetts (454 CMR 21.00), New Jersey (42 N.J.R. 1709(a)) and Pennsylvania (Chapter 323. Hazardous Substance List). |
| Other | In California, NMP is listed on Proposition 65 (Cal. Code Regs. title 27, section 27001) due to reproductive toxicity. California OEHHA lists a Maximum Allowable Dose Level (MADL) for inhalation exposure = 3,200 µg/day MADL for dermal exposure = 17,000 µg/day.<br><br>The California Department of Toxic Substances Control (DTSC) Safer Consumer Products Program lists NMP as a Candidate Chemical for development toxicity and reproductive toxicity. In addition, DTSC is moving to address paint strippers containing NMP and specifically cautioned against replacing Methylene Chloride with NMP. California is considering a separate rule on NMP.<br>California Department of Public Health's Hazard Evaluation System and Information Service (HESIS) issued a Health Hazard Advisory on NMP in 2006 and updated the Advisory in June 2014. The Advisory is aimed at workers and employers at sites where NMP is used. |

## A.3 International Laws and Regulations

**Table_Apx A-3. Regulatory Actions by Other Governments and Tribes**

| Country/Organization | Requirements and Restrictions |
|---|---|
| European Union | In 2011, NMP was listed on the Candidate list as a Substance of Very High Concern (SVHC) under regulation (EC) No 1907/2006 - REACH (Registration, Evaluation, Authorization and Restriction of Chemicals).<br>In March 2017, NMP was included in the public consultation of chemicals recommended for inclusion in Annex XIV of the European Chemicals Agency (ECHA) under Annex (Authorisation list) of regulation (EC) No 1907/2006 - REACH (Registration, Evaluation, Authorization and Restriction of Chemicals).<br>In 2013, the Netherlands submitted a proposal under REACH to restrict manufacturing and all industrial and professional uses of NMP where workers' exposure exceeds a level specified in the restriction (European Chemicals Agency (ECHA) database. Accessed April 18, 2017).<br>On April 18, 2018, the European Union added NMP to REACH Annex XVII, the restricted substances list. The action specifies three conditions of restriction. The conditions are: 1) NMP shall not be placed on the market as a substance on its own or in mixtures in concentrations greater than 0.3% after May 9, 2020, unless manufacturers, importers and downstream users have included chemical safety reports and safety data sheets with Derived No-Effect Levels (DNELs) relating to workers' exposures of 14.4 mg/m3 for exposure by inhalation and 4.8 mg/kg/day for dermal exposure; 2) NMP shall not be manufactured, or used, as a substance on its own or in mixtures in a concentration equal to or greater than 0.3% after May 9, 2020 unless manufacturers and downstream users take the appropriate risk management measures and provide the appropriate operational conditions to ensure that exposure of workers is below the DNELs specified above: and 3) the restrictions above shall apply from May 9, 2024 to placing on the market for use, or use, as a solvent or reactant in the process of coating wires. |
| Australia | NMP was assessed under Human Health Tier III of the Inventory Multi-tiered Assessment and Prioritisation (IMAP) (National Industrial Chemicals Notification and Assessment Scheme, NICNAS, 2017, Human Health Tier III assessment for 2-Pyrrolidinone, 1methyl-. Accessed April, 18 2017). |
| Japan | NMP is regulated in Japan under the following legislation:<br>• Act on the Evaluation of Chemical Substances and Regulation of their Manufacture, etc. (Chemical Substances Control Law; CSCL)<br>• Industrial Safety and Health Act<br>(National Institute of Technology and Evaluation (NITE) Chemical Risk Information Platform (CHIRP). Accessed April 18, 2017). |

| Country/Organization | Requirements and Restrictions |
|---|---|
| European Union and Australia, Austria, Belgium, Canada (Ontario), Denmark, Finland, France, Germany, Ireland, Italy, Latvia, New Zealand, Poland, Spain, Sweden, Switzerland, The Netherlands, Turkey and the United Kingdom. | Occupational exposure limits for NMP (GESTIS International limit values for chemical agents (Occupational exposure limits, OELs) database. Accessed April 18, 2017). |

# Appendix B PROCESS, RELEASE AND OCCUPATIONAL EXPOSURE INFORMATION

This appendix provides information and data found during preliminary data gathering for NMP.

## B.1 Process Information

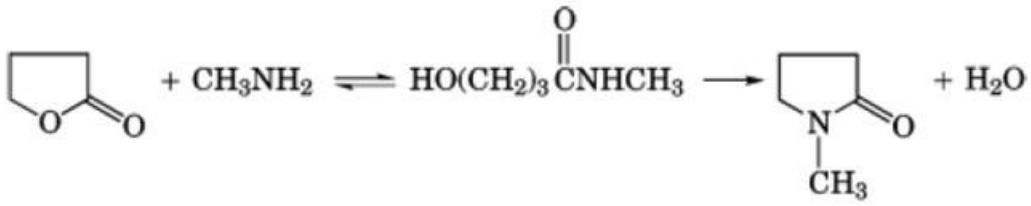
Process-related information potentially relevant to the risk evaluation may include process diagrams, descriptions and equipment. Such information may inform potential release sources and worker exposure activities for consideration. Note that the processing information below is representative of NMP, but not inclusive of all uses. EPA will consider this information and data in combination with other data and methods for use in the risk evaluation.

### B.1.1 Manufacture (Including Import)

According to 2016 public CDR data, NMP is both domestically manufactured in and imported into the United States (U.S. EPA, 2016b).

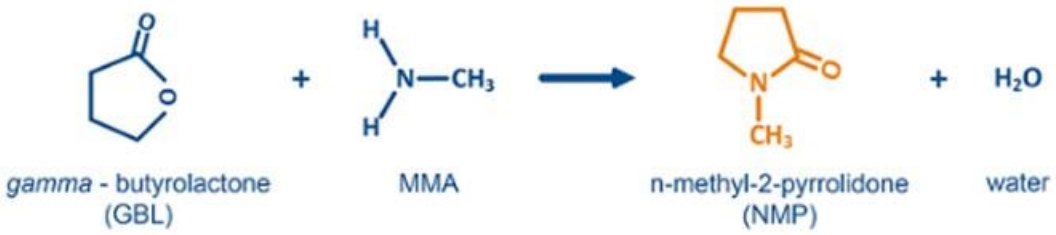
#### B.1.1.1 Domestic Manufacturing

NMP can be manufactured using different methods. One method involves reaction of butyrolactone with an excess of pure or aqueous methylamine in a high pressure tube (Harreus et al., 2011). This reaction is shown in Figure_Apx B-1 and is taken from (Anderson and Liu, 2000). This exothermic reaction takes place under adiabatic conditions, and produces a reaction product containing NMP that is subsequently distilled to purify the NMP produced. This method of manufacturing results in a 97% yield of NMP (Harreus et al., 2011).




**Figure_Apx B-1. NMP Manufacturing Under Adiabatic Conditions**

Another process for manufacturing NMP involves reacting gamma-butyrolactone (GBL) and monomethylamine (MMA), as shown in Figure_Apx B-2 (Johnson Matthey Process Technologies, 2017). This reaction is non-catalyzed and takes place in two stages. The first stage produces a long-chain amide that is cyclized, then dehydrated to form NMP during the second stage of the reaction. The reaction product which contains NMP is then distilled to purify the NMP.




**Figure_Apx B-2. NMP Manufacturing Using Gamma-Butyrolactone (GBL) and Monomethylamine (MMA)**

NMP is also manufactured from maleic anhydride in an integrated production process at a Mitsubishi plant in Japan (Mitsubishi Chemical, 2017).

#### B.1.1.2 Import

Typical import activities for NMP include storage in warehouses prior to distribution for further processing and use and quality control sampling.

Transfers of NMP are generally done with steel piping, as rubber hose is not suitable for handling. NMP may be transported in tank cars, tank trailers or drums. Shipping containers normally consist of unlined steel (Anderson and Liu, 2000).

### B.1.2 Processing

#### B.1.2.1 Reactant/Intermediate

The exact process operations involved during the use of NMP as a chemical intermediate are dependent on the final product that is being synthesized. For NMP use as a chemical intermediate, operations would typically involve unloading NMP from transport containers and feeding it into reaction vessel(s), where the NMP would either react fully or to a lesser extent. Following completion of the reaction, the produced substance may or may not be purified further, thus removing unreacted NMP (if present). The reacted NMP is assumed to be destroyed and therefore is not expected to be released to the environment or to present a potential for worker exposure.

#### B.1.2.2 Incorporation into Formulation, Mixture, or Reaction Product

NMP is incorporated into formulations for a wide range of products, including cleaning products, paints, coatings, adhesives, sealants, inks and toners (ECHA, 2011). Formulation processes for these products typically involve similar operations. First, the components of the product formulation are unloaded from transport containers, either directly into the mixing equipment or into an intermediate storage vessel. Transfer from transport containers may be manual or automated, through the use of a pumping system. An automated dispenser may be used to feed components into the mixing vessel to ensure that precise amounts are added at the proper time during the mixing process. Once in the mixing vessel, the components are then mixed in either a batch or continuous system. Evaporative losses of NMP and other volatile components will depend on whether a closed or open system is used during the mixing process (OECD, 2010a).

Depending on the specific product, the formulation may be further processed through filtering. Once the formulation is completed, it is sampled for quality purposes. The final formulation is then filled into containers, either through manual dispensing from transfer lines or through utilization of an automatic system. Automatic filling systems are generally used for the filling of smaller containers that are

intended for consumer and commercial applications, whereas manual filling is done for larger containers (e.g., tank trucks, totes, drums) which are typically used in an industrial setting (OECD, 2010a).

#### B.1.2.3 Incorporation into Article

EPA defines articles as manufactured items that are formed to a specific shape or design during manufacture and for which the end use is dependent in whole or in part upon their shape or design. The exact process operations involved in the incorporation of NMP are dependent on the article. Incorporation into an article typically refers to a process in which a chemical becomes an integral component of an article (as defined at 40 CFR 704.3) for distribution in commerce. The exact process operations involved in the incorporation of NMP-containing formulations or reaction products are dependent on the article. EPA identified the following processing activities that incorporate NMP and NMP formulations or reaction products into articles.

#### B.1.2.4 Repackaging

Typical repackaging operations involve transferring of NMP into appropriately sized containers to meet customer demands/needs.

#### B.1.2.5 Recycling

NMP is used as an extractive solvent for effective removal of various compounds by petrochemical and other industries (ECHA, 2011). In this capacity, NMP absorbs the compound being extracted and can be regenerated and recycled for reuse; this is described in further detail in the Petrochemical Processing Aid section.

### B.1.3 Uses

In this document, EPA has grouped uses based on CDR categories and identified examples within these categories as subcategories of use. Note that some subcategories may be grouped under multiple CDR subcategories. These differences will be further investigated and refined during risk evaluation.

#### B.1.3.1 Paints and Coatings

The physical-chemical properties of NMP make it miscible in water and many hydrocarbon solvents, allowing NMP to be used in a diverse range of paint and coating applications (ECHA, 2011). The components of the paint or coating are formulated as discussed in the previous section. Note that many paint and coating formulations are filtered to remove any undesired solids (such as gel, pigment or filler agglomerates) (OECD, 2010a) prior to packaging into transport containers.

Containers of formulated paints and coating products are then sent to the customer for application, where they may be diluted and mixed prior to application (OECD, 2011). Application techniques include brushing, rolling, spraying, printing, dipping and curtain coating, and may be manual or automated. Once applied to the substrate, the paint or coating is allowed to dry or “cure” during this time, the NMP in the coating evaporates completely (ECHA, 2011). The drying/curing process may be promoted through the use of heat or radiation (radiation can include ultraviolet and electron beam radiation), but this more common for waterborne coatings (OECD, 2010a). Due to its evaporation potential, NMP is not assumed to be present in articles after the drying/curing process is complete (ECHA, 2011).

NMP is used for paint removal in a variety of industries, such as the automotive, aircraft, construction and refinishing industries. Application methods include manual or automated, with techniques such as spraying, brushing, pouring, wiping and rolling. Additional details on this use of NMP can be found in the previous risk assessment which evaluated the use of NMP in paint and coating removal (U.S. EPA, 2015).

### B.1.3.2 Solvents for Cleaning and Degreasing

NMP is used in a variety of cleaning products, because of its high solvating power for plastics, resins, oil and grease (ECHA, 2011). NMP is used in industrial cleaners and degreasers, graffiti-removing products and consumer cleaning products. NMP is also used in the electronics industry as a solvent carrier in photoresist formulations, and for removal of excess photoresist from silicon wafers (ECHA, 2011).

Once formulated, cleaning solutions containing NMP can be applied to substrates using a variety of application methods, including roller application, brushing, dipping, pouring, spraying and wiping. NMP application may be automated or manual, depending on the cleaning product. Consumer cleaning solutions are likely to be applied manually, whereas industrial cleaning processes are often automated. The applied cleaning solution is then removed from the substrate, along with the contaminants, and discarded as waste.

Degreasing operations are used to remove dirt, grease and surface contaminants from the substrate. NMP is reportedly used as a solvent in degreasing tanks in the aerospace industry (ECHA, 2011). Industrial degreasing operations can involve batch or continuous processes; actual operation can include vapor-phase and/or liquid-phase degreasing (e.g., cold cleaning) (U.S. EPA, 2016b).

Photoresist formulations containing solvents, such as NMP, are applied using a dispensing apparatus that applies small amounts of photoresist formulations to wafers, which are then spun at a high speed to uniformly coat their surface. The excess photoresist that is spun off of the wafer is then disposed of as waste. The coated wafers are subsequently baked to evaporate the carrier solvent, exposed to form an image and then baked again to ensure that trace amounts of solvent are evaporated (OECD, 2010b). Wafers are then developed to dissolve unwanted portions of the photoresist and etched to remove unwanted areas of silicon substrate or deposited film before the residual photoresist is removed. Wet removal processes involve submersion of wafers in a bath solution containing chemicals such as solvents, acids or bases, to dissolve the photoresist. The waste bath containing the dissolved photoresist is collected, and potentially treated, prior to disposal (OECD, 2010b).

### B.1.3.3 Ink, Toner and Colorant Products

Printing inks are comprised of colorants (e.g., pigments, dyes and toners) dispersed in a formulation to form a paste, liquid or solid which can be applied to a substrate surface and dried (OECD, 2010c). In addition to colorants, ink formulations contain several types of substances including solvents such as NMP, binders, thinners, dispersing agents and drying agents. During product formulation, colorants are generally added after all of the other components have been combined and mixed. Dispersion usually involves a milling process, to break up and evenly distribute the colorant throughout the formulation.

Transport containers for inks and toners can vary widely depending on the intended end use of the product formulation. Consumer products are packaged into smaller containers, such as cartridges for printing or writing inks, whereas product formulations intended for industrial printing operations are generally packaged into larger (e.g., 1-5-gallon) containers (OECD, 2010c).

Industrial printing processes can be categorized as lithographic, flexographic, gravure, letterpress, screen printing or digital printing. Commercial printing may involve lithographic, flexographic, gravure and letterpress printing - all of which involve the transfer of images from printing plates to a substrate. Screen printing requires a mesh screen to transfer the ink to a substrate, whereas digital printing allows for the transfer of a digital image directly onto a substrate. Inkjet printing is the most common form of digital printing. It involves the application of small drops of ink onto a substrate, with direct contact

between the ink nozzle and the substrate. Consumer printing is generally limited to digital inkjet printing; however, consumers also use inks that are pre-loaded into a pen prior to distribution in commerce (ECHA, 2011).

#### B.1.3.4 Processing Aids Specific to Petroleum Production

NMP is used as a petrochemical processing aid in a variety of applications including extraction of aromatic hydrocarbons from lube oils; separation and recovery of aromatic hydrocarbons from mixed hydrocarbon feedstocks; recovery of acetylenes, olefins and diolefins; removal of sulfur compounds from natural gas and refinery gases; and dehydration of natural gas (Anderson and Liu, 2000).

Extractive distillation involves distillation in the presence of a solvent (or mixture of solvents) which acts as a separating agent, displaying both a selectivity for, and the capacity to solubilize components in a mixture to be separated (Doherty and Knapp, 2004). Solvents interact differently with the components of the mixture to be separated, thereby altering their relative volatility and allowing them to be separated. Solvent are added near the top of the extractive distillation column, while the mixture to be separated is added at a second feed point further down the column. The component with the higher volatility in the presence of a solvent is distilled overhead as the distillate and components with lower volatility are removed with the solvent in the column bottoms. The solvent is then separated from other components of the mixture, generally through distillation in a second column, and then recycled back to the extractive distillation column (Doherty and Knapp, 2004).

NMP is used both for the extraction of unwanted aromatics from lube oils and the recovery of hydrocarbons from feedstocks, via extractive distillation (ECHA, 2011). NMP is favorable for the extractive distillation of hydrocarbons because hydrocarbons are highly soluble in NMP, and the use of NMP for extraction does not lead to the formation of azeotropes. NMP also has high resistance to heat and chemicals (Stevens et al., 2007).

Other uses of NMP in petrochemical processing involve first using NMP to absorb specific compounds, then separating the NMP from the absorbed compounds, similar to the extractive distillation process (Anderson and Liu, 2000). Examples of absorptive processes include NMP use in the recovery of acetylenes, olefins and diolefins; removal of sulfur compounds from natural and refinery gases; and the dehydration of natural gas.

Absorption using a solvent, such as NMP, generally involves two towers, an absorption tower and a removal tower. The mixture to be separated and the solvent are first introduced into the absorption tower. Here the solvent absorbs the miscible compound and this heavier stream leaves in the bottoms of the column. The solvent mixture is then sent to another column where the absorbed compound is recovered from the solvent. The solvent may undergo further processes, such as scrubbing, to be fully regenerated before being recycled back into the absorption column (Gannon and Schaffer, 2003). (Information specific to the use of NMP for hydraulic fracturing operations was not identified.)

#### B.1.3.5 Adhesives and Sealants

NMP is used as a component in the formulation of solvent-based adhesives and sealants (OECD, 2009a). Once the adhesive or sealant is received by the user, it may be diluted or mixed prior to application (OECD, 2015). The adhesive formulation is then loaded into the application reservoir or apparatus and applied to the substrate via spray, roll, curtain, syringe or bead application which may be manual or automated. After application, the adhesive or sealant is allowed to dry, usually at ambient temperature. During this time the solvent completely evaporates and a bond is formed between the

substrates. In some instances, heat is applied to the substrate to promote the drying or curing of the adhesive or sealant (OECD, 2015).

#### B.1.3.6 Other Uses

A number of other uses have been identified for NMP, including laboratory use for various research and cleaning purposes. These activities typically occur within a fume hood, on a bench with local exhaust ventilation, or under conditions that include general ventilation (ECHA, 2011).

***Lithium Ion Battery Manufacturing***

NMP use as a solvent for electrode preparation and in electrolyte formulations used for lithium ion battery manufacturing is growing (Daniel, 2008). Electrolyte formulations usually include a lithium salt dissolved in a solvent-based solution (Kamienski, 2004). The electrolyte is formulated separately, then filled into the assembled cell, which consists of the electrode structures. Once the electrolyte solution is added, the battery is sealed.

***Pharmaceuticals***

NMP is increasingly being used as a solvent and extraction medium for the manufacture and formulation of pharmaceuticals (ECHA, 2011).

***Reaction Medium***

in industry, NMP is often used as a reaction medium for polymerization reactions, because many polymers are soluble in NMP (Anderson and Liu, 2000). Specific polymers that are soluble in NMP include polyvinyl acetate, polyvinyl fluoride, polystyrene, nylon, polyimides, polyesters, acrylics, polycarbonates and synthetic elastomers. Depending on the intended product, once the polymer is synthesized in the NMP-containing reaction medium, it may be isolated and precipitated. However, some polymer-based resin and coating formulations, such as polyurethane dispersions, will include NMP in the final formulation (BPI, 2017). Additional uses of NMP as a reaction medium have not been identified.

***Textiles and Clothing***

NMP has been found in textiles; however, EPA has not identified information specific to the use of NMP in the textile industry.

### B.1.4 Disposal

NMP is not designated as a hazardous substance under federal regulations thus, there are no federal regulations determining how NMP and NMP-containing products may be disposed. However, three states, Massachusetts, New Jersey and Pennsylvania have designated NMP as a hazardous substance, thereby regulating NMP disposal. EPA has not identified other specific NMP disposal information.

## B.2 Occupational Exposure Data

EPA presents herein some examples of occupational exposure-related information for NMP obtained from preliminary data gathering. EPA expects to consider this information in combination with other readily available data and methods for use in risk evaluation.

Table_Apx B-1 and Table_Apx B-2 show mappings of release and worker exposure scenarios to industry sectors with available OSHA monitoring data obtained from OSHA inspections between 2002 and 2016 for personal monitoring data and area monitoring data, respectively. EPA attempted to group industry sectors, designated by North American Industry Classification System (NAICS) code,

according to possible release/exposure scenarios, but there is a great degree of uncertainty where and how NMP may be used in these industries. The industry sectors in Table_Apx B-1 and Table_Apx B-2 were extracted from the OSHA CEHD (OSHA, 2017a).

EPA also found some NIOSH HHE data since 2000 that are summarized and included in Table_Apx B-3.

**Table_Apx B-1. Mapping of Scenarios to Industry Sectors with NMP Personal Monitoring Air Samples Obtained from OSHA Inspections Conducted Between 2012 and 2016**

| Possible Release/Exposure Scenario | NAICS | NAICS Description |
|---|---|---|
| Paint stripping; Adhesive removal by contractors; Roll/curtain, spray, or manual application of lacquers, stains, varnishes, and primers | 811420 | Reupholstery and Furniture Repair |
| Aerosol degreasing; Wipe cleaning; Spray, manual (brushing), or dip application of metal finishing products; | 333249 | Other Industrial Machinery Manufacturing |
| Unknown – this establishment is an OSHA facility | 923110 | Administration of Education Programs |

[a] Samples are not 8-hr TWA. Results include non-detects (below limit of quantification) and exclude blank samples.

**Table_Apx B-2. Mapping of Scenarios to Industry Sectors with NMP Area Monitoring Air Samples Obtained from OSHA Inspections Conducted Between 2012 and 2016**

| Possible Release/Exposure Scenario | NAICS | NAICS Description |
|---|---|---|
| Paint stripping; Adhesive removal by contractors; Roll/curtain, spray, or manual application of lacquers, stains, varnishes, and primers | 811420 | Re-upholstery and Furniture Repair |

[a] Samples are not 8-hr TWA. Results include non-detects (below limit of quantification) and exclude blank samples.

**Table_Apx B-3. Summary of NIOSH HHE NMP Data**

| Exposure/Release Scenario | Facility Description | Number of Exposure Samples | Minimum of Exposure Values (ppm) | Maximum of Exposure Values (ppm) | Comments | Source |
|---|---|---|---|---|---|---|
| Paint and coating removal | Floor refinishing | 7 (PBZ)<br>13 (Area) | 1.4 (PBZ)<br>2.2 (Area) | 5.2 (PBZ)<br>9.3 (Area) | Samples are a mix of full-shift and short-term exposures. | Kiefer (1994) |
| Spray application of paints, coatings, and adhesives | Spray application of paints onto automotive seals | 48 (PBZ)<br>20 (Area) | 0.01 (PBZ)<br>0.01 (Area) | 1.27 (PBZ)<br>25.0 (Area) | Individual data points not provided. Source only includes range and average of exposure values by job function. | NIOSH (1998) |

PBZ – Personal Breathing Zone

## B.3 Sources Containing Potentially Relevant Data or Information

Some sources of information and data related to releases and worker exposure were found during the Systematic review literature search. Sources of data or information identified in the Analysis Plan Sections 2.6.1.1 (releases) and 2.6.1.3 (occupational exposures) are shown in the four tables below. The data sources identified are based on preliminary results to date of the full-text screening step of the systematic review process. Further screening and quality evaluation are on-going. These sources will be reviewed to determine the utility of the data and information in the Risk Evaluation.

**Table_Apx B-4. Potentially Relevant Data Sources for Information Related to Process Description**

| Bibliography | url |
|---|---|
| Nishimura, S., et al. (2009). "A cross-sectional observation of effect of exposure to N-methyl-2-pyrrolidone (NMP) on workers' health." Industrial Health **47**(4): 355-362. | Nishimura et al. (2009) |
| Solomon, G. M., et al. (1996). "Stillbirth after occupational exposure to N-methyl-2-pyrrolidone: A case report and review of the literature." Journal of Occupational and Environmental Medicine **38**(7): 705-713. | Solomon et al. (1996) |
| Bader, M., et al. (2006). "Ambient monitoring and biomonitoring of workers exposed to N-methyl-2-pyrrolidone in an industrial facility." International Archives of Occupational and Environmental Health **79**(5): 357-364. | Bader et al. (2006) |
| Meier, S., et al. (2013). "Biomonitoring of exposure to N-methyl-2-pyrrolidone in workers of the automobile industry." Annals of Occupational Hygiene **57**(6): 766-773. | Meier et al. (2013) |
| Muenter, J. and R. Blach (2010). "Ecological technology: NMP-free leather finishing." American Leather Chemists Association. Journal **105**(9): 303-308. | Muenter and Blach (2010) |
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| RIVM (2013). Annex XV Restriction Report: Proposal for a Restriction. RIVM, Bureau REACH. The Netherlands, National Institute for Public Health and the Environment (RIVM). | RIVM (2013) |
| OECD (2009). Emission scenario document on adhesive formulation. Paris, France. | OECD (2009a) |
| U.S. EPA (1998). Environmental profile for N-methylpyrrolidone. Washington, DC. | U.S. EPA (1998b) |
| ECHA (2014). Background document to the opinion on the annex XV dossier proposing restrictions on 1-methyl-2-pyrrolidone (NMP). Helsinki, Finland. | ECHA (2014a) |
| OECD (2017). Emission Scenario Document (ESD) on the use of textile dyes. | OECD (2017) |
| OECD (2015). Emission scenario document on use of adhesives. Paris, France. | OECD (2015) |
| OECD (2010). Emission Scenario Document on Formulation of Radiation Curable Coatings, Inks and Adhesives. Series on Emission Scenario Documents No. 21. Paris, OECD Environmental Health and Safety Publications. | OECD (2010a) |
| OECD (2010). Emission Scenario Document on Photoresist Use in Semiconductor Manufacturing. Series on Emission Scenario Documents No. 9. Paris, OECD Environmental Health and Safety Publications. | OECD (2010b) |

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|---|---|
| OECD (2010). Scoping Document for Emission Scenario Document on Manufacturing and Use of Printing Inks, OECD Environmental Health and Safety Publications. | OECD (2010c) |
| OECD (2011). EMISSION SCENARIO DOCUMENT ON RADIATION CURABLE COATING, INKS AND ADHESIVES. Series on Emission Scenario Documents No. 27. Paris, OECD Environmental Health and Safety Publications. | OECD (2011) |
| White, D. L. and J. A. Bardole (2004). Paint and finish removers. | White and Bardole (2004) |
| (2017). PubChem: 1-Methyl-2-pyrrolidinone. Washington, DC, National Institute of Health, U.S. National Library of Medicine, National Center for Biotechnology Information. | NCBI (2017) |
| ECHA (2017). Uses as industrial sites: 1-Methyl-2-pyrrolidone. Helsinki, Finland. | ECHA (2017a) |
| ECHA (2017). Uses by professional workers: 1-Methyl-2-pyrrolidone. Helsinki, Finland. | ECHA (2017b) |
| NIOSH (2014). Health hazard evaluation report no. HHE-2011-0099-3211, evaluation of employee exposures during sea lamprey pesticide application. Cincinnati, OH. | NIOSH (2014a) |
| NICNAS (1997). Full public report: Polymer in byk-410. | NICNAS (1997) |
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| Johnson Matthey Process Technologies (2017). "N-methyl-2-pyrrolidone (NMP)." from http://davyprotech.com/what-we-do/licensed-processes-and-core-technologies/licensed-processes/nmp/specification/. | Johnson Matthey Process Technologies (2017) |
| European Chemicals Agency (ECHA) (2016). 1-methyl-2-pyrrolidone brief profile. | European Chemicals Agency (ECHA) (2016) |
| BASF (1990). Technical information: N-methylpyrrolidone handling and storage. Parsippany, NJ. | BASF (1990) |
| TURI (1996). N-methyl pyrrolidone: Chemical profile. Lowell, MA, The Toxics Use Reduction Institute. | TURI (1996) |
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| ERG (2000). Preferred and alternative methods for estimating air emissions from paint and ink manufacturing facilities. Durham, NC, Emission Inventory Improvement Program. | ERG (2000) |
| Technikon LLC (2001). Core box cleaner study: Evaporative emission study of specialty systems' solvent FC-47-G1. McClellan, CA, Casting Emission Reduction Program. | Technikon LLC (2001) |
| EC (2004). Effectiveness of vapour retardants in reducing risks to human health from paint strippers containing dichloromethane. Brussels, Belgium. | EC (2004a) |
| ERM (2017). Life cycle assessment of used oil management. London, UK. | ERM (2017) |

**Table_Apx B-5. Measured or Estimated Release Data**

| Bibliography | url |
|---|---|
| Kim, B. R., et al. (2000). "Henry's law constants for paint solvents and their implications on volatile organic compound emissions from automotive painting." Water Environment Research **72**(1): 65-74. | Kim et al. (2000) |
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| OECD (2015). Emission scenario document on use of adhesives. Paris, France. | OECD (2015) |
| OECD (2010). Emission Scenario Document on Formulation of Radiation Curable Coatings, Inks and Adhesives. Series on Emission Scenario Documents No. 21. Paris, OECD Environmental Health and Safety Publications. | OECD (2010a) |
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| OECD (2010). Scoping Document for Emission Scenario Document on Manufacturing and Use of Printing Inks, OECD Environmental Health and Safety Publications. | OECD (2010c) |

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| (2016). Toxic release inventory: N-methyl-2-pyrrolidone. | U.S. EPA (2016c) |
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| Chemistry Industry Association of Canada (2017). All substances emissions for 2012 and projections for 2015. Ottawa, Canada. | Chemistry Industry Association of Canada (2017b) |
| Chemistry Industry Association of Canada (2017). All substances emissions for 2011 and projections for 2014. Ottawa, Canada. | Chemistry Industry Association of Canada (2017a) |

**Table_Apx B-6. Personal Exposure Monitoring and Area Monitoring Data**

| Bibliography | url |
|---|---|
| Nishimura, S., et al. (2009). "A cross-sectional observation of effect of exposure to N-methyl-2-pyrrolidone (NMP) on workers' health." Industrial Health **47**(4): 355-362. | Nishimura et al. (2009) |
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| OEHHA (2007). Occupational health hazard risk assessment project for California: Identification of chemicals of concern, possible risk assessment methods, and examples of health protective occupational air concentrations. Sacramento, CA. | OEHHA (2007) |
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**Table_Apx B-7. Engineering Controls and Personal Protective Equipment**

| Bibliography | url |
|---|---|
| Nishimura, S., et al. (2009). "A cross-sectional observation of effect of exposure to N-methyl-2-pyrrolidone (NMP) on workers' health." Industrial Health **47**(4): 355-362. | Nishimura et al. (2009) |
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# Appendix C SURFACE WATER ANALYSIS OF NMP RELEASES

This appendix provides an analysis of surface water concentrations based on reported surface water releases of NMP.

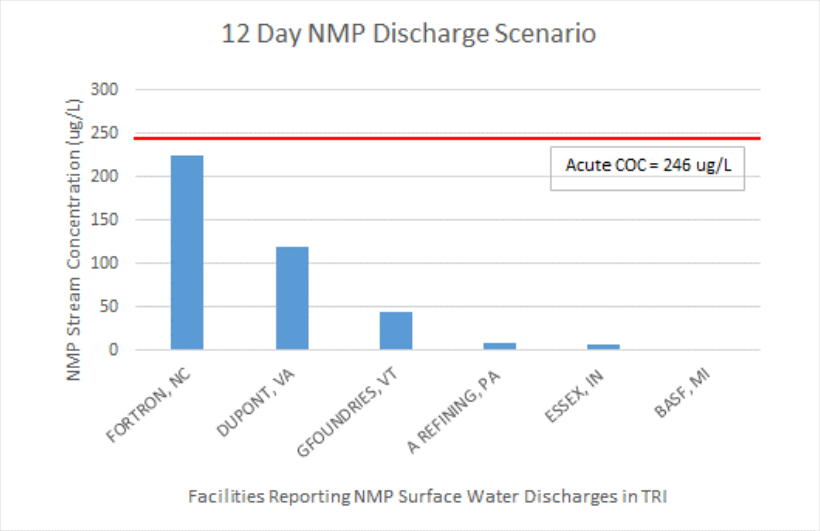
EPA considered several scenarios to estimate NMP concentrations in surface water resulting from industrial discharges. Using 2015 TRI available data and EPA's first-tier, Probabilistic Dilution Model (PDM) within the EPA Exposure and Fate Assessment Screening Tool (E-FAST), facilities with the largest releases of NMP were modeled for 12 days of release, and 250 days of release. The 12-day release scenario represents an acute scenario in which periodic maintenance and cleaning activities result in periodic releases. The 250-day scenario represents a chronic scenario in which operations consist of fairly constant discharges of NMP. Six facilities had reported direct discharges of NMP to surface waters and seven facilities reported indirect discharges, that is discharges sent to a municipal treatment facility also known as a public-owned treatment works (POTW) for treatment and discharge into surface waters. The single day release was considered the most conservative scenario since the NMP surface water concentrations were highest (see Table_Apx C-1).

**Table_Apx C-1. Estimated NMP Surface Water Concentrations**

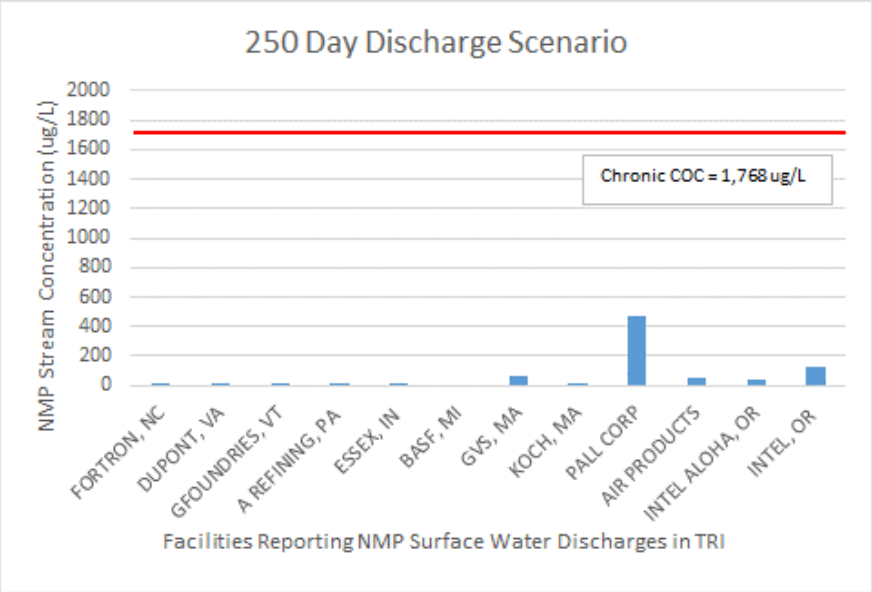
| Top Facility Discharges (2015) | | Direct TRI | Indirect TRI | PDM; input loadings (kg/site/day) | | PDM; stream NMP concentrations | |
|---|---|---|---|---|---|---|---|
| Facility Location | State | Pounds (lbs/yr) | Pounds (lbs/yr) | 12 day scenario | 250 day scenario | 12 day (ug/L) | 250 day (ug/L) |
| WILMINGTON | NC | 8,987 | 0 | 339.71 | 16.31 | 224.00 | 10.75 |
| RICHMOND | VA | 4,602 | 0 | 173.96 | 8.35 | 119.70 | 5.75 |
| ESSEX JUNCTION | VT | 451 | 0 | 17.05 | 0.82 | 44.49 | 2.14 |
| BRADFORD | PA | 26.83 | 0 | 1.01 | 0.05 | 8.49 | 0.4 |
| FORT WAYNE | IN | 22.1 | 0 | 0.84 | 0.04 | 5.56 | 0.27 |
| WYANDOTTE | MI | 2 | 21.52 | 0.08 | 0.00 | 0.0011 | 0.0000538 |
| WESTBOROUGH | MA | | 8,048 | 304.21 | 14.60 | | 69.03 |
| WILMINGTON | MA | | 42,682 | 1613.38 | 77.44 | | 4.79 |
| PENSACOLA | FL | | 12,384 | 468.12 | 22.47 | | 467.92 |
| SAINT LOUIS | MO | | 12,001 | 453.64 | 21.77 | | 50.86 |
| ALOHA | OR | | 13,600 | 514.08 | 24.68 | | 39.91 |
| HILLSBORO | OR | | 40,800 | 1542.24 | 74.03 | | 119.72 |

EPA then compared the surface water concentrations with the aquatic organism acute and chronic COCs estimated during problem formulation, 246 ppb and 1,768 ppb, respectively.

**Figure_Apx C-1. Estimated Surface Water Concentration for 12-Day NMP Discharge**




**Figure_Apx C-2. Estimated Surface Water Concentration for 250 Day NMP Discharge**




For all modeled NMP release scenarios, none of the facility discharges resulted in an exceedance of the acute or chronic levels of concern identified for ecological receptors.

# Appendix D SUPPORTING TABLE FOR INDUSTRIAL AND COMMERCIAL ACTIVITIES AND USES CONCEPTUAL MODEL

**Table_Apx D-1. Worker Exposure Conceptual Model Supporting Table (Note that rows shaded in gray are excluded from the scope of this risk evaluation)**

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | | Exposure Pathway | Exposure Route | Receptor / Population | Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|---|
| Manufacture | Domestic Manufacture | Domestic Manufacture | | Manufacture of NMP | Liquid Contact | Dermal | Workers | Yes | Dermal exposure is expected to be a primary pathway. The number of sites manufacturing NMP is limited per CDR (11 sites). |
| | | | | | Vapor | Inhalation | Workers, ONU | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | | Vapor | Dermal | Workers, ONU | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015). Vapor-through-skin is a pathway of concern. |
| | | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | | Mist / Dust | Dermal/Inhalation | Workers, ONU | No | Generation of mist and dust containing NMP is not expected during this operation. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | | Exposure Pathway | Exposure Route | Receptor / Population | Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|---|
| Manufacture | Import | Import | | Repackaging of import containers | Liquid Contact | Dermal | Workers | Yes | Exposure expected only in the event the imported material is repackaged into different sized containers. Exposure frequency may be low. However, the number of workers potentially exposed may be high per CDR (13 submissions reporting <10 workers, 1 submission reporting 10 to 25 workers, 5 submissions reporting 50 to 100 workers, 1 submission reporting 100 to 500 workers, and 9 submissions claiming CBI or NKRA for number of workers). |
| | | | | | Vapor | Inhalation | Workers, ONU | Yes | Exposure expected only in the event the imported material is repackaged into different sized containers. EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | | Vapor | Dermal | Workers, ONU | Yes | Exposure expected only in the event the imported material is repackaged into different sized containers. NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015). Vapor-through-skin is a pathway of concern. |
| | | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | | Mist / Dust | Dermal/Inhalation | Workers, ONU | No | Generation of mist and dust containing NMP is not expected during this operation. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | | Exposure Pathway | Exposure Route | Receptor / Population | Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|---|
| Processing | Processing as a reactant or intermediate | Intermediate in Pharmaceutical and Medicine Manufacturing; Other Chemical Manufacturing | | Pharmaceutical manufacturing; Chemical Manufacturing | Liquid Contact | Dermal | Workers | Yes | Dermal exposure is expected to be a primary pathway. The number of workers potentially exposed may be high per CDR (1 submission reporting 500 to 1,000 workers and 1 submission reporting NKRA for number of workers). |
| | | | | | Vapor | Inhalation | Workers, ONU | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | | Vapor | Dermal | Workers, ONU | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015). Vapor-through-skin is a pathway of concern. |
| | | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | | Mist / Dust | Dermal/Inhalation | Workers, ONU | No | Generation of mist and dust containing NMP is not expected during this operation. |
| Processing | Incorporated into formulation, mixture or reaction product | Adhesives and sealant chemicals in Adhesive Manufacturing; Anti-adhesive agents in Printing and Related Support Activities; Paint additives and coating additives not described by other codes in Paint and Coating Manufacturing; Print Ink Manufacturing; Plating agents and surface treating agents in Fabricated Metal Product Manufacturing; Solvents (for cleaning or degreasing) in Non-Metallic Mineral Product Manufacturing, Machinery Manufacturing, Plastic | | Formulation of adhesives; Formulation of chemical mixtures; Formulation of paints, and coatings; Formulation of printing inks; Formulation of metal finishing chemicals; Formulation of cleaning and degreasing products; Formulation of cleaning fluids; | Liquid Contact | Dermal | Workers | Yes | Dermal exposure is expected to be a primary pathway. The number of workers potentially exposed may be high per CDR (34 submissions reporting number of workers ranging from <10 to 500 to 1,000 workers). |
| | | | | | Vapor | Inhalation | Workers, ONU | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | | Vapor | Dermal | Workers, ONU | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015). |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | | Exposure Pathway | Exposure Route | Receptor / Population | Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|---|
| | | Material and Resin Manufacturing, Primary Metal Manufacturing, Soap, Cleaning Compound and Toilet Preparation Manufacturing, Transportation Equipment Manufacturing, All Other Chemical Product and Preparation Manufacturing, Printing and Related Support Activities, Services, Wholesale and Retail Trade; Solvents (which become part of product formulation or mixture) in Electrical Equipment, Appliance and Component Manufacturing, Other Manufacturing, Paint and Coating Manufacturing, Print Ink Manufacturing, Soap, Cleaning Compound and Toilet Preparation Manufacturing, Transportation Equipment Manufacturing, All Other Chemical Product and Preparation Manufacturing, Printing and Related Support Activities, Wholesale and Retail Trade; Surface active agents in Soap, Cleaning Compound and Toilet Preparation Manufacturing; Other uses in Oil and Gas Drilling, Extraction and Support Activities. | | Formulation of petrochemical products | | | | | Vapor-through-skin is a pathway of concern. |
| | | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | | Mist / Dust | Dermal/Inhalation | Workers, ONU | No | Generation of mist and dust containing NMP is not expected during this operation. |
| Processing | Incorporated into formulation, mixture or reaction product | Solvents (which become part of product formulation or mixture) in Other Manufacturing, All Other Chemical Product and Preparation Manufacturing. | | Formulation of granular agricultural products | Liquid Contact | Dermal | Workers | Yes | Dermal exposure is expected to be a primary pathway. The number of workers potentially exposed may be high per CDR (34 submissions reporting number of workers ranging from <10 to 500 to 1,000 workers). |
| | | | | | Vapor | Inhalation | Workers, ONU | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | | Exposure Pathway | Exposure Route | Receptor / Population | Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | | Dust | Inhalation | Workers, ONU | Yes | Dust formation is possible during manufacturing of solid products. |
| | | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | | Vapor | Dermal | Workers, ONU | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015). Vapor-through-skin is a pathway of concern. |
| | | | | | Mist | Dermal/Inhalation | Workers, ONU | No | Mist generation not expected during this operation. |
| Processing | Incorporated into article | Lubricants and lubricant additives in Machinery Manufacturing; Paint additives and coating additives not described by other codes in Transportation Equipment Manufacturing; Solvents (which become part of product formulation or mixture), including in Textiles, Apparel and Leather Manufacturing | | Formulation of lubricants; Formulation of Paints and Coatings; Formulation of textile finishing chemicals | Liquid Contact | Dermal | Workers | Yes | Dermal exposure is expected to be a primary pathway. |
| | | | | | Vapor | Inhalation | Workers, ONU | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | | Vapor | Dermal | Workers, ONU | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015). Vapor-through-skin is a pathway of concern. |
| | | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | | Mist / Dust | Dermal/Inhalation | Workers, ONU | No | Generation of mist and dust containing NMP is not expected during this operation. |
| Processing | Incorporated into article | Other, including in Plastic Product Manufacturing | | Plastics compounding | Liquid Contact | Dermal | Workers | Yes | Dermal exposure is expected to be a primary pathway. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | | Exposure Pathway | Exposure Route | Receptor / Population | Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|---|
| | | | | and Plastics converting | Vapor | Inhalation | Workers, ONU | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | | Dust | Inhalation | Workers, ONU | Yes | Dust formation is possible during plastic processing activities. |
| | | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | | Vapor | Dermal | Workers, ONU | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015). Vapor-through-skin is a pathway of concern. |
| | | | | | Mist | Dermal/Inhalation | Workers, ONU | No | Mist generation not expected during this operation. |
| Processing | Repackaging | Wholesale and Retail Trade | | Repackaging into large and small containers | Liquid Contact | Dermal | Workers | Yes | Low ranking - screening-level analysis will be done |
| | | | | | Vapor | Inhalation | Workers, ONU | Yes | Low ranking - screening-level analysis will be done |
| | | | | | Vapor | Dermal | Workers, ONU | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015). Vapor-through-skin is a pathway of concern. |
| | | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | | Mist / Dust | Dermal/Inhalation | Workers, ONU | No | Generation of mist and dust containing NMP is not expected during this operation. |
| Processing | Recycling | Recycling | | | Liquid Contact | Dermal | Workers | Yes | Dermal exposure is expected to be a primary pathway. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | | Exposure Pathway | Exposure Route | Receptor / Population | Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Recycling of process solvents containing NMP | Vapor | Inhalation | Workers, ONU | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | | Vapor | Dermal | Workers, ONU | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015). Vapor-through-skin is a pathway of concern. |
| | | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | | Mist / Dust | Dermal/Inhalation | Workers, ONU | No | Generation of mist and dust containing NMP is not expected during this operation. |
| Distribution in commerce | Distribution | Distribution | | Distribution of bulk shipments of NMP; Distribution of formulated products | Liquid Contact, Vapor / Dust | Dermal/ Inhalation | Workers, ONU | No | Low priority for assessment. Exposure will only occur in the event of spills. |
| Industrial, commercial, and consumer use | Paints and coatings; Paint additives and coating additives not described by other codes; Adhesives and sealants | Adhesive and paint and coating removers; Lacquers, stains, varnishes, primers and floor finishes; Powder coatings (surface preparation); Paint and Coating Use in Computer and Electronic Product Manufacturing, Construction, Fabricated Metal Product Manufacturing, Machinery Manufacturing, Other Manufacturing, Paint and Coating Manufacturing, Primary Metal | | Adhesive and paint and coating removal by contractors; Roll/curtain application and spray application of paints, coatings, adhesives, and sealants and removers | Liquid Contact | Dermal | Workers | Yes | Dermal exposure is expected to be a primary pathway. The number of workers potentially exposed may be high per CDR (16 submissions reporting the number of workers ranging from <10 workers to >10,000 workers). |
| | | | | | Vapor | Inhalation | Workers, ONU | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | | Mist | Inhalation | Workers, ONU | Yes | Mist generation is expected to occur during this operation. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | | Exposure Pathway | Exposure Route | Receptor / Population | Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|---|
| | | Manufacturing, Transportation Equipment Manufacturing, Wholesale and Retail Trade; Adhesives and sealant chemicals including binding agents; Single component glues and adhesives, including lubricant adhesives; Two-component glues and adhesives, including some resins | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | | Vapor | Dermal | Workers, ONU | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015). Vapor-through-skin is a pathway of concern. |
| | | | | | Dust | Dermal/Inhalation | Workers, ONU | No | Generation of dust containing NMP is not expected during this operation. |
| Industrial, commercial, and consumer use | Paints and coatings; Paint additives and coating additives not described by other codes; Adhesives and sealants | Lacquers, stains, varnishes, primers and floor finishes; Powder coatings (surface preparation); Paint and Coating Use in Computer and Electronic Product Manufacturing, Construction, Fabricated Metal Product Manufacturing, Machinery Manufacturing, Other Manufacturing, Paint and Coating Manufacturing, Primary Metal Manufacturing, Transportation Equipment Manufacturing, Wholesale and Retail Trade; Adhesives and sealant chemicals including binding agents; Single component glues and adhesives, including lubricant adhesives; Two-component glues and adhesives, including some resins | | Manual (roller/brush) application and syringe/bead application of paints, coatings, adhesives, and sealants and removers | Liquid Contact | Dermal | Workers | Yes | Dermal exposure is expected to be a primary pathway. The number of workers potentially exposed may be high per CDR (16 submissions reporting the number of workers ranging from <10 workers to >10,000 workers). |
| | | | | | Vapor | Inhalation | Workers, ONU | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | | Vapor | Dermal | Workers, ONU | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015). Vapor-through-skin is a pathway of concern. |
| | | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | | Mist / Dust | Dermal/Inhalation | Workers, ONU | No | Generation of mist and dust containing NMP is not expected during this operation. |
| Industrial, commercial, | | | | Aerosol degreasing | Liquid Contact | Dermal | Workers | Yes | Dermal exposure is expected to be a primary pathway. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | | Exposure Pathway | Exposure Route | Receptor / Population | Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|---|
| and consumer use | Solvents (for cleaning or degreasing) | Use in Electrical Equipment, Appliance and Component Manufacturing | | | Vapor | Inhalation | Workers, ONU | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | | Mist | Inhalation | Workers, ONU | Yes | Mist generation is expected to occur during this operation. |
| | | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | | Vapor | Dermal | Workers, ONU | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015). Vapor-through-skin is a pathway of concern. |
| | | | | | Dust | Dermal/Inhalation | Workers, ONU | No | Generation of dust containing NMP is not expected during this operation. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | | Exposure Pathway | Exposure Route | Receptor / Population | Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|---|
| Industrial, commercial, and consumer use | Solvents (for cleaning or degreasing) | Use in Electrical Equipment, Appliance and Component Manufacturing | | Wipe cleaning | Liquid Contact | Dermal | Workers | Yes | Dermal exposure is expected to be a primary pathway. |
| | | | | | Vapor | Inhalation | Workers, ONU | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | | Vapor | Dermal | Workers, ONU | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015). Vapor-through-skin is a pathway of concern. |
| | | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | | Mist / Dust | Dermal/Inhalation | Workers, ONU | No | Generation of mist and dust containing NMP is not expected during this operation. |
| Industrial, commercial, and consumer use | Ink, toner and colorant products | Printer ink | | Industrial / commercial printing | Liquid Contact | Dermal | Workers | Yes | Dermal exposure is expected to be a primary pathway. The number of workers is limited per CDR (1 submission reporting <10 workers and 1 submission reporting 100 to 500 workers). |
| | | | | | Vapor | Inhalation | Workers, ONU | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | | Vapor | Dermal | Workers, ONU | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015). Vapor-through-skin is a pathway of concern. |
| | | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | | Exposure Pathway | Exposure Route | Receptor / Population | Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | Mist / Dust | Dermal/Inhalation | Workers, ONU | No | Generation of mist and dust containing NMP is not expected during this operation. |
| Industrial, commercial, and consumer use | Processing aids, specific to petroleum production | Petrochemical Manufacturing | | Oil and gas extraction; Petrochemical purifications | Liquid Contact | Dermal | Workers | Yes | Dermal exposure is expected to be a primary pathway. The number of workers potentially exposed is limited per CDR (1 submission reporting 50 to 100 workers and 2 submissions reporting NKRA for number of workers). |
| | | | | | Vapor | Inhalation | Workers, ONU | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | | Vapor | Dermal | Workers, ONU | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015). Vapor-through-skin is a pathway of concern. |
| | | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | | Mist / Dust | Dermal/Inhalation | Workers, ONU | No | Generation of mist and dust containing NMP is not expected during this operation. |
| Industrial, commercial, and consumer use | Adhesives and sealants | Soldering materials | | Industrial and commercial soldering | Liquid Contact | Dermal | Workers | Yes | Dermal exposure is expected to be a primary pathway. The number of workers potenitally exposed is limited per CDR (1 submission reporting 50 to 100 workers and 2 submissions reporting NKRA for number of workers). |
| | | | | | Vapor | Inhalation | Workers, ONU | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | | Exposure Pathway | Exposure Route | Receptor / Population | Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | Vapor | Dermal | Workers, ONU | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015). Vapor-through-skin is a pathway of concern. |
| | | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | | Mist / Dust | Dermal/Inhalation | Workers, ONU | Yes | EPA will further evaluate to determine if mist and dust generation is applicable. |
| Industrial, commercial, and consumer use | Other uses | Other non-aerosol uses, e.g. anti-freeze and de-icing products; automotive care products; lubricants and greases; Lubricant and lubricant additives, including hydrophilic coatings; Metal products not covered elsewhere; Laboratory chemicals; Lithium ion batteries; Cleaning and furniture care products, including wood cleaners, gasket removers; Pharmaceutical and Medicine Manufacturing - functional fluids (closed systems); Wood preservatives | | Commercial automotive servicing, including application of lubricants; Manual (brushing) and dip application of metal finishing products; Laboratory use; Industrial battery use; Wipe cleaning; Pharmaceutical chemical extractions; Manual (paste/brush) application of wood preservatives | Liquid Contact | Dermal | Workers | Yes | Dermal exposure is expected to be a primary pathway. However, the potential for exposure is unknown where NMP is incorporated into articles. |
| | | | | | Vapor | Inhalation | Workers, ONU | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | | Vapor | Dermal | Workers, ONU | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015). Vapor-through-skin is a pathway of concern. |
| | | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | | Mist / Dust | Dermal/Inhalation | Workers, ONU | No | Generation of mist and dust containing NMP is not expected during this operation. |
| Industrial, commercial, | Other uses | Other aerosol uses, e.g. metal products not covered | | Spray application of | Liquid Contact | Dermal | Workers | Yes | Dermal exposure is expected to be a primary pathway. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | | Exposure Pathway | Exposure Route | Receptor / Population | Further Analysis | Rationale for Further Analysis / no Further Analysis |
|---|---|---|---|---|---|---|---|---|---|
| and consumer use | | elsewhere; Cleaning and furniture care products, including wood cleaners, gasket removers; Fertilizer and other agricultural chemical manufacturing - processing aids and solvents | | metal finishing products; Spray/aerosol application of cleaning products; Commercial fertilizer application | Vapor | Inhalation | Workers, ONU | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | | Mist | Inhalation | Workers, ONU | Yes | Mist generation is expected to occur during this operation. |
| | | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | | Vapor | Dermal | Workers, ONU | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015). Vapor-through-skin is a pathway of concern. |
| | | | | | Dust | Dermal/Inhalation | Workers, ONU | No | Chemical is not expected to be in solid form. |
| Disposal | Waste Handling, Treatment and Disposal | Disposal of NMP wastes | | Worker handling and disposal of waste | Liquid Contact | Dermal | Workers | Yes | Dermal exposure is expected to be a primary pathway. Frequency of exposure and the potential for dermal immersion needs to be evaluated. |
| | | | | | Vapor | Inhalation | Workers, ONU | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | | Vapor | Dermal | Workers, ONU | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015). Vapor-through-skin is a pathway of concern. |

# Appendix E SUPPORTING TABLE FOR CONSUMER ACTIVITES AND USES CONCEPTUAL MODEL

**Table_Apx E-1. Supporting Table for Consumer Activities and Uses Conceptual Model**

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor | Proposed for Further Analysis | Rationale for Further Analysis/ No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| Consumer Use | Paints and Coatings | Paint and coating removers | Evaporation from surface | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Paints and Coatings | Paint and coating removers | Spray Application | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor | Proposed for Further Analysis | Rationale for Further Analysis/ No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| Consumer Use | Paints and Coatings | Paint and coating removers | Spray Application | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Paints and Coatings | Adhesive removers | Evaporation from surface | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor | Proposed for Further Analysis | Rationale for Further Analysis/ No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Paints and Coatings | Adhesive removers | Spray Application | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Paints and Coatings | Lacquers, stains, varnishes, primers and floor finishes | Evaporation from surface | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor | Proposed for Further Analysis | Rationale for Further Analysis/ No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Vapor/Mist | Inhalation | Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| Consumer Use | Paints and Coatings | Lacquers, stains, varnishes, primers and floor finishes | Spray Application | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor | Proposed for Further Analysis | Rationale for Further Analysis/ No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Paint additives and coating additives | Construction; Wholesale and Retail Trade | Evaporation from surface | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Paint additives and coating additives | Construction; Wholesale and Retail Trade | Spray Application | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor | Proposed for Further Analysis | Rationale for Further Analysis/ No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Solvents (for cleaning and degreasing) | Use in Electrical Equipment, Appliance and Component Manufacturing | Evaporation from surface | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor | Proposed for Further Analysis | Rationale for Further Analysis/ No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| Consumer Use | Solvents (for cleaning and degreasing) | Use in Electrical Equipment, Appliance and Component Manufacturing | Spray Application | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Ink, toner and colorant products | Printer ink | Evaporation from surface | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor | Proposed for Further Analysis | Rationale for Further Analysis/ No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Ink, toner and colorant products | Inks in writing equipement | Evaporation from surface | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor | Proposed for Further Analysis | Rationale for Further Analysis/ No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| Consumer Use | Adhesives and sealants | Adhesives and sealant chemicals including binding agents | Evaporation from surface | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Adhesives and sealants | Adhesives and sealant chemicals including binding agents | Spray Application | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor | Proposed for Further Analysis | Rationale for Further Analysis/ No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Adhesives and sealants | Single component glues and adhesives, including lubricant adhesives | Evaporation from surface | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Adhesives and sealants | Single component glues and | Spray Application | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor | Proposed for Further Analysis | Rationale for Further Analysis/ No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | adhesives, including lubricant adhesives | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Adhesives and sealants | Two-component glues and adhesives, including some resins | Evaporation from surface | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor | Proposed for Further Analysis | Rationale for Further Analysis/ No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Adhesives and sealants | Soldering materials | Evaporation from surface | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Other uses | Automotive care products | Evaporation from surface | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor | Proposed for Further Analysis | Rationale for Further Analysis/ No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Other uses | Automotive care products | Spray Application | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor | Proposed for Further Analysis | Rationale for Further Analysis/ No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| Consumer Use | Other uses | Lubricants and greases | Evaporation from surface | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Other uses | Lubricants and greases | Spray Application | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor | Proposed for Further Analysis | Rationale for Further Analysis/ No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | | certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Other uses | Cleaning and furniture care products, including wood cleaners, gasket removers | Evaporation from surface | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Other uses | Cleaning and furniture care products, | Spray Application | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor | Proposed for Further Analysis | Rationale for Further Analysis/ No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | including wood cleaners, gasket removers | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Other uses | Lubricant and lubricant additives, including hydrophilic coatings | Evaporation from surface | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor | Proposed for Further Analysis | Rationale for Further Analysis/ No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Other uses | Lubricant and lubricant additives, including hydrophilic coatings | Spray Application | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Other uses | Wood preservatives | Evaporation from surface | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor | Proposed for Further Analysis | Rationale for Further Analysis/ No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Other uses | Wood preservatives | Spray Application | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor | Proposed for Further Analysis | Rationale for Further Analysis/ No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| Consumer Use | Other uses | Arts and Crafts, Hobby Materials | Evaporation from surface | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Other uses | Arts and Crafts, Hobby Materials | Spray Application | Liquid contact | Dermal | Consumers | Yes | Dermal exposure is expected to be a primary pathway since NMP is well absorbed following dermal exposures. |
| | | | | Vapor through skin | Dermal | Consumers/ Bystanders | Yes | NMP is well absorbed following dermal exposures and dermal absorption including NMP from the vapor phase typically contributes significantly to human exposure (U.S. EPA, 2015a). Vapor-through-skin is a pathway of concern. |
| | | | | Liquid contact | Oral | Consumers | Yes | NMP contamination of hands resulting from product use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be low. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor | Proposed for Further Analysis | Rationale for Further Analysis/ No Further Analysis |
|---|---|---|---|---|---|---|---|---|
| | | | | Vapor/Mist | Inhalation | Consumers/ Bystanders | Yes | EPA will further evaluate vapor generation potential, as inhalation exposures are expected to be limited for certain conditions of use due to the low volatility of NMP (VP = 0.345 mmHg). |
| | | | | Liquid contact | Dermal | Bystanders | No | Bystanders are not expected to have direct contact with liquids containing NMP |
| | | | | Liquid contact | Oral | Bystanders | Yes | NMP contamination of hands resulting from near-field use may result in consumer exposure to NMP via ingestion. NMP exposure via oral route is expected to be unlikely for bystanders. |
| Consumer Use | Other uses | Articles | Children's soft toys, blankets, etc | Liquid contact | Dermal | Consumers (Children) | Yes | Residual NMP in article could be source of dermal exposure. NMP is well absorbed following dermal exposures. |
| | | | | Liquid contact | Oral (mouthing) | Consumers (Children) | Yes | Residual NMP in article could be source of exposure due to children's mouthing behavior. |

# Appendix F SUPPORTING TABLE FOR ENVIRONMENTAL RELEASES AND WASTES CONCEPTUAL MODEL

**Table_Apx F-1. Supporting Table for Environmental Releases and Wastes Conceptual Model**

| Life Cycle Stage | Release | Exposure Pathway/ Media | Exposure Routes | Receptor / Population | Further Analysis? | Rationale for Further Analysis/ No Further Analysis |
|---|---|---|---|---|---|---|
| Disposal | Industrial wastewater treatment operations | Direct release into surface water | Surface water | Aquatic Species | No | Conservative Tier 1 screening indicates low risk concern for aquatic organisms (see section 2.3.4) |
| | | | | Terrestrial Species | No | Conservative Tier 1 screening indicates low concentrations of NMP in surface water. Ingestion of water is not expected to be a significant route of NMP exposure for terrestrial organisms. |
| | Industrial wastewater treatment operations | Direct release into surface water and indirect partitioning to sediment | Sediment | Aquatic Species | No | NMP has low sorption to soil, sludge, and sediment (log Koc = 0.9) and will instead stay in the associated aqueous phases due to high water solubility (1,000 g/L). |
| | | | | Terrestrial Species | No | |
| Disposal | Industrial pre-treatment, then transfer to Publicly Owned Treatment Works (POTW) | Direct release into surface water | Surface water | Aquatic Species | No | Conservative Tier 1 screening indicates low risk concern for aquatic organisms (see section 2.3.4) |
| | | | | Terrestrial Species | No | NMP exposure via ingestion of water and inhalation of air are expected to present a low risk concern for terrestrial organisms. |
| Disposal | Industrial pre-treatment, then transfer to Publicly Owned Treatment Works (POTW) | Direct release into surface water and indirect partitioning to sediment | Sediment | Aquatic Species | No | NMP has low sorption to soil, sludge, and sediment (log Koc = 0.9) and will instead stay in the associated aqueous phases (solubility = 1,000 g/L). |
| Disposal | Industrial pre-treatment, then transfer to Publicly Owned Treatment Works (POTW) | Direct release into surface water and indirect partitioning to sediment | Sediment | Terrestrial Species | No | Based on physical-chemical properties (log Koc = 0.9), NMP is not expected to partition to soil, sludge, and sediment. NMP is expected to remain in the aqueous phase (water solubility = 1,000 g/L). |

| Life Cycle Stage | Release | Exposure Pathway/ Media | Exposure Routes | Receptor / Population | Further Analysis? | Rationale for Further Analysis/ No Further Analysis |
|---|---|---|---|---|---|---|
| Disposal | Biosolids and land disposal to soil | Migration from biosolids via soil deposition | Soil | Terrestrial Species | No | Due to NMP's physical-chemical properties, (log Koc = 0.9, and water solubility = 1,000 g/L), NMP is not expected to partition to soil; aerobic biodegradation and mobility in soil are expected to limit accumulation in this environmental compartment. |
| | | | Groundwater - Ingestion | General Population: Adults and children living near facilities | No | Conservative Tier 1 screening indicates low concentrations of NMP in surface water. NMP releases from land application of biosolids are expected to be much less than those associated with direct release of wastewater treatment plant effluents to surface water. |
| All | Emissions to Air | Near facility ambient air concentrations | Inhalation | General Population: Adults and children living near facilities | No | Conservative Tier 1 screening indicates low risk concern to general population (see section 2.5.3.1) |
| | | Indirect deposition to nearby bodies of water and soil catchments | Soil | Terrestrial Species | No | NMP is not expected to remain in soil for long periods of time due to aerobic biodegradation and migration to groundwater due to the log Koc (0.9) and water solubility (1,000 g/L). |

# Appendix G INCLUSION AND EXCLUSION CRITERIA FOR FULL TEXT SCREENING

Appendix G contains the eligibility criteria for various data streams informing the TSCA risk evaluation: environmental fate; engineering and occupational exposure; exposure to consumers; and human health hazard. The criteria are applied to the *on-topic* references that were identified following title and abstract screening of the comprehensive search results published on June 22, 2017.

Systematic reviews typically describe the study eligibility criteria in the form of PECO statements or a modified framework. PECO stands for Population, Exposure, Comparator and Outcome and the approach is used to formulate explicit and detailed criteria about those characteristics in the publication that should be present in order to be eligible for inclusion in the review. EPA/OPPT adopted the PECO approach to guide the inclusion/exclusion decisions during full text screening.

Inclusion and exclusion criteria were also used during the title and abstract screening, and documentation about the criteria can be found in the *Strategy for Conducting Literature Searches* document published in June 2017 along with each of the TSCA Scope documents. The list of *on-topic* references resulting from the title and abstract screening is undergoing full text screening using the criteria in the PECO statements. The overall objective of the screening process is to select the most relevant evidence for the TSCA risk evaluation. As a general rule, EPA is excluding non-English data/information sources and will translate on a case by case basis.

The inclusion and exclusion criteria for ecotoxicological data have been documented in the ECOTOX SOPs. The criteria can be found at https://cfpub.epa.gov/ecotox/help.cfm?helptabs=tab4) and in the *Strategy for Conducting Literature Searches* document published along with each of the TSCA Scope documents.

## G.1 Inclusion Criteria for Data Sources Reporting Environmental Fate Data

EPA/OPPT developed a generic PESO statement to guide the full text screening of environmental fate data sources. PESO stands for Pathways and Processes, Exposure, Setting or Scenario, and Outcomes. Subsequent versions of the PESO statement may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the inclusion criteria in the PESO statement are eligible for inclusion, considered for evaluation, and possibly included in the environmental fate assessment. On the other hand, data sources are excluded if they do not meet the criteria in the PESO statement.

Assessors seek information on various chemical-specific fate endpoints and associated fate processes, environmental media and exposure pathways as part of the process of developing the environmental fate assessment.

## G.2 Inclusion Criteria for Data Sources Reporting Releases and Occupational Exposure Data

EPA/OPPT developed a generic RESO statement to guide the full text screening of releases and occupational exposure literature (Table_Apx G1). RESO stands for Receptors, Exposure, Setting or Scenario, and Outcomes. Subsequent versions of the RESO statement may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the inclusion criteria specified in the RESO statement will be eligible for inclusion, considered for evaluation, and possibly included in the environmental release and occupational exposure assessments, while those that do not meet these criteria will be excluded.

The RESO statement should be used along with the engineering, release and occupational exposure data needs table (Table_Apx G2) when screening the literature.

Since full text screening commenced right after the publication of the TSCA Scope document, the criteria for engineering and occupational exposure data were set to be broad to capture relevant information that would support the risk evaluation. Thus, the inclusion and exclusion criteria for full text screening do not reflect the refinements to the conceptual model and analysis plan resulting from problem formulation. As part of the iterative process, EPA is in the process of refining the results of the full text screening to incorporate the changes in information/data needs to support the risk evaluation.

**Table_Apx G-1. Inclusion Criteria for Data Sources Reporting Release and Occupational Exposure Data**

| RESO Element | **Evidence** |
|---|---|
| **R**eceptors | • **Humans:**<br>Workers, including occupational non-users<br><br>Please refer to the conceptual models for more information about the ecological and human receptors included in the TSCA risk evaluation. |
| **E**xposure | • Worker exposure to and relevant occupational environmental releases of the chemical substance of interest<br>  ○ Dermal and inhalation exposure routes (as indicated in the conceptual model)<br><br>Please refer to the conceptual models for more information about the routes and media/pathways included in the TSCA risk evaluation. |
| **S**etting or **S**cenario | • Any occupational setting or scenario resulting in worker exposure and environmental releases (includes all manufacturing, processing, use, disposal indicated in Table_Apx G below. |
| **O**utcomes | • Quantitative estimates* of worker exposures and of relevant environmental releases from occupational settings<br>• General information and data related and relevant to the occupational estimates* |

* Metrics (e.g., mg/kg/day or $mg/m^3$ for worker exposures, kg/site/day for releases) are determined by toxicologists for worker exposures and by exposure assessors for releases; also, the Engineering, Release, and Occupational Exposure Data Needs (Table_Apx G2) provides a list of related and relevant general information.
TSCA=Toxic Substances Control Act

**Table_Apx G-2. Engineering, Environmental Release and Occupational Data Necessary to Develop the Environmental Release and Occupational Exposure Assessments**

| Objective Determined during Scoping | Type of Data |
|---|---|
| General Engineering Assessment (may apply for either or both Occupational Exposures and / or Environmental Releases) | 1. Description of the life cycle of the chemical(s) of interest, from manufacture to end-of-life (e.g., each manufacturing, processing, or use step), and material flow between the industrial and commercial life cycle stages. {Tags: Life cycle description, Life cycle diagram} [a]<br>2. The total annual U.S. volume (lb/yr or kg/yr) of the chemical(s) of interest manufactured, imported, processed, and used; and the share of total annual manufacturing and import volume that is processed or used in each life cycle step. {Tags: Production volume, Import volume, Use volume, Percent PV} [a]<br>3. Description of processes, equipment, unit operations, and material flows and frequencies (lb/site-day or kg/site-day and days/yr; lb/site-batch and batches/yr) of the chemical(s) of interest during each industrial/ commercial life cycle step. Note: if available, include weight fractions of the chemical of interest and material flows of all associated primary chemicals (especially water). {Tags: Process description, Process material flow rate, Annual operating days, Annual batches, Weight fractions (for each of above, manufacture, import, processing, use)} [a]<br>4. Basic chemical properties relevant for assessing exposures and releases, e.g., molecular weight, normal boiling point, melting point, physical form, and room temperature vapor pressure. {Tags: Molecular weight, Boiling point, Melting point, Physical form, Vapor pressure, Water solubility} [a]<br>5. Number of sites that manufacture, process, or use the chemical(s) of interest for each industrial/ commercial life cycle step and site location. {Tags: Numbers of sites (manufacture, import, processing, use), Site locations} [a] |
| Occupational Exposures | 6. Description of worker activities with exposure potential during the manufacture, processing, or use of the chemical(s) of interest in each industrial/commercial life cycle stage. {Tags: Worker activities (manufacture, import, processing, use)} [a]<br>7. Potential routes of exposure (e.g., inhalation, dermal). {Tags: Routes of exposure (manufacture, import, processing, use)} [a]<br>8. Physical form of the chemical(s) of interest for each exposure route (e.g., liquid, vapor, mist) and activity. {Tags: Physical form during worker activities (manufacture, import, processing, use)} [a]<br>9. Breathing zone (personal sample) measurements of occupational exposures to the chemical(s) of interest, measured as time-weighted average (TWA), short-term exposures, or peak exposures in each occupational life cycle stage (or in a workplace scenario similar to an occupational life cycle stage). {Tags: PBZ measurements (manufacture, import, processing, use)} [a]<br>10. Area or stationary measurements of airborne concentrations of the chemical(s) of interest in each occupational setting and life cycle stage (or in a workplace scenario similar to the life cycle stage of interest). {Tags: Area measurements (manufacture, import, processing, use)} [a]<br>11. For solids, bulk and dust particle size distribution (PSD) data. {Tags: PSD measurements (manufacture, import, processing, use)} [a]<br>12. Dermal exposure data. {Tags: Dermal measurements (manufacture, import, processing, use)}<br>Data needs associated with mathematical modeling (will be determined on a case-by-case basis). {Tags: Worker exposure modeling data needs (manufacture, import, processing, use)} [a]<br>13. Exposure duration (hrs/day). {Tags: Worker exposure durations (manufacture, import, processing, use)} [a]<br>14. Exposure frequency (days/yr). {Tags: Worker exposure frequencies (manufacture, import, processing, use)} [a]<br>15. Number of workers who potentially handle or have exposure to the chemical(s) of interest in each life cycle stage. {Tags: Numbers of workers exposed (manufacture, import, processing, use)} [a]<br>16. Personal protective equipment (PPE) types employed by industries within the scope. {Tags: Worker PPE (manufacture, import, processing, use)} [a]<br>17. Engineering controls employed to reduce occupational exposures in each occupational life cycle stage (or in a workplace scenario similar to the life cycle stage of interest), and associated data or estimates of exposure reductions. {Tags: Engineering controls (manufacture, import, processing, use), Engineering control effectiveness data} [a] |

| | |
|---|---|
| Environmental Releases (to relevant environmental media) | 18. Description of sources of potential environmental releases, including cleaning of residues from process equipment and transport containers involved during the manufacture, processing, or use of the chemical(s) of interest in each life cycle stage. {Tags: Release sources (manufacture, import, processing, use)} [a]<br>19. Estimated mass (lb or kg) of the chemical(s) of interest released from industrial and commercial sites to each environmental medium (water) and treatment and disposal methods (POTW), including releases per site and aggregated over all sites (annual release rates, daily release rates) {Tags: Release rates (manufacture, import, processing, use)} [a]<br>20. Release or emission factors. {Tags: Emission factors (manufacture, import, processing, use)} [a]<br>21. Number of release days per year. {Tags: Release frequencies (manufacture, import, processing, use)} [a]<br>22. Data needs associated with mathematical modeling (will be determined on a case-by-case basis). {Tags: Release modeling data needs (manufacture, import, processing, use)} [a]<br>23. Waste treatment methods and pollution control devices employed by the industries within scope and associated data on release/emission reductions. {Tags: Treatment/ emission controls (manufacture, import, processing, use), Treatment/ emission controls removal/ effectiveness data} [a] |

**Notes:**

[a] These are the tags included in the full text screening form. The screener makes a selection from these specific tags, which describe more specific types of data or information.

**Abbreviations:**

hr = Hour
kg = Kilogram(s)
lb = Pound(s)
yr = Year
PV = Production volume
PBZ = Personal breathing zone
POTW = Publicly owned treatment works
PPE = Personal protective equipment
PSD = Particle size distribution
TWA = Time-weighted average

## G.3 Inclusion Criteria for Data Sources Reporting Exposure Data on Consumers and Ecological Receptors

EPA/OPPT developed PECO statements to guide the full text screening of exposure data/information for human (i.e., consumers, potentially exposed or susceptible subpopulations) and ecological receptors. Subsequent versions of the PECO statements may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the inclusion criteria in the PECO statement are eligible for inclusion, considered for evaluation, and possibly included in the exposure assessment. On the other hand, data sources are excluded if they do not meet the criteria in the PECO statement. The NMP-specific PECO is provided in Table_Apx G1 thru Table_Apx G4.

Since full text screening commenced right after the publication of the TSCA Scope document, the criteria for exposure data were set to be broad to capture relevant information that would support the risk evaluation. Thus, the inclusion and exclusion criteria for full text screening do not reflect the refinements to the conceptual model and analysis plan resulting from problem formulation. As part of the iterative process, EPA is in the process of refining the results of the full text screening to incorporate the changes in information/data needs to support the risk evaluation.

**Table_Apx G-3. Inclusion Criteria for the Data Sources Reporting N-Methylpyrrolidone Exposure Data on Consumers and Ecological Receptors**

| PECO Element | Evidence |
|---|---|
| **P**opulation | **Human:** Consumers (i.e., individuals who use a product directly) and bystanders (i.e., those individuals who happen to be in close proximity during use of NMP-containing products), including, susceptible populations (e.g., lifestages, preexisting conditions, genetic factors), such as infants, children, pregnant women, women of child bearing age; do-it-yourself (DIY) or high-end consumers. |
| | **Ecological:** Aquatic and terrestrial biota (organisms and plants). |
| **E**xposure | **Expected Primary Exposure Sources, Pathways, Routes**<br>**Sources:** Consumer uses in the home producing releases of NMP to air and dermal contact; industrial and commercial activities that generate releases to surface water; NMP remaining primarily in aqueous media of biosolids after wastewater treatment.<br>**Pathways**: Indoor/outdoor air and dermal contact with NMP in consumer products (e.g., liquid contact), vapor/mist/dust, dust; biosolids application to soil.<br>**Routes**: oral (dust or by mouthing), inhalation (vapor/mist), dermal (liquid contact); dermal (vapor to skin). |
| **C**omparator (Scenario) | **Human:** Consider media-specific background exposure scenarios and use/source-specific exposure scenarios as well as which receptors are and are not reasonably exposed across the projected exposure scenarios. |
| | **Ecological:** Aquatic and terrestrial species exposure via contact with or ingestion of surface water; terrestrial species exposure via contact with soil. |

| PECO Element | Evidence |
|---|---|
| **O**utcomes for Exposure Concentration or Dose | **Human:** Acute, subchronic, and/or chronic external exposure dose estimates (mg/kg/day); acute, subchronic, and/or chronic air concentration estimates ($mg/m^3$ or mg/L). Both external potential dose and internal dose based on biomonitoring and reverse dosimetry mg/kg/day will be considered. |
| | **Ecological:** A range of ecological receptors will be considered using surface water concentrations, sediment concentrations, and soil concentrations. |

Abbreviations:
NMP = N-Methylpyrrolidone

## G.4 Inclusion Criteria for Data Sources Reporting Human Health Hazards

EPA/OPPT developed chemical-specific PECO statements Table_Apx G1 thru Table_Apx G4) to guide the full text screening of the human health hazard literature. Subsequent versions of the PECOs may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the criteria specified in the PECO statement will be eligible for inclusion, considered for evaluation, and possibly included in the human health hazard assessment, while those that do not meet these criteria will be excluded according to the exclusion criteria.

In general, the PECO statements were based on (1) information accompanying the TSCA Scope document, and (2) preliminary review of the health effects literature from authoritative sources cited in the TSCA Scope documents. When applicable, these authoritative sources (e.g., IRIS assessments, EPA/OPPT's Work Plan problem formulations or risk assessments) will serve as starting points to identify PECO-relevant studies.

**Table_Apx G-4. Inclusion Criteria for Data Sources Reporting Human Health Hazards Related to N-Methylpyrrolidone (NMP) [a]**

| PECO Element | Evidence Stream | Papers/Features Included | Papers/Features Excluded |
|---|---|---|---|
| **Population [b]** | *Human* | • Any population<br>• All lifestages<br>• Study designs:<br>  ○ Controlled exposure, cohort, case-control, cross-sectional, case-crossover<br>  ○ Case studies and case series that are related to deaths from acute exposure | • Case studies and case series for all endpoints ***other than*** death from acute exposure |
| | *Animal* | • All non-human whole-organism mammalian species<br>• All lifestages | • Non-mammalian species |
| ***Exposure*** | *Human* | • Exposure based on administered dose or concentration of NMP, biomonitoring data (e.g., urine, blood or other specimens), environmental or occupational-setting monitoring data (e.g., air, water levels), job title or residence<br>• Primary metabolites of interest as identified in biomonitoring studies (5-hydroxy-N-methyl-2-pyrrolidone (5-HNMP) and 2-hydroxy-N-methylsuccinimide (2-HMSI))<br>• Exposure identified as ***or presumed to be*** from oral, dermal, inhalation routes<br>• Any number of exposure groups<br>• Quantitative, semi-quantitative or qualitative estimates of exposure<br>• Exposures to multiple chemicals/mixtures only if NMP or related metabolites were independently measured and analyzed | • Route of exposure ***not*** by inhalation, oral or dermal type (e.g., intraperitoneal, injection)<br>• Multiple chemical/mixture exposures with no independent measurement of or exposure to NMP (or related metabolite) |

| PECO Element | Evidence Stream | Papers/Features Included | Papers/Features Excluded |
|---|---|---|---|
| | *Animal* | • A minimum of 2 quantitative dose or concentration levels of NMP plus a negative control group[a]<br>• Acute, subchronic, chronic exposure from oral, dermal, inhalation routes<br>• Exposure to NMP only (no chemical mixtures)<br>• Quantitative or semi-quantitative estimates of exposure are included | • Only 1 quantitative dose or concentration level in addition to the control<br>• Route of exposure ***not*** by inhalation, oral or dermal type (e.g., intraperitoneal, injection)<br>• No duration of exposure stated<br>• Exposure to NMP in a chemical mixture |
| **Comparator** | *Human* | • A comparison population [not exposed, exposed to lower levels, exposed below detection] for endpoints ***other than*** death from acute exposure | • No comparison population for endpoints other than death from acute exposure |
| | *Animal* | • Negative controls that are vehicle-only treatment and/or no treatment | • Negative controls ***other than*** vehicle-only treatment or no treatment |
| **Outcome** | *Human* | • Endpoints described in the NMP scope document [c]:<br>o Acute toxicity (neurotoxicity and lethality)<br>o Reproductive toxicity<br>o Growth (early life) and developmental toxicity<br>o Immunotoxicity<br>o Neurotoxicity<br>o Irritation<br>• Other endpoints [d] | |
| | *Animal* | | |
| **General Considerations** | | **Papers/Features Included** | **Papers/Features Excluded** |
| | | • Written in English [e]<br>• Reports primary data<br>• Full text available<br>• Reports both NMP exposure ***and*** a health outcome | • Not written in English<br>• Reports secondary data (e.g., review papers) [a]<br>• No full text available (e.g., only a study description/abstract, out-of-print text)<br>• Reports NMP-related exposure ***or*** a health outcome, but not both (e.g. incidence, prevalence report) |

[a] Some of the studies that are excluded based on the PECO statement may be considered later during the systematic review process. For NMP, EPA will evaluate studies related to susceptibility and may evaluate, toxicokinetics and physiologically based pharmacokinetic models after other data (e.g., human and animal data identifying adverse health outcomes) are reviewed. EPA may need to evaluate mechanistic data depending on the review of health effects data. Finally, EPA may also review other data as needed (e.g., animal studies using one concentration, review papers).

[b] Mechanistic data are excluded during the full text screening phase of the systematic review process but may be considered later (see footnote *a*).

[c] EPA will review key and supporting studies in EPA's 2015 Work Plan Chemical Risk Assessment for non-cancer and cancer endpoints as well as studies published after the assessment.

[d] EPA may screen for hazards other than those listed in the scope document if they were identified in the updated literature search that accompanied the scope document.

[e] EPA may translate studies as needed.

Abbreviations: NMP= N-Methylpyrrolidone

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Office of Chemical Safety and
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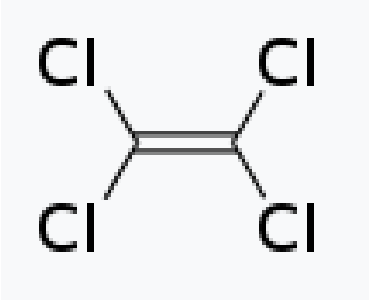
States
Environmental Protection Agency

# Problem Formulation of the Risk Evaluation for Perchloroethylene (Ethene, 1,1,2,2-Tetrachloro)

# CASRN: 127-18-4




***May 2018***

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**Docket**
Supporting information can be found in public docket: EPA-HQ-OPPT-2016-0732

**Disclaimer**
Reference herein to any specific commercial products, process or service by trade name, trademark, manufacturer or otherwise does not constitute or imply its endorsement, recommendation or favoring by the United States Government.

# ABBREVIATIONS

| | |
|---|---|
| °C | Degrees Celsius |
| 1-BP | 1-Bromopropane |
| ACGIH | American Conference of Government Industrial Hygienists |
| AEGL | Acute Exposure Guideline Level |
| ATSDR | Agency for Toxic Substances and Disease Registries |
| atm | Atmosphere(s) |
| BAF | Bioaccumulation Factor |
| BCF | Bioconcentration Factor |
| CAA | Clean Air Act |
| CASRN | Chemical Abstracts Service Registry Number |
| CBI | Confidential Business Information |
| $CCL_4$ | Carbon Tetrachloride |
| CDC | Centers for Disease Control |
| CDR | Chemical Data Reporting |
| CEHD | Chemical Exposure Health Data |
| CEPA | Canadian List of Toxic Substances |
| CERCLA | Comprehensive Environmental Response, Compensation and Liability Act |
| CFC | Chlorofluorocarbon |
| CHIRP | Chemical Risk Information Platform |
| $cm^3$ | Cubic Centimeter(s) |
| COC | Concentration of Concern |
| CoRAP | Community Rolling Action Plan |
| cP | Centipoise |
| CPCat | Chemical and Product Categories |
| CPSC | Consumer Product Safety Commission |
| CSCL | Chemical Substances Control Law |
| CWA | Clean Water Act |
| DNAPL | Dense Non-Aqueous Phase Liquid |
| ECHA | European Chemicals Agency |
| EDC | Ethylene Dichloride |
| EG | Effluent Guidelines |
| EPA | Environmental Protection Agency |
| EPCRA | Emergency Planning and Community Right-to-Know Act |
| ESD | Emission Scenario Documents |
| EU | European Union |
| FDA | Food and Drug Administration |
| FFDCA | Federal Food, Drug and Cosmetic Act |
| FHSA | Federal Hazardous Substance Act |
| FIFRA | Federal Insecticide, Fungicide and Rodenticide Act |
| g | Gram(s) |
| GACT | Generally Available Control Technology |
| HAP | Hazardous Air Pollutant |
| HCFC | Hydrochlorofluorocarbon |
| HCl | Hydrochloric Acid |
| HFC | Hydrofluorocarbon |
| HSIA | Halogenated Solvents Industry Association |
| HPV | High Production Volume |

| | |
|---|---|
| Hr | Hour |
| IARC | International Agency for Research on Cancer |
| IDLH | Immediately Dangerous to Life and Health |
| i.p. | Intraperitoneal |
| IRIS | Integrated Risk Information System |
| ISHA | Industrial Safety and Health Act |
| kg | Kilogram(s) |
| L | Liter(s) |
| lb | Pound(s) |
| Log $K_{oc}$ | Logarithmic Organic Carbon:Water Partition Coefficient |
| Log $K_{ow}$ | Logarithmic Octanol:Water Partition Coefficient |
| $m^3$ | Cubic Meter(s) |
| MACT | Maximum Achievable Control Technology |
| MCL | Maximum Contaminant Level |
| MCLG | Maximum Contaminant Level Goal |
| mg | Milligram(s) |
| µg | Microgram(s) |
| mmHg | Millimeter(s) of Mercury |
| MOA | Mode of Action |
| MSDS | Material Safety Data Sheet |
| n | Number |
| NAAQS | National Ambient Air Quality Standards |
| NAC | National Advisory Committee |
| NAICS | North American Industry Classification System |
| NCEA | National Center for Environmental Assessment |
| NEI | National Emissions Inventory |
| NESHAP | National Emission Standards for Hazardous Air Pollutants |
| NHANES | National Health and Nutrition Examination Survey |
| NICNAS | National Industrial Chemicals Notification and Assessment Scheme |
| NIH | National Institutes of Health |
| NIOSH | National Institute of Occupational Safety and Health |
| NITE | National Institute of Technology and Evaluation |
| NPL | National Priorities List |
| NTP | National Toxicology Program |
| OAQPS | Office of Air Quality Planning and Standards |
| OCSPP | Office of Chemical Safety and Pollution Prevention |
| ODS | Ozone Depleting Substance |
| OECD | Organisation for Economic Co-operation and Development |
| OEHHA | Office of Environmental Health Hazard Assessment |
| OEL | Occupational Exposure Limit |
| ONU | Occupational Non-User |
| OPPT | Office of Pollution Prevention and Toxics |
| OSHA | Occupational Safety and Health Administration |
| PBZ | Personal Breathing Zone |
| PCE | Perchloroethylene |
| PEL | Permissible Exposure Limit |
| PESS | Potentially Exposed Susceptible Subpopulation |
| POD | Point of Departure |

| | |
|---|---|
| POTW | Publicly Owned Treatment Works |
| ppb | Part(s) per Billion |
| PPE | Personal Protective Equipment |
| ppm | Part(s) per Million |
| PWS | Public Water System |
| RCRA | Resource Conservation and Recovery Act |
| SARA | Superfund Amendments and Reauthorization Act |
| SCHER | Scientific Committee on Health and Environmental Risks |
| SDS | Safety Data Sheet |
| SDWA | Safe Drinking Water Act |
| SIDS | Screening Information Data Set |
| SNAP | Significant New Alternatives Policy |
| STEL | Short-Term Exposure Limit |
| $t_{1/2}$ | Half-life |
| TCCR | Transparent, Clear, Consistent, and Reasonable |
| TCE | Trichloroethylene |
| TLV | Threshold Limit Value |
| TRI | Toxics Release Inventory |
| TSCA | Toxic Substances Control Act |
| TTO | Total Toxic Organics |
| TWA | Time-Weighted Average |
| U.S. | United States |
| VOC | Volatile Organic Compound |
| WHO | World Health Organization |
| Yr | Year(s) |

# EXECUTIVE SUMMARY

TSCA § 6(b)(4) requires the U.S. Environmental Protection Agency (EPA) to establish a risk evaluation process. In performing risk evaluations for existing chemicals, EPA is directed to "determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of costs or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator under the conditions of use." In December of 2016, EPA published a list of 10 chemical substances that are the subject of the Agency's initial chemical risk evaluations (81 FR 91927), as required by TSCA § 6(b)(2)(A). Perchloroethylene was one of these chemicals.

TSCA § 6(b)(4)(D) requires that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use and potentially exposed or susceptible subpopulations that the Administrator expects to consider. In June 2017, EPA published the Scope of the Risk Evaluation for perchloroethylene. As explained in the scope document, because there was insufficient time for EPA to provide an opportunity for comment on a draft of the scope, as EPA intends to do for future scope documents, EPA is publishing and taking public comment on a problem formulation document to refine the current scope, as an additional interim step prior to publication of the draft risk evaluation for perchloroethylene. Comments received on this problem formulation document will inform development of the draft risk evaluation.

This problem formulation document refines the conditions of use, exposures and hazards presented in the scope of the risk evaluation for perchloroethylene and presents refined conceptual models and analysis plans that describe how EPA expects to evaluate the risk for perchloroethylene.

Perchloroethylene, also known as ethene, 1,1,2,2-tetrachloro, tetrachloroethylene and PCE, is a high production volume (HPV) solvent. Perchloroethylene is subject to a number of federal and state regulations and reporting requirements. For example, perchloroethylene has been a Toxics Release Inventory (TRI) reportable chemical under Section 313 of the Emergency Planning and Community Right-to-Know Act (EPCRA) since 1995. It is designated a Hazardous Air Pollutant (HAP) under the Clean Air Act (CAA), a hazardous waste under the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA) and a regulated drinking water contaminant under the Safe Drinking Water Act (SDWA).

Information on the domestic manufacture, processing and use of perchloroethylene is available to EPA through its Chemical Data Reporting (CDR) Rule, issued under TSCA. According to the 2016 CDR, more than 324 million pounds of perchloroethylene were manufactured (including imported) in the United States in 2015. According to the *Use and Market Profile for Tetrachloroethylene* (EPA-HQ-OPPT-2016-0732), perchloroethylene is primarily used to produce fluorinated compounds, such as hydrofluorocarbons (HFCs) and hydrochlorofluorocarbons (HCFCs) (65%) followed by dry cleaning (15%) and vapor degreasing solvents (10%). Other uses can be quite varied, including:

- Adhesives
- Degreasing
- Brake cleaner
- Laboratories
- Lubricants
- Mold cleaners, releases and protectants
- Oil refining

- Sealants
- Stainless steel polish
- Tire buffers and cleaners and
- Vandal mark removers.

This document presents the potential exposures that may result from the conditions of use of perchloroethylene. Exposures may occur to workers and occupational non-users (workers who do not directly handle the chemical but perform work in an area where the chemical is used), consumers and bystanders (non-product users that are incidentally exposed to the product) and the general population through inhalation, dermal and oral pathways. Workers and occupational non-users (ONU), who do not directly handle the chemical but perform work in an area where the chemical is used, may be exposed to perchloroethylene during a variety of conditions of use, such as manufacturing, processing and industrial and commercial uses, including uses in degreasing and adhesives. EPA expects that the highest exposures to perchloroethylene generally involve workers in industrial and commercial settings. Perchloroethylene can be found in numerous products and can, therefore, result in exposures to commercial and consumer users in indoor or outdoor environments. For perchloroethylene, EPA considers workers, occupational non-users, consumers, bystanders, and certain other groups of individuals who may experience greater exposures than the general population due to proximity to conditions of use to be potentially exposed or susceptible subpopulations. Exposures to the general population may occur from industrial and/or commercial uses; industrial releases to air, water or land; and other conditions of use. EPA will evaluate whether groups of individuals within the general population may be exposed via pathways that are distinct from the general population due to unique characteristics (e.g., life stage, behaviors, activities, duration) that increase exposure and whether groups of individuals have heightened susceptibility, and should therefore be considered potentially exposed or susceptible subpopulations for purposes of the risk evaluation. EPA plans to further analyze inhalation exposures to vapors and mists for workers and occupational non-users and dermal exposures for skin contact with liquids in occluded situations for workers in the risk evaluation. For environmental release pathways, EPA plans to further analyze surface water exposure to aquatic vertebrates, invertebrates and aquatic plants and exposure to sediment-dwelling organisms.

Perchloroethylene has been the subject of several prior health hazard and risk assessments, including EPA's Integrated Risk Information System (IRIS) Toxicological Review and a draft Agency for Toxic Substances and Disease Registry's (ATSDR's) Toxicological Profile. A number of targets of toxicity from exposures to perchloroethylene have been identified in animal and human studies for both oral and inhalation exposures. EPA plans to evaluate all potential hazards for perchloroethylene, using the primary literature identified in human health reviews and including any found in recent literature. Hazard endpoints identified in previous assessments include: acute toxicity, neurotoxicity, kidney toxicity, liver toxicity, developmental and reproductive toxicity and cancer. Support for an association with immune and blood effects was less well characterized. Perchloroethylene is also considered to be irritating.

The revised conceptual models presented in this problem formulation identify conditions of use; exposure pathways (e.g., media); exposure routes (e.g., inhalation, dermal, oral); potentially exposed or susceptible subpopulations; and hazards EPA expects to consider in the risk evaluation. The initial conceptual models provided in the scope document were revised during problem formulation based on evaluation of reasonably available information for physical and chemical properties, fate, exposures, hazards and conditions of use, and based upon consideration of other statutory and regulatory authorities. In each problem formulation document for the first 10 chemical substances, EPA also

refined the activities, hazards and exposure pathways that will be included in and excluded from the risk evaluation.

EPA's overall objectives in the risk evaluation process are to conduct timely, relevant, high-quality, and scientifically credible risk evaluations within the statutory deadlines, and to evaluate the conditions of use that raise greatest potential for risk 82 FR 33726, 33728 (July 20, 2017).

# 1 INTRODUCTION

This document presents for comment the problem formulation of the risk evaluation to be conducted for perchloroethylene under the Frank R. Lautenberg Chemical Safety for the 21st Century Act. The Frank R. Lautenberg Chemical Safety for the 21st Century Act amended the Toxic Substances Control Act (TSCA), the nation's primary chemicals management law, on June 22, 2016. The new law includes statutory requirements and deadlines for actions related to conducting risk evaluations of existing chemicals.

In December of 2016, EPA published a list of 10 chemical substances that are the subject of the Agency's initial chemical risk evaluations (81 FR 91927), as required by TSCA § 6(b)(2)(A). These 10 chemical substances were drawn from the 2014 update of EPA's TSCA Work Plan for Chemical Assessments, a list of chemicals that EPA identified in 2012 and updated in 2014 (currently totaling 90 chemicals) for further assessment under TSCA. EPA's designation of the first 10 chemical substances constituted the initiation of the risk evaluation process for each of these chemical substances, pursuant to the requirements of TSCA § 6(b)(4).

TSCA § 6(b)(4)(D) requires that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use and potentially exposed or susceptible subpopulations that the Administrator expects to consider, within 6 months after the initiation of a risk evaluation. The scope documents for all first 10 chemical substances were issued on June 22, 2017. The first 10 problem formulation documents are a refinement of what was presented in the first 10 scope documents. TSCA § 6(b)(4)(D) does not distinguish between scoping and problem formulation, and requires EPA to issue scope documents that include information about the chemical substance, including the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations that the Administrator expects to consider in the risk evaluation. In the future, EPA expects scoping and problem formulation to be completed prior to the issuance of scope documents and intends to issue scope documents that include problem formulation.

As explained in the scope document, because there was insufficient time for EPA to provide an opportunity for comment on a draft of the scope, as EPA intends to do for future scope documents, EPA is publishing and taking public comment on a problem formulation document to refine the current scope, as an additional interim step prior to publication of the draft risk evaluation for perchloroethylene. Comments received on this problem formulation document will inform development of the draft risk evaluation.

The Agency defines problem formulation as the analytical phase of the risk assessment in which "the purpose for the assessment is articulated, the problem is defined, and a plan for analyzing and characterizing risk is determined" (see Section 2.2 of the Framework for Human Health Risk Assessment to Inform Decision Making). The outcome of problem formulation is a conceptual model(s) and an analysis plan. The conceptual model describes the linkages between stressors and adverse human health effects, including the stressor(s), exposure pathway(s), exposed life stage(s) and population(s), and endpoint(s) that will be addressed in the risk evaluation (U.S. EPA, 2014e). The analysis plan follows the development of the conceptual model(s) and is intended to describe the approach for conducting the risk evaluation, including its design, methods and key inputs and intended outputs as described in the EPA Human Health Risk Assessment Framework (U.S. EPA, 2014e). The problem formulation documents refine the initial conceptual models and analysis plans that were provided in the scope documents.

First, EPA has removed from the risk evaluation any activities and exposure pathways that EPA has concluded do not warrant inclusion in the risk evaluation. For example, for some activities which were listed as "conditions of use" in the scope document, EPA has insufficient information following the further investigations during problem formulation to find they are circumstances under which the chemical is actually "intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of."

Second, EPA also identified certain exposure pathways that are under the jurisdiction of regulatory programs and associated analytical processes carried out under other EPA-administered environmental statutes – namely, the Clean Air Act (CAA), the Safe Drinking Water Act (SDWA), the Clean Water Act (CWA), and the Resource Conservation and Recovery Act (RCRA) – and which EPA does not expect to include in the risk evaluation.

As a general matter, EPA believes that certain programs under other Federal environmental laws adequately assess and effectively manage the risks for the covered exposure pathways. To use Agency resources efficiently under the TSCA program, to avoid duplicating efforts taken pursuant to other Agency programs, to maximize scientific and analytical efforts, and to meet the three-year statutory deadline, EPA is planning to exercise its discretion under TSCA 6(b)(4)(D) to focus its analytical efforts on exposures that are likely to present the greatest concern and consequently merit a risk evaluation under TSCA, by excluding, on a case-by-case basis, certain exposure pathways that fall under the jurisdiction of other EPA-administered statutes.[1] EPA does not expect to include tany such excluded pathways as further explained below in the risk evaluation. The provisions of various EPA-administered environmental statutes and their implementing regulations represent the judgment of Congress and the Administrator, respectively, as to the degree of health and environmental risk reduction that is sufficient under the various environmental statutes.

Third, EPA identified any conditions of use, hazards, or exposure pathways which were included in the scope document and that EPA expects to include in the risk evaluation but which EPA does not expect to further analyze in the risk evaluation. EPA expects to be able to reach conclusions about particular conditions of use, hazards or exposure pathways without further analysis and therefore expects to conduct no further analysis on those conditions of use, hazards or exposure pathways in order to focus the Agency's resources on more extensive or quantitative analyses. Each risk evaluation will be "fit-for-purpose," meaning not all conditions of use will warrant the same level of evaluation and the Agency may be able to reach some conclusions without comprehensive or quantitative risk evaluations 82 FR 33726, 33734, 33739 (July 20, 2017).

EPA received comments on the published scope document for perchloroethylene and has considered the comments specific to perchloroethylene in this problem formulation document. EPA is soliciting public comment on this problem formulation document and when the draft risk evaluation is issued the Agency intends to respond to comments that are submitted. In its draft risk evaluation, EPA may revise the conclusions and approaches contained in this problem formulations, including the conditions of use and pathways covered and the conceptual models and analysis plans, based on comments received.

[1] As explained in the final rule for chemical risk evaluation procedures, "EPA may, on a case-by case basis, exclude certain activities that EPA has determined to be conditions of use in order to focus its analytical efforts on those exposures that are likely to present the greatest concern, and consequently merit an unreasonable risk determination." [82 FR 33726, 33734, 33729 (July 20, 2017)]

## 1.1 Regulatory History

EPA conducted a search of existing domestic and international laws, regulations and assessments pertaining to perchloroethylene. EPA compiled this summary from data available from federal, state, international and other government sources, as cited in Appendix A. EPA has evaluated and considered the impact of these existing laws and regulations (e.g., regulations on landfill disposal, design, and operations) in the problem formulation step to determine what, if any, further analysis might be necessary as part of the risk evaluation. Consideration of the nexus between these existing regulations and TSCA conditions of use may additionally be made as detailed/specific conditions of use and exposure scenarios are developed in conducting the analysis phase of the risk evaluation.

***Federal Laws and Regulations***

Perchloroethylene is subject to federal statutes or regulations, other than TSCA, that are implemented by other offices within EPA and/or other federal agencies/departments. A summary of federal laws, regulations and implementing authorities is provided in Appendix A.1.

***State Laws and Regulations***

Perchloroethylene is subject to state statutes or regulations implemented by state agencies or departments. A summary of state laws, regulations and implementing authorities is provided in Appendix A.2.

***Laws and Regulations in Other Countries and International Treaties or Agreements***

Perchloroethylene is subject to statutes or regulations in countries other than the United States. A summary of these laws and regulations is provided in Appendix A.3.

## 1.2 Assessment History

EPA has identified assessments conducted by other EPA Programs and other organizations (see Table 1-1). Depending on the source, these assessments may include information on conditions of use, hazards, exposures and potentially exposed or susceptible subpopulations. Table 1-1 shows the assessments that have been conducted. This table includes one additional document identified since the publication of the Scope document from the Office of Health and Environmental Assessment.

In addition to using this information, EPA intends to conduct a full review of the relevant data/information collected in the initial comprehensive search [see *Perchloroethylene (CASRN 127-18-4) Bibliography: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0732)], using the literature search strategy [see *Strategy for Conducting Literature Searches for Perchloroethylene: Supplemental File for the TSCA Scope Document,* (EPA-HQ-OPPT-2016-0732)]. This will ensure that EPA considers data/information that has been made available since these assessments were conducted.

**Table 1-1. Assessment History of Perchloroethylene**

| Authoring Organization | Assessment |
|---|---|
| **EPA Assessments** | |
| Integrated Risk Information System (IRIS) | Toxicological Review of Tetrachloroethylene (Perchloroethylene) (CAS No. 127-18-4) U.S. EPA (2012e) |
| Office of Air Quality Planning and Standards (OAQPS) | Perchloroethylene Dry Cleaners Refined Human Health Risk Characterization U.S. EPA (2005b) |

| Authoring Organization | Assessment |
|---|---|
| National Center for Environmental Assessment (NCEA) | Sources, Emission and Exposure for Trichloroethylene (TCE) and Related Chemicals U.S. EPA (2001c) |
| Office of Air Toxics | Tetrachloroethylene (Perchloroethylene); 127-18-4 U.S. EPA (2000b) |
| Office of Pesticides and Toxic Substances (now, Office of Chemical Safety and Pollution Prevention [OCSPP]) | Occupational Exposure and Environmental Release Assessment of Tetrachloroethylene U.S. EPA (1985b) |
| Office of Health and Environmental Assessment | Final Health Effects Criteria Document for Tetrachloroethylene U.S. EPA (1985a) |
| Office of Water (OW) | Update of Human Health Ambient Water Quality Criteria: Tetrachloroethylene (Perchloroethylene) 127-18-4 U.S. EPA (2015b) |
| Office of Water (OW) | Ambient Water Quality Criteria for Tetrachloroethylene U.S. EPA (1980a) |
| **Other U.S.-Based Organizations** | |
| California Environmental Protection Agency, Office of Environmental Health Hazard Assessment (OEHHA), Air Toxics Hot Spots Program | Perchloroethylene Inhalation Cancer Unit Risk Factor Cal/EPA (2016) |
| Agency for Toxic Substances and Disease Registry (ATSDR) | Toxicological Profile for Tetrachloroethylene (PERC) (Draft) ATSDR (2014) |
| National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances (NAC/AEGL Committee) | Tetrachloroethylene NAC/AEGL (2009) |
| California Environmental Protection Agency, OEHHA, Pesticide and Environmental Toxicology Section | Public Health Goal for Tetrachloroethylene in Drinking Water Cal/EPA (2001) |
| National Toxicology Program (NTP) | Toxicology and Carcinogenesis Studies of Tetrachloroethylene (Perchloroethylene); (CAS No. 127-18-4) in F344/N Rats and B6C3F1 Mice NTP (1986) |
| **International** | |
| International Agency for Research on Cancer (IARC) | IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Tetrachloroethylene IARC (2014b) |
| European Union (EU), Scientific Committee on Health and Environmental Risks (SCHER) | SCHER, Scientific Opinion on the Risk Assessment Report on Tetrachloroethylene, Human Health Part, CAS No.: 127-18-4, 12 SCHER (2008) |

| Authoring Organization | Assessment |
|---|---|
| World Health Organization (WHO) | Concise International Chemical Assessment Document 68; Tetrachloroethylene WHO (2006) |
| EU, European Chemicals Bureau (ECB) | EU Risk Assessment Report; Tetrachloroethylene, Part 1 - environment (2005a) |
| National Industrial Chemicals Notification and Assessment Scheme (NICNAS), Australia | Tetrachloroethylene; Priority Existing Chemical Assessment Report No. 15 NICNAS (2001) |

## 1.3 Data and Information Collection

EPA/OPPT generally applies a systematic review process and workflow that includes: (1) data collection (2) data evaluation and (3) data integration of the scientific data used in risk evaluations developed under TSCA. Scientific analysis is often iterative in nature as new knowledge is obtained. Hence, EPA/OPPT expects that multiple refinements regarding data collection may occur during the process of risk evaluation. Additional information that may be considered and was not part of the initial comprehensive bibliographies will be documented in the Draft Risk Evaluation for perchloroethylene.

***Data Collection: Data Search***

EPA/OPPT conducted chemical-specific searches for information on: physical and chemical properties; environmental fate and transport; conditions of use information; environmental and human exposures, including potentially exposed or susceptible subpopulations; ecological hazard, human health hazard, including potentially exposed or susceptible subpopulations.

EPA/OPPT designed its initial data search to be broad enough to capture a comprehensive set of sources containing data and/or information potentially relevant to the risk evaluation. Generally, the search was not limited by date and was conducted on a wide range of data sources, including but not limited to: peer-reviewed literature and gray literature (e.g., publicly-available industry reports, trade association resources, government reports). For human health hazard, EPA/OPPT relied on the search strategies from recent assessments, such as EPA Integrated Risk Information System (IRIS) assessments, to identify relevant information published after the end date of the previous search to capture more recent literature. The *Strategy for Conducting Literature Searches for Perchloroethylene: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0732) provides details about the data and information sources and search terms that were used in the literature search.

***Data Collection: Data Screening***

Following the data search, references were screened and categorized using selection criteria outlined in the *Strategy for Conducting Literature Searches for Perchloroethylene: Supplemental File for the TSCA Scope Document* (U.S. EPA, 2017d). Titles and abstracts were screened against the criteria as a first step with the goal of identifying a smaller subset of the relevant data to move into the subsequent data extraction and data evaluation steps. Prior to full-text review, EPA/OPPT anticipates refinements to the search and screening strategies, as informed by an evaluation of the performance of the initial title/abstract screening and categorization process.

The categorization scheme (or tagging structure) used for data screening varies by scientific discipline (i.e., physical and chemical properties; environmental fate and transport; chemical use/conditions of use information; human and environmental exposures, including potentially exposed or susceptible subpopulations identified by virtue of greater exposure; human health hazard, including potentially

exposed or susceptible subpopulations identified by virtue of greater susceptibility; and ecological hazard), but within each data set, there are two broad categories or data tags: (1) o*n-topic* references or (2) *off-topic* references. *On-topic* references are those that may contain data and/or information relevant to the risk evaluation. O*ff-topic* references are those that do not appear to contain data or information relevant to the risk evaluation. The supplemental document: *Strategy for Conducting Literature Searches for Perchloroethylene: Supplemental File for the TSCA Scope Document* discusses the inclusion and exclusion criteria that EPA/OPPT used to categorize references as *on-topic* or *off-topic* (U.S. EPA, 2017d).

Additional data screening using sub-categories (or sub-tags) was also performed to facilitate further sorting of data/information, for example, identifying references by source type (e.g., published peer-reviewed journal article, government report); data type (e.g., primary data, review article); human health hazard (e.g., liver toxicity, cancer, reproductive toxicity); or chemical-specific and use-specific data or information. These sub-categories are described in supplemental document: *Strategy for Conducting Literature Searches for Perchloroethylene: Supplemental File for the TSCA Scope Document* and will be used to organize the different streams of data during the stages of data evaluation and data integration steps of systematic review (U.S. EPA, 2017d).

Results of the initial search and categorization can be found in the supplemental document *Perchloroethylene (CASRN 127-18-4) Bibliography: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0732) (U.S. EPA, 2017b). This document provides a comprehensive list (bibliography) of the sources of data identified by the initial search and the initial categorization for *on-topic* and *off-topic* references. Because systematic review is an iterative process, EPA/OPPT expects that some references may move from the *on-topic* to the *off-topic* categories, and vice versa. Moreover, targeted supplemental searches may also be conducted to address specific needs for the analysis phase (e.g., to locate specific data needed for modeling); hence, additional *on-topic* references not initially identified in the initial search may be identified as the systematic review process proceeds.

## 1.4 Data Screening During Problem Formulation

EPA/OPPT is in the process of completing the full text screening of the on-topic references identified in the *Perchloroethylene (CASRN: 127-18-4) Bibliography: Supplemental File for the TSCA Scope Document* (U.S. EPA, 2017b). The screening process at the full-text level is described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a). Appendix F provides the inclusion and exclusion criteria applied at the full text screening. The eligibility criteria are guided by the analytical considerations in the revised conceptual models and analysis plan, as discussed in the problem formulation document. Thus, it is expected that the number of data/information sources entering evaluation is reduced to those that are relevant to address the technical approach and issues described in the analysis plan of this document.

Following the screening process, the quality of the included data/information sources will be assessed using the evaluation strategies that are described in *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018b).

# 2 PROBLEM FORMULATION

As required by TSCA, the scope of the risk evaluation identifies the conditions of use, hazards, exposures and potentially exposed or susceptible subpopulations that the Administrator expects to consider. To communicate and visually convey the relationships between these components, EPA included in the scope document a life cycle diagram and conceptual models that describe the actual or potential relationships between perchloroethylene and human and ecological receptors. During the problem formulation, EPA revised the conceptual models based on further data gathering and analysis as presented in this problem formulation document. An updated analysis plan is also included which identifies, to the extent feasible, the approaches and methods that EPA may use to assess exposures, effects (hazards) and risks under the conditions of use of perchloroethylene.

## 2.1 Physical and Chemical Properties

Physical-chemical properties influence the environmental behavior and the toxic properties of a chemical, thereby informing the potential conditions of use, exposure pathways and routes and hazards that EPA intends to consider. For scope development, EPA considered the measured or estimated physical-chemical properties set forth in Table 2-1; EPA found no additional information during problem formulation that would change these values.

**Table 2-1. Physical and Chemical Properties of Perchloroethylene**

| Property | Value[a] | References |
|---|---|---|
| Molecular formula | $C_2Cl_4$ | |
| Molecular weight | 165.833 | |
| Physical form | Colorless liquid; ether-like, mildly sweet odor | Lewis (2007); NIOSH (2005); U.S. Coast Guard (1984) |
| Melting point | -22.3°C | Lide (2007) |
| Boiling point | 121.3°C | Lide (2007) |
| Density | 1.623 g/cm$^3$ at 20°C | Lide (2007) |
| Vapor pressure | 18.5 mmHg at 25°C | Riddick et al. (1985) |
| Vapor density | 5.7 (relative to air) | Browning (1965) |
| Water solubility | 206 mg/L at 25°C | Horvath (1982) |
| Octanol:water partition coefficient ($K_{ow}$) | 3.40 | Hansch et al. (1995) |
| Henry's Law constant | 0.0177 atmm$^3$/mole | Gossett (1987) |
| Flash point | Not applicable | NFPA (2010) |
| Autoflammability | Not readily available | |
| Viscosity | 0.839 cP @at 25°C | Hickman (2000) |
| Refractive index | 1.4775 | Lide (2007) |
| Dielectric constant | 0 D | |

[a] Measured unless otherwise noted.

## 2.2 Conditions of Use

TSCA § 3(4) defines the conditions of use as ‘‘the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of.’’

### 2.2.1 Data and Information Sources

In the scope documents, EPA identified, based on reasonably available information, the conditions of use for the subject chemicals. As further described in this document, EPA searched a number of available data sources (e.g., *Use and Market Profile for Tetrachloroethylene*, EPA-HQ-OPPT-2016-0732). Based on this search, EPA published a preliminary list of information and sources related to chemical conditions of use [see *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: Tetrachloroethylene (Perchloroethylene) and Use*, EPA-HQ-OPPT-2016-0732] prior to a February 2017 public meeting on scoping efforts for risk evaluation convened to solicit comment and input from the public. EPA also convened meetings with companies, industry groups, chemical users and other stakeholders to aid in identifying conditions of use and verifying conditions of use identified by EPA. The information and input received from the public and stakeholder meetings has been incorporated into this problem formulation document to the extent appropriate. Thus, EPA believes the manufacture, processing, distribution, use and disposal activities identified in these documents constitute the intended, known, and reasonably foreseeable activities associated with the subject chemical, based on reasonably available information.

### 2.2.2 Identification of Conditions of Use

To determine the current conditions of use of perchloroethylene and inversely, activities that do not qualify as conditions of use, EPA conducted extensive research and outreach. This included EPA’s review of published literature and online databases including the most recent data available from EPA’s Chemical Data Reporting program (CDR) and Safety Data Sheets (SDSs). EPA also conducted online research by reviewing company websites of potential manufacturers, importers, distributors, retailers, or other users of perchloroethylene and queried government and commercial trade databases. EPA also received comments on the Scope of the Risk Evaluation for perchloroethylene (EPA-HQ-OPPT-2016-0732) that were used to determine the conditions of use. In addition, EPA convened meetings with companies, industry groups, chemical users, states, environmental groups, and other stakeholders to aid in identifying conditions of use and verifying conditions of use identified by EPA. Those meetings included a February 14, 2017 public meeting with such entities (EPA-HQ-OPPT-2016-0732).

EPA has removed from the risk evaluation any activities that EPA concluded do not constitute conditions of use – for example because EPA has insufficient information to find certain activities are circumstances under which the chemical is actually “intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used or disposed of.” EPA has also identified any conditions of use that EPA does not expect to include in the risk evaluation. As explained in the final rule for Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act, TSCA Section 6(b)(4)(D) requires EPA to identify "the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations the Administrator expects to consider” in a risk evaluation, suggesting that EPA is not required to consider all conditions of use, and EPA may exclude certain activities that EPA has determined to be conditions of use on a case-by-case basis 82 FR 33736, 33729 (July 20, 2017). For example, EPA may exclude conditions of use that the Agency has sufficient basis to conclude would present only de minimus exposures or otherwise insignificant risks (such as use in a closed system that effectively precludes exposure or as an intermediate).

The activities that EPA no longer believes are conditions of use or were otherwise excluded during problem formulation are described in Section 2.2.2.1. The conditions of use included in the scope of the risk evaluation are summarized in Section 2.2.2.2.

### 2.2.2.1 Categories and Subcategories Determined Not to be Conditions of Use During Problem Formulation

For perchloroethylene, EPA has conducted public outreach and literature searches to collect information about perchloroethylene's conditions of use and has reviewed reasonably available information obtained or possessed by EPA concerning activities associated with perchloroethylene. Based on the foregoing research and outreach, EPA does not have reason to believe that any categories or subcategories identified in the perchloroethylene scope should be excluded from the scope of the risk evaluation. Therefore, no categories or subcategories of use for perchloroethylene will be excluded from the scope of the risk evaluation.

**Table 2-2. Categories and Subcategories Determined Not to be Conditions of Use During Problem Formulation**

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| No categories or subcategories have been excluded from the risk evaluation. | | | |

### 2.2.2.2 Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation

The uses of perchloroethylene include the production of fluorinated compounds, dry cleaning and vapor degreasing, as well as a number of smaller uses. Nearly 65% of the production volume of perchloroethylene is used as an intermediate in industrial gas manufacturing, more specifically to produce fluorinated compounds, such as hydrofluorocarbons (HFCs) and hydrochlorofluorocarbons (HCFCs) (NTP, 2014; ICIS, 2011). HFCs 134a and 125 are alternatives to chlorofluorocarbons (CFCs) and HCFCs, which are ozone depleting substances (ODSs), and the subject of a phase-out (https://www.epa.gov/ods-phaseout). HCFCs are transitional substances in the phase-out of ODSs (ICIS, 2011) (Public Comment, EPA-HQ-OPPT-2016-0732-0033). Previously, perchloroethylene was widely used to manufacture CFCs (esp. trichlorotrifluoroethane (CFC-113)) until production and importation of CFCs for most uses were phased out in the United States by regulations implementing the Montreal Protocol (40 CFR part 82). A relatively small amount of CFC-113 is still produced for exempted uses (teleconference with Honeywell, 2017; summary is available in the docket: EPA-HQ-OPPT-2016-0732).

The second largest use of perchloroethylene (~15%) is as a solvent in dry cleaning facilities (NTP, 2014). Perchloroethylene is non-flammable and effectively dissolves fats, greases, waxes and oils, without harming natural or human-made fibers. These properties enabled it to replace traditional petroleum solvents(ATSDR, 2014; Dow Chemical Co, 2008; Tirsell, 2000). The demand for perchloroethylene dry cleaning solvents has steadily declined as a result of the improved efficiency of dry cleaning equipment, increased chemical recycling and the popularity of wash-and-wear fabrics that eliminate the need for dry cleaning (ATSDR, 2014). Perchloroethylene is also used in dry cleaning detergent and dry cleaning sizing.

Approximately 60% of dry cleaning machines now use perchloroethylene as a solvent (DLI and NCA, 2017). In 1991, EPA estimated that 83% of all dry cleaning facilities used perchloroethylene as solvent (U.S. EPA, 1991). In 2008, the Halogenated Solvents Industry Association (HSIA) estimated that 70% of dry cleaners used perchloroethylene as dry cleaning solvent (EPA-HQ-OPPT-2016-0732-0027). Similarly, in 2011, King County, WA conducted a profile of the dry cleaning industry and found that 69% of respondents (105 of the 152 respondents) used perchloroethylene in their primary machine (Whittaker and Johanson, 2011). Hence, there appears to be a trend towards alternatives to perchloroethylene in dry cleaning. According to the dry cleaning industry, a majority of new perchloroethylene dry cleaning machines are sold in locations where local fire codes preclude the use of Class III combustible alternative solvents or where the nature of the dry cleaning operation requires the use of perchloroethylene (DLI and NCA, 2017).

The third most prevalent use of perchloroethylene (~10%) is as a vapor degreasing solvent (NTP, 2014). Perchloroethylene can be used to dissolve many organic compounds, select inorganic compounds and high-melting pitches and waxes making it ideal for cleaning contaminated metal parts and other fabricated materials (ATSDR, 2014). It is a very good solvent for greases, fats, waxes, oils, bitumen, tar and many natural and synthetic resins for use in chemical cleaning systems, degreasing light and heavy metals, degreasing pelts and leather (tanning), extraction of animal and vegetable fats and oils and textile dyeing (solvent for dye baths)(Stoye, 2000). Perchloroethylene is also used in cold cleaning, which is similar to vapor degreasing, except that cold cleaning does not require the solvent to be heated to its boiling point in order to clean a given component. Vapor degreasing and cold cleaning scenarios may include a range of open-top or closed systems, conveyorized/enclosed/inline systems, spray wands, dip containers and wipes.

Perchloroethylene has many other uses, which collectively constitute ~10% of the production volume. EPA's search of safety data sheets, government databases and other sources found over 375 products containing perchloroethylene. These uses include (but are not limited to):

- Adhesives
- Aerosol degreasing
- Brake cleaner
- Laboratories
- Lubricants
- Mold cleaners, releases and protectants
- Oil refining
- Sealants
- Stainless steel polish
- Tire buffers and cleaners
- Vandal mark removers

Many of these uses include consumer products, such as adhesives (arts and crafts, as well as light repairs), aerosol degreasing, brake cleaners, aerosol lubricants, sealants, sealants for gun ammunition, stone polish, stainless steel polish and wipe cleaners. The uses of perchloroethylene in consumer adhesives and brake cleaners are especially prevalent; EPA has found 16 consumer adhesive products and 14 consumer brake cleaners containing perchloroethylene [see *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: Tetrachloroethylene (Perchloroethylene)* and *Use and Market Profile for Tetrachloroethylene*, EPA-HQ-OPPT-2016-0732-0003].

Table 2-3 summarizes each life cycle stage and the corresponding categories and subcategories of conditions of use for perchloroethylene that EPA expects to consider in the risk evaluation. Using the 2016 CDR (U.S. EPA, 2016b), EPA identified industrial processing or use activities, industrial function categories and commercial and consumer use product categories. EPA identified the subcategories by supplementing CDR data with other published literature and information obtained through stakeholder consultations. For risk evaluations, EPA intends to consider each life cycle stage (and corresponding use categories and subcategories) and assess certain relevant potential sources of release and human exposure associated with that life cycle stage.

Beyond the uses identified in the *Scope of the Risk Evaluation for Perchloroethylene*, EPA has received no additional information identifying additional current conditions of use for perchloroethylene from public comment and stakeholder meetings.

**Table 2-3. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation**

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| Manufacture | Domestic manufacture | Domestic manufacture | U.S. EPA (2016b) |
| | Import | Import | U.S. EPA (2016b) |
| Processing | Processing as a reactant or intermediate | Intermediate in industrial gas manufacturing | U.S. EPA (2016b); Market Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0013; Public Comment, Public Comment, EPA-HQ-OPPT-2016-0732-DRAFT-0018; Public Comment, Public Comment, EPA-HQ-OPPT-2016-0732-0033 |
| | | Intermediate in basic organic chemical manufacturing | U.S. EPA (2016b); Market Profile, EPA-HQ-OPPT-2016-0732; |
| | | Intermediate in petroleum refineries | U.S. EPA (2016b); Market Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0018 |
| | | Residual or byproduct | Public Comment, EPA-HQ-OPPT-2016-0732-0013 |
| | Incorporated into formulation, mixture or reaction product | Cleaning and degreasing products | U.S. EPA (2016b); Public Comment, EPA-HQ-OPPT-2016-0732-0017 |
| | | Adhesive and sealant products | U.S. EPA (2016b) |
| | | Paint and coating products | U.S. EPA (2016b) |
| | | Other chemical products and preparations | U.S. EPA (2016b) |
| | Incorporated into articles | Plastic and rubber products | Use Document, EPA-HQ-OPPT-2016-0732-0003 |
| | Repackaging | Solvent for cleaning or degreasing | U.S. EPA (2016b) |
| | | Intermediate | U.S. EPA (2016b) |
| | Recycling | Recycling | U.S. EPA (2016b) |
| Distribution in commerce | Distribution | Distribution | Use Document, EPA-HQ-OPPT-2016-0732-0003 |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| Industrial use | Solvents (for cleaning or degreasing) | Solvents and/or Degreasers (cold, aerosol spray or vapor degreaser; not specified in comment) | Market Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0022; Public Comment, EPA-HQ-OPPT-2016-0732-0029 |
| | | Batch vapor degreaser (e.g., open-top, closed-loop) | U.S. EPA (1985b); Public Comment, EPA-HQ-OPPT-2016-0732-0015; Public Comment, EPA-HQ-OPPT-2016-0732-0027 |
| | | In-line vapor degreaser (e.g., conveyorized, web cleaner) | U.S. EPA (1985b); Public Comment, EPA-HQ-OPPT-2016-0732-0014 |
| | Solvents (for cleaning or degreasing) | Cold cleaner | Market Profile, EPA-HQ-OPPT-2016-0732; ; Public Comment, EPA-HQ-OPPT-2016-0732-0017 |
| | | Aerosol spray degreaser/cleaner | Use Document, EPA-HQ-OPPT-2016-0732-0003; Market Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0009; Public Comment, EPA-HQ-OPPT-2016-0732-0017 |
| | | Dry cleaning solvent | Market Profile, EPA-HQ-OPPT-2016-0732; U.S. EPA (2006a) |
| | | Spot cleaner | Market Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0009 |
| | Lubricants and greases | Lubricants and greases (e.g., penetrating lubricants, cutting tool coolants, aerosol lubricants) | U.S. EPA (2016b); Market Profile, ; Public Comment, EPA-HQ-OPPT-2016-0732-0027; Public Comment, EPA-HQ-OPPT-2016-0732-0029; Public Comment, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0027; Public |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| | | | Comment, EPA-HQ-OPPT-2016-0732-0029 |
| | Adhesive and sealant chemicals | Solvent-based adhesives and sealants | U.S. EPA (2016b); Use Document, EPA-HQ-OPPT-2016-0732-0003; Market Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0009; Public Comment, EPA-HQ-OPPT-2016-0732-0015; Public Comment, EPA-HQ-OPPT-2016-0732-0022; Public Comment, EPA-HQ-OPPT-2016-0732-0027 |
| | Paints and coatings including paint and coating removers | Solvent-based paints and coatings, including for chemical milling | U.S. EPA (2016b); Use Document, EPA-HQ-OPPT-2016-0732-0003; Market Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0006; Public Comment, EPA-HQ-OPPT-2016-0732-0009; Public Comment, EPA-HQ-OPPT-2016-0732-0015; Public Comment, EPA-HQ-OPPT-2016-0732-0020; Public Comment, EPA-HQ-OPPT-2016-0732-0027; Public Comment,EPA-HQ-OPPT-2016-0732-0062 |
| | Processing aids, not otherwise listed | Pesticide, fertilizer and other agricultural chemical manufacturing | U.S. EPA (2016b) |
| | Processing aids, specific to petroleum production | Catalyst regeneration in petrochemical manufacturing | U.S. EPA (2016b); Use Document, EPA-HQ-OPPT-2016-0732-0003; Market Profile, EPA-HQ-OPPT-2016-0732; Dow Chemical Co (2008); Public Comment, EPA-HQ-OPPT-2016-0732-0018; Public Comment, EPA-HQ-OPPT-2016-0732-0027 |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| | Other uses | Textile processing | Use Document, EPA-HQ-OPPT-2016-0732-0003; Market Profile, EPA-HQ-OPPT-2016-0732 |
| | | Wood furniture manufacturing | Use Document, EPA-HQ-OPPT-2016-0732-0003 |
| | | Laboratory chemicals | Use Document, EPA-HQ-OPPT-2016-0732-0003; Market Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0015 |
| | | Foundry applications | Use Document, EPA-HQ-OPPT-2016-0732-0003; Market Profile, EPA-HQ-OPPT-2016-0732 |
| Commercial/consumer use | Cleaning and furniture care products | Cleaners and degreasers (other) | Market Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0009; Public Comment, EPA-HQ-OPPT-2016-0732-0017; Public Comment, EPA-HQ-OPPT-2016-0732-0022; EPA-HQ-OPPT-2016-0732-0023; Public Comment, EPA-HQ-OPPT-2016-0732-0027; Public Comment, EPA-HQ-OPPT-2016-0732-0029 |
| | | Dry cleaning solvent | Market Profile, EPA-HQ-OPPT-2016-0732; U.S. EPA (2006a); Public Comment, EPA-HQ-OPPT-2016-0732-0007; Public Comment, EPA-HQ-OPPT-2016-0732-0009 |
| | | Spot cleaner | Market Profile, EPA-HQ-OPPT-2016-0732; U.S. EPA (2006a); Public Comment, EPA-HQ-OPPT-2016-0732-0009 |
| | | Automotive care products (e.g., engine degreaser and brake cleaner) | U.S. EPA (2016b), Use Document, EPA-HQ-OPPT-2016-0732-0003; Market |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| | | | Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0017; Public Comment, EPA-HQ-OPPT-2016-0732-0027 |
| | | Aerosol cleaner | Use Document, EPA-HQ-OPPT-2016-0732-0003; Market Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0009 |
| | | Non-aerosol cleaner | Use Document, EPA-HQ-OPPT-2016-0732-0003; Market Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0009 |
| | Lubricants and greases | Lubricants and greases (e.g., penetrating lubricants, cutting tool coolants, aerosol lubricants) | U.S. EPA (2016b); Market Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0027; Public Comment, EPA-HQ-OPPT-2016-0732-0029 |
| | Adhesives and sealant chemicals | Adhesives for arts and crafts | U.S. EPA (2016b); Use Document, EPA-HQ-OPPT-2016-0732-0003; Market Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0009 |
| | | Light repair adhesives | U.S. EPA (2016b); Use Document, EPA-HQ-OPPT-2016-0732-0003 |
| | Paints and coatings | Solvent-based paints and coatings | U.S. EPA (2016b); Use Document, EPA-HQ-OPPT-2016-0732-0003; Market Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0009; Public Comment, EPA-HQ-OPPT-2016-0732-0020; Public Comment, EPA-HQ-OPPT-2016-0732-0027 |
| | Other uses | Carpet cleaning | Use Document, EPA-HQ-OPPT-2016-0732-0003; Market |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| | | | Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0009 |
| | | Laboratory chemicals | Use Document, EPA-HQ-OPPT-2016-0732-0003; Market Profile, EPA-HQ-OPPT-2016-0732 |
| | | Metal (e.g., stainless steel) and stone polishes | Use Document, EPA-HQ-OPPT-2016-0732-0003; Market Profile, EPA-HQ-OPPT-2016-0732 |
| | | Inks and ink removal products | Use Document, EPA-HQ-OPPT-2016-0732-0003; Market Profile, EPA-HQ-OPPT-2016-0732 |
| | | Welding | Use Document, EPA-HQ-OPPT-2016-0732-0003; Market Profile, EPA-HQ-OPPT-2016-0732; |
| | | Photographic film | Use Document, EPA-HQ-OPPT-2016-0732-0003 |
| | | Mold cleaning, release and protectant products | Use Document, EPA-HQ-OPPT-2016-0732-0003; Market Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0017 |
| Disposal | Disposal | Industrial pre-treatment | Use Document, EPA-HQ-OPPT-2016-0732-0003 |
| | | Industrial wastewater treatment | |
| | | Publicly owned treatment works (POTW) | |
| | | Underground injection | |
| | | Municipal landfill | |
| | | Hazardous landfill | |
| | | Other land disposal | |
| | | Municipal waste incinerator | |
| | | Hazardous waste incinerator | |
| | | Off-site waste transfer | |
| | | Off-site waste transfer | |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|

[a] These categories of conditions of use appear in the initial life cycle diagram, reflect CDR codes and broadly represent conditions of use for perchloroethylene in industrial and/or commercial settings.
[b] These subcategories reflect more specific uses of perchloroethylene.

#### 2.2.2.3 Overview of Conditions of Use and Lifecycle Diagram

The life cycle diagram provided in Figure 2-1 depicts the conditions of use that are considered within the scope of the risk evaluation during various life cycle stages including manufacturing, processing, distribution, use (industrial, commercial, consumer, where distinguishable) and disposal. Additions or changes to conditions of use based on additional information gathered or analyzed during problem formulation were described in Sections 2.2.2.1 and 2.2.2.2. The information is grouped according to Chemical Data Reporting (CDR) processing codes and use categories (including functional use codes for industrial uses and product categories for industrial, commercial and consumer uses), in combination with other data sources (e.g., published literature and consultation with stakeholders), to provide an overview of conditions of use. EPA notes that some subcategories of use may be grouped under multiple CDR categories.

Use categories include the following: "industrial use" means use at a site at which one or more chemicals or mixtures are manufactured (including imported) or processed. "Commercial use" means the use of a chemical or a mixture containing a chemical (including as part of an article) in a commercial enterprise providing saleable goods or services. "Consumer use" means the use of a chemical or a mixture containing a chemical (including as part of an article, such as furniture or clothing) when sold to or made available to consumers for their use (U.S. EPA, 2016a).

To understand conditions of use relative to one another and associated potential exposures under those conditions of use, the life cycle diagram includes the production volume associated with each stage of the life cycle, as reported in the 2016 CDR (U.S. EPA, 2016b), when the volume was not claimed confidential business information (CBI).

The 2016 CDR reporting data for perchloroethylene are provided in Table 2-4 from EPA's CDR database (U.S. EPA, 2016b). This information has not changed from that provided in the scope document.

**Table 2-4. Production Volume of Perchloroethylene in CDR Reporting Period (2012 to 2015) [a]**

| Reporting Year | 2012 | 2013 | 2014 | 2015 |
|---|---|---|---|---|
| Total Aggregate Production Volume (lbs) | 387,623,401 | 391,403,540 | 355,305,850 | 324,240,744 |

[a] The CDR data for the 2016 reporting period is available via ChemView (https://java.epa.gov/chemview) (U.S. EPA, 2016b). The CDR data presented in the problem formulation is more specific than currently available in ChemView.

Descriptions of the industrial, commercial and consumer use categories identified from the 2016 CDR (U.S. EPA, 2016b) and included in the life cycle diagram (Figure 2-1) are summarized below. The descriptions provide a brief overview of the use category; Appendix B contains more detailed descriptions (e.g., process descriptions, worker activities, process flow diagrams, equipment illustrations) for each manufacture, processing, distribution, use and disposal category. The descriptions provided below are primarily based on the corresponding industrial function category and/or commercial and consumer product category descriptions from the 2016 CDR and can be found in EPA's *Instructions for Reporting 2016 TSCA Chemical Data Reporting* (U.S. EPA 2016) (U.S. EPA, 2016b).

The "**Cleaning and Furniture Care Products**" category encompasses chemical substances contained in products that are used to remove dirt, grease, stains and foreign matter from furniture and furnishings or to cleanse, sanitize, bleach, scour, polish, protect or improve the appearance of surfaces (U.S. EPA,

2016a)). This category includes a wide variety of uses, including, but not limited to, the use of perchloroethylene as a commercial dry cleaning solvent, in spot cleaning formulations, in automotive care products such as brake cleaners and engine degreasers, and other aerosol and non-aerosol type cleaners.

The "**Solvents for Cleaning and Degreasing**" category encompasses chemical substances used to dissolve oils, greases and similar materials from a variety of substrates including metal surfaces, glassware and textile (U.S. EPA, 2016a). This category includes the use of perchloroethylene in vapor degreasing, cold cleaning, in industrial and commercial aerosol degreasing products and in industrial dry cleaning applications, including spot cleaning.

The "**Lubricants and Greases**" category encompasses chemical substances contained in products used to reduce friction, heat generation and wear between solid surfaces (U.S. EPA, 2016a). This category covers a variety of lubricants and greases that contain perchloroethylene including, but not limited to, penetrating lubricants, cutting tool coolants, aerosol lubricants, red greases, white lithium greases, silicone-based lubricants and chain and cable lubricants.

The "**Adhesives and Sealants**" category encompasses chemical substances contained in adhesive and sealant products used to fasten or bond other materials together (U.S. EPA, 2016a). EPA anticipates that the primary subcategory will be the use of perchloroethylene in solvent-based adhesives and sealants. This category covers industrial, commercial and consumer uses of adhesives and sealants.

The "**Paints and Coatings**" category encompasses chemical substances contained in paints, lacquers, varnishes and other coating products that are applied as a thin continuous layer to a surface (U.S. EPA, 2016a; OECD, 2009c). Coating may provide protection to surfaces from a variety of effects such as corrosion and UV degradation; may be purely decorative; or provide other functions (OECD, 2009c). EPA anticipates that the primary subcategory will be the use of perchloroethylene in solvent-based coatings. This category covers industrial, commercial and consumer uses of paints and coatings.

The "**Processing aids for agricultural product manufacturing**" category encompasses a variety of chemical substances that are used to improve the processing characteristics or operation of process equipment or to alter or buffer the pH of the substance (U.S. EPA, 2016a). Processing aids do not become a part of the final reaction product and are not intended to affect the function of the product (U.S. EPA, 2016a). Based on the 2016 CDR, EPA anticipates the primary subcategory will be the use in pesticide, fertilizer or other agricultural product manufacturing; however, the exact use in this subcategory has yet to be identified be EPA. Examples of processing aids include buffers, dehumidifiers, dehydrating agents, sequestering agents and chelators (U.S. EPA, 2016a).

The "**Processing aid for petrochemical manufacturing**" category is similar to the "Processing aid for agricultural product manufacturing" category except the chemicals are used specifically during the production of oil, gas and other similar products (U.S. EPA, 2016a). Based on the U.S. EPA (2016a) and a Dow Chemical Company Product Safety Assessment (Dow Chemical Co, 2008), EPA anticipates the primary subcategory will be the use of perchloroethylene for catalyst regeneration in petrochemical manufacturing.

Figure 2-1 depicts the life cycle diagram for perchloroethylene from manufacture to the point of disposal. Activities related to distribution (e.g., loading, unloading) will be considered throughout the perchloroethylene life cycle, rather than using a single distribution scenario.

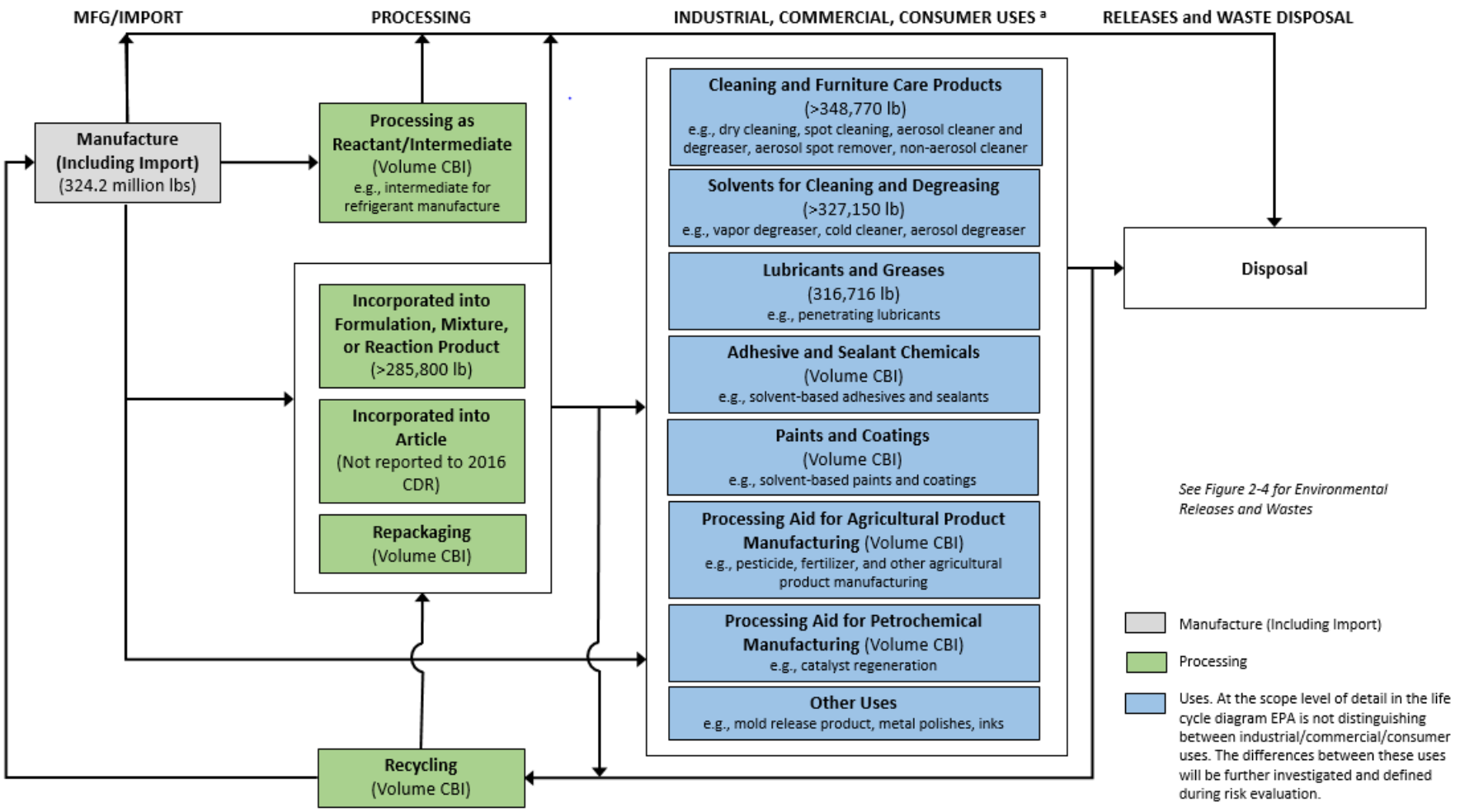


**Figure 2-1. Perchloroethylene Life Cycle Diagram**

The life cycle diagram depicts the conditions of use that are within the scope of the risk evaluation during various life cycle stages including manufacturing, processing, use (industrial, commercial, consumer, where distinguishable), distribution and disposal. The production volumes shown are for reporting year 2015 from the 2016 CDR reporting period (U.S. EPA, 2016b). Activities related to distribution (e.g., loading, unloading) will be considered throughout the perchloroethylene life cycle, rather than using a single distribution scenario.

[a] See Table 2-3 for additional uses not mentioned specifically in this diagram.

## 2.3 Exposures

For TSCA exposure assessments, post-release pathways and routes will be described to characterize the relationship or connection between the conditions of use of perchloroethylene and the exposure to human receptors, including potentially exposed or susceptible subpopulations, and ecological receptors. EPA will take into account, where relevant, the duration, intensity (concentration), frequency and number of exposures in characterizing exposures to perchloroethylene.

### 2.3.1 Fate and Transport

Environmental fate includes both transport and transformation processes. Environmental transport is the movement of the chemical within and between environmental media. Transformation occurs through the degradation or reaction of the chemical with other species in the environment. Hence, knowledge of the environmental fate of the chemical informs the determination of the specific exposure pathways and potential human and environmental receptors EPA expects to consider in the risk evaluation. Table 2-5 provides environmental fate data that EPA identified and considered in developing the scoping and problem formulation for perchloroethylene.

Fate data including volatilization during wastewater treatment, volatilization from lakes and rivers, biodegradation rates, and organic carbon:water partition coefficient (log $K_{OC}$) were used when considering changes to the conceptual models. Model results and basic principles were used to support the fate data used in problem formulation while the literature review is currently underway through the systematic review process.

The environmental fate and transport of perchloroethylene has been assessed by WHO (2006); (ECB, 2005a). This section was prepared, in part, based on these reviews, supplemented by information from EPI Suite™ (U.S. EPA, 2012b) modules.

Based on its vapor pressure and Henry's Law constant, perchloroethylene will tend to partition from water to air and, to a lesser extent, soil to air. The persistence of perchloroethylene is highly dependent on specific environmental and microbial conditions (WHO, 2006; ECB, 2005a). In the vapor phase, perchloroethylene can be slowly transformed by reaction with hydroxyl and other radicals with half-lives of months or greater, and long-range transport may occur. In water, perchloroethylene is generally stable. Aqueous photolysis has not been observed and is not expected to be a significant degradation process. Hydrolysis, if it occurs, is expected to be slow with a half-life of greater than months to years.

Chemicals that enter wastewater treatment plants (WWTP) may be incorporated into sludge if they are not rapidly degraded or transferred into the vapor phase. Sorption to organic and inorganic solids will result in the chemical being settled out during coagulation and flocculation. EPI Suite™ (U.S. EPA, 2012b) modules were used to predict volatilization of perchloroethylene from wastewater treatment plants, lakes, and rivers and to confirm the data showing slow biodegradation. The EPI Suite™ module that estimates chemical removal in sewage treatment plants ("STP" module) was run using default settings to evaluate the potential for perchloroethylene to volatilize to air or adsorb to sludge during wastewater treatment. The STP module estimates that about 80% of perchloroethylene in wastewater will be removed by volatilization. Based on measured log $K_{oc}$ = 1.6-2.7 perchloroethylene is not expected to sorb to a large extent but may also be settled out by entrainment and incorporation into flocs. During sludge processing perchloroethylene will tend to be transferred to air during dewatering and volume reduction processes. When biosolids (processed sludge) are land applied perchloroethylene will be transferred to air during spraying and over time by volatilization from solids and liquid phases.

Perchloroethylene in surface waters can be expected to volatilize into the atmosphere. However, perchloroethylene is denser than water and only slightly soluble in water. In soil and aquifers, it will tend to remain in the aqueous phase and be transported to ground water. Anaerobic biodegradation is expected to be a significant degradation mechanism in soil and ground water.

The EPI Suite™ module that estimates volatilization from lakes and rivers ("Volatilization" module) was run using default settings to evaluate the volatilization half-life of perchloroethylene in surface water. The parameters required for volatilization (evaporation) rate of an organic chemical from the water body to air are water depth, wind, and current velocity of the river or lake. The volatilization module estimates that the half-life of perchloroethylene in a model river will be 0.05 days and the half-life in a model lake will be 5 days.

In ground water, perchloroethylene may be present as a dense non-aqueous phase liquid (DNAPL), which, because it is denser than water, means that it will form a separate phase, often at the base of an aquifer. The half-life degradation rate in ground water is estimated to be between one to two years, based on aqueous aerobic biodegradation (Howard, 1991) but may be considerably longer under certain conditions.

**Table 2-5. Environmental Fate Characteristics of Perchloroethylene**

| Property or Endpoint | Value [a] | References |
|---|---|---|
| Direct photodegradation | 3 years (atmosphere) | ECB (2005a) |
| Indirect photodegradation | 96 days (atmosphere) | ECB (2005a) |
| Hydrolysis half-life | Months-years | ECB (2005a) |
| Biodegradation | No degradation (aerobic in mixed and pure culture, modified shake flask, river die-away study, sewage inoculated).<br><br><1 day to weeks (anaerobic, based on multiple studies). | ECB (2005a) |
| Bioconcentration factor (BCF) | 40 and 49 (fish)<br>312 and 101 (marine algae) | ECB (2005a) |
| Bioaccumulation factor (BAF) | 46 (estimated) | U.S. EPA (2012b); ECB (2005a) |
| Organic carbon:water partition coefficient (log $K_{oc}$) | 1.62.7<br>2.9 (estimated) | U.S. EPA (2012b); ECB (2005a) |

[a] Measured unless otherwise noted.

The EPI Suite™ module that predicts biodegradation rates ("BIOWIN" module) was run using default settings to estimate biodegradation rates of perchloroethylene in soil and sediment. Mixed results were obtained: four of the models built into the BIOWIN module (BIOWIN 1, 2, 5 and 6) estimate that perchloroethylene will not rapidly biodegrade in aerobic environments, while two (BIOWIN 3 and 4) estimate that perchloroethylene will rapidly biodegrade in aerobic environments. These results support the biodegradation data presented in the perchloroethylene Scope Document (U.S. EPA, 2017c), which

indicated that in soil and sediment, aerobic and anaerobic degradation can occur but is generally slow. Several microbial species have been identified that are capable of degrading perchloroethylene under certain conditions but overall biodegradation in these environments is expected to be slow with half-life of months or greater. The model that estimates anaerobic biodegradation (BIOWIN 7) predicts that perchloroethylene will degrade more rapidly under anaerobic conditions.

With BCFs and BAFs ranging from 40 to 100, ECB (2005a),WHO (2006) and ECB (2005a) indicate that there is limited potential for perchloroethylene to bioaccumulate in plants and animals.

### 2.3.2 Releases to the Environment

Releases to the environment from conditions of use (e.g., industrial and commercial processes, commercial or consumer uses resulting in down-the-drain releases) are one component of potential exposure and may be derived from reported data that are obtained through direct measurement, calculations based on empirical data and/or assumptions and models.

A source of information that EPA considered in evaluating exposure are data reported under the Toxics Release Inventory (TRI) program. Under the Emergency Planning and Community Right-to-Know Act (EPCRA) Section 313 rule, perchloroethylene is a TRI-reportable substance effective January 1, 1987. During problem formulation, EPA further analyzed the TRI data and examined the definitions of elements in the TRI data to determine the level of confidence that a release would result from certain types of disposal to land (e.g., RCRA Subtitle C hazardous landfill and Class I underground Injection wells) and incineration. EPA also examined how perchloroethylene is treated at industrial facilities.

Table 2-6 provides production-related waste managed data (also referred to as waste managed) for perchloroethylene reported by industrial facilities to the TRI program for 2015. Table 2-7 provides more detailed information on the quantities released to air or water or disposed of on land.

**Table 2-6. Summary of Perchloroethylene TRI Production-Related Waste Managed in 2015 (lbs)**

| Number of Facilities | Recycling | Energy Recovery | Treatment | Releases [a, b, c] | Total Production Related Waste |
|---|---|---|---|---|---|
| 27 | 46,406,761 | 2,341,981 | 15,132,768 | 1,177,484 | 65,058,994 |

Data source: 2015 TRI Data [updated March 2017 (U.S. EPA, 2017f)].
[a] Terminology used in these columns may not match the more detailed data element names used in the TRI public data and analysis access points.
[b] Does not include releases due to one-time event not associated with production such as remedial actions or earthquakes.
[c] Counts all releases including release quantities transferred and release quantities disposed of by a receiving facility reporting to TRI.

In 2015, 27 facilities reported a total of 65 million pounds of perchloroethylene waste managed. Of this total, roughly 46 million pounds were recycled, 2.3 million pounds were recovered for energy, 15 million pounds were treated and 1.18 million pounds were released into the environment.

Release quantities in Table 2-7 are more representative of actual releases during the year. Production-related waste managed shown in Table 2-6 excludes any quantities reported as catastrophic or one-time releases (TRI Section 8 data), while release quantities shown in Table 2-7 include both production-related and non-routine quantities (TRI Section 5 and 6 data). Table 2-6 counts all release quantities reported to TRI while Table 2-7 counts releases once at final disposition, accounting for transfers of chemical waste from one TRI reporting facility and received by another TRI reporting facility for final

disposal. As a result, release quantities may differ slightly and may further reflect differences in TRI calculation methods for reported release range estimates (U.S. EPA, 2017e).

**Table 2-7. Summary of Perchloroethylene TRI Releases to the Environment in 2015 (lbs)**

| | Number of Facilities | Air Releases | | Water Releases | Land Releases | | | Other Releases [a] | Total Releases [b, c] |
|---|---|---|---|---|---|---|---|---|---|
| | | Stack Air Releases | Fugitive Air Releases | | Class I Under-ground Injection | RCRA Subtitle C Landfills | All other Land Disposal [a] | | |
| Subtotal | | 435,558 | 279,073 | | 272 | 78,121 | 414 | | |
| Totals | 27 | 714,631 | | 10,393 | 78,807 | | | 373,653 | 1,177,484 |

Data source: 2015 TRI Data [updated March 2017) (U.S. EPA, 2017e)].
[a] Terminology used in these columns may not match the more detailed data element names used in the TRI public data and analysis access points.
[b] These release quantities do include releases due to one-time events not associated with production such as remedial actions or earthquakes.
[c] Counts release quantities once at final disposition, accounting for transfers to other TRI reporting facilities that ultimately dispose of the chemical waste.

While production-related waste managed shown in Table 2-6 excludes any quantities reported as catastrophic or one-time releases (TRI Section 8 data), release quantities shown in Table 2-7 include both production-related and non-routine quantities (TRI Section 5 and 6 data). As a result, release quantities may differ slightly and may further reflect differences in TRI calculation methods for reported release range estimates (U.S. EPA, 2017e).

Table 2-8 provides an additional representation of TRI data including the volume of perchloroethylene sent to each release, disposal, and waste treatment method.

**Table 2-8. Summary of 2015 TRI Releases for Perchloroethylene (CASRN 127-18-4)**

| Waste Type | Conceptual Model Release Category | TRI Category | Volume from TRI (lbs) | Number of Reporting Sites from TRI | % of Total Production Related Waste Managed |
|---|---|---|---|---|---|
| Wastewater or Liquid Wastes | Industrial Pre-Treatment (indirect discharge) | POTW | 857 | 15 | <0.001% |
| | Industrial WWT (indirect discharge) | Off-site WWT (non-POTW) | 9,187 | 5 | <0.001% |
| | Industrial WWT (direct discharge) | Water | 349 | 19 | <0.001% |
| | Underground Injection | Class I Underground Injection | 271 | 6 | <0.001% |
| Solid Wastes and Liquid Wastes | Hazardous and Municipal Waste Landfill | RCRA Subtitle C Landfill | 78,120 | 20 | 0.12% |
| | | Other Landfills, Land Treatment, and Disposal | 413 | 19 | <0.001% |
| | Hazardous and Municipal Waste Incinerators, Recycling and Other Treatment | Off-site Incineration | 1,098,035 | 65 | 1.7% |
| | | Energy Recovery | 2,341,981 | 44 | 3.6% |
| | | Other Treatment and Management Methods | 269,529 | 19 | 0.41% |
| | | Transfers to Waste Broker | 138,052 | 16 | 0.21% |
| | | Recycling | 46,406,761 | 51 | 71.3% |
| | | Unspecified Treatment Methods[2] | 14,000,805 | 44 | 21.5% |
| Emissions to Air | Emissions to Air | Fugitive Air[1] | 279,073 | 152 | 0.43% |
| | | Stack Air[1] | 435,558 | 119 | 0.70% |
| Total Production Related Waste Managed | | | 65,067,293 | 219 | |
| Total One-Time Release Waste | | | 31,082 | 6 | <0.001% |
| Total Waste Managed | | | 65,098,375 | 219 | |

[2] Because sites such as treatment, storage, and disposal facilities (TSDFs) are required to report to TRI, the total volumes for these categories may include volumes reported as transferred to off-site treatment, such as off-site incineration.

***Releases to Air***
TRI data in Table 2-8 show air as a primary medium of environmental release. These releases include both fugitive air emissions and point source (stack) air emissions. Fugitive air emissions (totaling 279,073 pounds from 2015 TRI data) are emissions that do not occur through a confined air stream, which may include equipment leaks, releases from building ventilation systems, and evaporative losses from surface impoundments and spills. Point source (stack) air emissions (totaling 435,558 pounds from TRI reporting year 2015 data) are releases to air that occur through confined air streams, such as stacks, ducts or pipes.

***Releases to Water***
In the 2015 TRI, 349 lbs of perchloroethylene were reported as directly released to surface water discharge, 857 lbs were sent to POTWs, and 9,187 lbs were sent to off-site non-POTW wastewater treatment.

***Releases to Land***
As shown in Table 2-8, TRI reports approximately 78,000 pounds transferred to RCRA Subtitle C landfills. EPA will not further analyze releases to hazardous waste landfills because these types of landfill mitigate exposure to the wastes. TRI also reports approximately 414 pounds transferred to other land disposal methods. As discussed in Section 2.3.5.3, perchloroethylene will not appreciably bind to sediment, soil or biosolids.

***Incineration***
During problem formulation, EPA reviewed air emissions from on-site incineration and energy recovery. Air emissions resulting from these operations are already included in the TRI reports and will be used in the analysis of air releases.

### 2.3.3 Presence in the Environment and Biota

Monitoring studies or a collection of relevant and reliable monitoring studies provide(s) information that can be used in an exposure assessment. Monitoring studies that measure environmental concentrations or concentrations of chemical substances in biota provide evidence of exposure. Monitoring and biomonitoring data were identified in EPA's data search for perchloroethylene:

***Environment***
Perchloroethylene has been found in air, soil, surface water, salt water, drinking water, aquatic organisms and terrestrial organisms (WHO, 2006). Historic industrial, commercial and military use of perchloroethylene, including unregulated or improper disposal of perchloroethylene wastes, has resulted in location-specific soil and ground water contamination. Perchloroethylene is a common ground water contaminant at hazardous waste sites in the U.S. (ATSDR, 2014) and a common drinking water contaminant (U.S. EPA, 2016b). EPA will analyze manufacturing, processing, distribution, use, disposal and recycling to identify and characterize current sources of release and contamination.

Urban and industrial areas are prone to higher perchloroethylene air concentrations than rural areas due to the concentration of sources (ATSDR, 2014; U.S. EPA, 2012e; WHO, 2006). EPA air monitoring data from 2013 reported detection of perchloroethylene in 77% of ambient air samples, with 58% of detects above the method detection limit (U.S. EPA, 2015a)(Table 4.1). Indoor air concentrations of perchloroethylene tend to be greater than concentrations in outdoor air (ATSDR, 2014; U.S. EPA, 2012e).

Perchloroethylene is a common contaminant in municipal drinking water supplies and ground water, with some of the highest measured concentrations in ground water occurring near perchloroethylene contaminated sites (for some examples, see (ATSDR, 2014; WHO, 2006) and references therein). EPA and the USGS National Water Quality Assessment Program (Cycle 1, 1992-2001) reported perchloroethylene contamination in U.S. surface water and ground water in 19.6% of samples (n=5,911) and at 13.2% of sites (n=4,295), with detection in surface water occurring more frequently than in ground water (U.S. EPA, 2009). EPA's Second Six-Year Review Contaminant Occurrence Data reported occurrence of monitored chemicals in U.S. drinking water supplies from 1998 to 2005. The Second Six-Year Review data showed perchloroethylene occurrence in 2.5% of roughly 50,000 public water systems, with thirty-six states reporting drinking water systems with at least one detection above the maximum contaminant level (MCL: 5 µg/L) (U.S. EPA, 2009).

***Air***

Urban and industrial areas are prone to higher perchloroethylene air concentrations than rural areas due to the concentration of sources (ATSDR, 2014; U.S. EPA, 2012e; WHO, 2006). Monitoring data (measured) from EPA's Air Quality System (AQS) and the open literature, as well as modeled estimates based on the National Air Toxics Assessment (NATA) and TRI emissions data suggest that perchloroethylene (tetrachloroethylene) is present in ambient air. The 2011 NATA analysis indicates perchloroethylene concentrations range from non-detect to 5.07 µg/m$^3$, with a mean 0.1 µg/m$^3$. EPA air monitoring data from 2013 reported detection of perchloroethylene in 77% of ambient air samples, with 58% of detects above the method detection limit (U.S. EPA, 2015a) (Table 4.1). The EPA Report on the Environment (U.S. EPA, 2017a) evaluated perchloroethylene concentrations from ambient air monitoring data, 2003-2013, and demonstrated that the annual average perchloroethylene air concentration is decreasing over time, from 0.429 µg/m$^3$ to 0.115 µg/m$^3$ (https://cfpub.epa.gov/roe/index.cfm).

Indoor air concentrations of perchloroethylene tend to be greater than concentrations in outdoor air (ATSDR, 2014; U.S. EPA, 2012e). In a multi-city study that evaluated the relationship between indoor and outdoor air pollutant concentrations, perchloroethylene was measured in 44.3% of 555 homes in three US cities (Weisel et al., 2005). In this study, the median concentration was 0.56 µg/m$^3$ and the 99$^{th}$ percentile was 20.9 µg/m$^3$. The median indoor air level of perchloroethylene in about 400 Dutch homes was 4 µg/m$^3$, while maximum levels varied between 49 and 205 µg/m$^3$. Levels can be much higher in buildings housing dry cleaning facilities. For example, sampling (over 100 samples) of air in six residential apartments in two buildings where dry cleaning was carried out on the ground floor revealed tetrachloroethene concentrations ranging from 50 to 6100 µg/m$^3$, with means ranging from 358 to 2408 µg/m$^3$ (ECB, 2005a).

***Surface Water***

Discharge Monitoring data (measured) were reported in EPA's Discharge Monitoring Report (DMR) Pollutant Loading Tool (https://cfpub.epa.gov/dmr/ez_search.cfm). The tool uses discharge monitoring report (DMR) data from ICIS-NPDES to calculate pollutant discharge amounts. This tool includes the top facility discharges for 2017. This information was used as a screening tool to evaluate some preliminary drinking concentrations. Using this tool an average concentration from the top discharger (total of 70 samples) would be 0.019 mg/L (19 ug/L) and the average maximum concentration for discharge would be 0.05 mg/L (50 ug/L). Note that this would only report the discharge to stream based on permits and would not report the actual stream concentrations. Reporting discharge would likely overestimate the actual stream concentrations.

A search was done through the European IPCheM database which is a single access point for locating and retrieving chemical surface water monitoring data collections (https://ec.europa.eu/jrc/en/event/conference/ipchem). Using this tool, an average concentration from the top dischargers (total of 20 samples) in surface water was 0.0058 mg/L (5.8 ug/L) and the average of the maximum concentration for 20 dischargers would be 0.0089 mg/L (8.9 ug/L) with >1000 samples collected indicating that ICIS-NPDES discharges would result in an overestimate to actual stream concentrations.

According to WHO (2006), perchloroethylene has been measured in surface (river) waters in Germany, Finland, the Netherlands, Italy, France, Switzerland, the United Kingdom, and the USA. Concentrations ranged from 0.01 to 168 µg/l, with levels typically below 5 µg/l.

***Groundwater***

Although groundwater can be higher than concentrations in surface water, this could reflect the fact that groundwater measurements tend to be taken where a problem (e.g. a spill) is thought to exist. Groundwater levels are usually below 10 µg/l, but concentrations as high as 1300 µg/l have been reported for a legacy contaminated site. Historic industrial, commercial, and military use of perchloroethylene, including unregulated or improper disposal of perchloroethylene wastes are considered legacy uses, but have resulted in location-specific soil and groundwater contamination (ECB, 2005a).

***Sediment***

Perchloroethylene is not likely to be in the sediment based on its physical and chemical properties. Nevertheless, perchloroethylene has been measured in sediment samples at 1–50 µg/kg wet weight in Germany and at <5 µg/kg wet weight in the USA (WHO, 2006). A search was done through the European IPCheM database. Using this tool, an average sediment concentration (from only 12 samples collected) was <15 µg/kg.

***Soil***

According to ECB (2005a), volatilization of perchloroethylene from dry soil is likely to be rapid due to its high vapor pressure and low adsorption to soil.

***Biota***

The EU Risk Assessment Report (ECB, 2005a) summarized data on measured levels of perchloroethylene in biota, including algae, invertebrates, fish and terrestrial plants. Nearly all reported concentrations are from locations in the EU and are below ~25 µg/kg.

***Biomonitoring***

Perchloroethylene has been measured in biomonitoring samples of U.S. populations. A subset of National Health and Nutrition Examination Survey (NHANES) data (1999-2000) reported in Lin et al. (2008) show the presence of perchloroethylene in 77% of human blood samples from non-smoking U.S. adults. Updated biomonitoring data reported by the Centers for Disease Control (CDC), sampled between 2001 and 2008, show a possible decline in the prevalence of perchloroethylene in U.S. population human blood samples, however limits of detection differ between the two data sets, complicating direct comparison. The CDC data show a decreasing concentration trend over the timeframe of data collection (CDC, 2017).

### 2.3.4 Environmental Exposures

The manufacturing, processing, use and disposal of perchloroethylene can result in releases to the environment. In this section, EPA presents exposures to aquatic and terrestrial organisms.

***Aquatic Environmental Exposures***

EPA identified and reviewed national scale monitoring data to support this problem formulation. EPA and the USGS National Water Quality Assessment Program (Cycle 1, 1992-2001) reported perchloroethylene contamination in U.S. surface water and ground water in 19.6% of samples (n=5,911) and at 13.2% of sites (n=4,295), with detection in surface water occurring more frequently than in ground water (U.S. EPA, 2009). More recently measured, national-scale monitoring data was from EPA's STOrage and RETreival (STORET) and National Water Information System (NWIS). Based on STORET query for perchloroethylene for the past ten years, perchloroethylene is detected in surface water in the United States. The data showed a detection rate (above quantification limit and/or above reporting limit) of approximately 15% for surface water, with detections ranging from 0.02 µg/L to 26.7 µg/L.

***Terrestrial Environmental Exposures***

Terrestrial species populations living near industrial and commercial facilities using perchloroethylene may be exposed via multiple routes such as ingestion of surface waters and inhalation of outdoor air. As described in Section 2.3.3, perchloroethylene is present and measurable through monitoring in a variety of environmental media including ambient and indoor air, surface water and ground water.

### 2.3.5 Human Exposures

In this section EPA presents occupational, consumer exposures and general population exposures. Subpopulations, including potentially exposed and susceptible subpopulations, within these exposure categories are also presented.

#### 2.3.5.1 Occupational Exposures

Exposure pathways and exposure routes are listed below for worker activities under the various conditions of use (industrial or commercial) described in Section 2.2. In addition, exposures to occupational non-users (ONU) who do not directly handle the chemical but perform work in an area where the chemical is present are listed. Engineering controls and/or personal protective equipment may impact occupational exposure levels.

Workers and occupational non-users may be exposed to perchloroethylene when performing activities associated with the conditions of use described in Section 2.2, including, but not limited to:

- Unloading and transferring perchloroethylene to and from storage containers to process vessels;
- Handling, transporting and disposing of waste containing perchloroethylene;
- Using perchloroethylene in process equipment (e.g., vapor degreasing machine);
- Cleaning and maintaining equipment;
- Sampling chemicals, formulations or products containing perchloroethylene for quality control;
- Repackaging chemicals, formulations or products containing perchloroethylene;
- Applying formulations and products containing perchloroethylene onto substrates (e.g., spray applying coatings or adhesives containing perchloroethylene);
- Use in dry cleaning processes; and
- Performing other work activities in or near areas where perchloroethylene is used.

During problem formulation, EPA further analyzed the expected physical form, associated exposure route, and exposure pathway for each condition of use.

***Key Data***
Key data that inform occupational exposure assessment include: the OSHA Chemical Exposure Health Data (CEHD) and NIOSH Health Hazard Evaluation (HHE) Program data. OSHA data are workplace monitoring data from OSHA inspections. The inspections can be random or targeted or can be the result of a worker complaint. OSHA data can be obtained through the OSHA Occupational Safety and Health Information System (OIS) at https://ois.osha.gov/portal/server.pt Appendix B includes a summary of perchloroethylene personal monitoring air samples obtained from OSHA inspections conducted between 2011 and 2016. NIOSH HHEs are conducted at the request of employees, union officials or employers and help inform potential hazards at the workplace. HHEs can be downloaded at https://www.cdc.gov/niosh/hhe/. HHE will be considered during risk evaluation.

***Inhalation***
Based on these occupational exposure scenarios, inhalation exposure to vapor is expected. EPA anticipates this is the most important perchloroethylene exposure pathway for workers and occupational nonusers based on the high volatility of perchloroethylene. Based on the potential for spray application of some products containing perchloroethylene exposures to mists are also expected for workers and ONU and will be incorporated into the occupational inhalation exposure estimates.

The United States has several regulatory and non-regulatory exposure limits for perchloroethylene: An OSHA Permissible Exposure Limit (PEL) of 100 ppm (685 mg/m$^3$), the ceiling is 200 ppm and the peak for a single time period up to 5 minutes for any 3 hours is 300 ppm, based on central nervous system effects, eye and skin irritation and liver and kidney damage.(OSHA, 1997) and an American Conference of Government Industrial Hygienists (ACGIH) Threshold Limit Value (TLV) of 25 ppm 8-hour TWA (ACGIH, 2001). A NIOSH Recommended Exposure Limit (REL) has not been established, but California has set its PEL at 25 ppm (170 mg/m$^3$) as a time weighted average, 100 ppm (685 mg/m$^3$) as a short term exposure limit (STEL) and 300 ppm as a ceiling.
The influence of these exposure limits on occupational exposures will be considered in the occupational exposure assessment. Also, the National Institute for Occupational Safety and Health (NIOSH) indicates that perchloroethylene has an immediately dangerous to life and health (IDLH) value of 150 ppm based on effects that might occur from a 20-30-minute exposure, and NIOSH provides a notation that perchloroethylene is a potential occupational carcinogen (NIOSH, 1994a).

***Dermal***
Based on the conditions of use, EPA expects dermal exposures for workers who have skin contact with liquids and vapors. Occupational non-users are not directly handling perchloroethylene; therefore, skin contact with liquid perchloroethylene is not expected for occupational non-users but skin contact with vapors is expected for occupational nonusers.

#### 2.3.5.2 Consumer Exposures

Perchloroethylene can be found in consumer and/or commercial products that are readily available for public purchase at common retailers (EPA-HQ-OPPT-2016-0732-0003, Sections 3 and 4 and Table 2-3) and can therefore result in exposures to consumers and bystanders (non-product users that are incidentally exposed to the product). The magnitude of exposure will depend upon the concentration of perchloroethylene products, use patterns (including frequency, duration, amount of product used, room of use) and application methods. Several consumer products need to be analyzed including solvents for

cleaning and degreasing, lubricants and greases, adhesives and sealant chemicals, paints and coatings, cleaning and furniture care products, and other uses such as mold release products, metal polishes and inks. Application activities include using aerosol and non-aerosol spraying, wiping, and painting. Other activities include mixing, pouring, and placing various types of liquids, slurries and pastes. Information regarding use patterns and application methods will be needed to build exposure scenarios. Any products which are spray applied are likely to result in some level of inhalation exposure to the consumer user and bystander in the room of use. Products used in the liquid form are also likely to result in some level of inhalation exposure to the consumer given the high vapor pressure of perchloroethylene. Consumer exposures are expected to be acute in nature, however, there may be a subset of consumers who use products on a frequent or regular basis resulting in sub-chronic or chronic exposures.

Although perchloroethylene is a liquid at room temperature, it has a high vapor pressure and tends to volatilize to air. It should be noted that the nature of the consumer solvent (whether the solvent has a high vapor pressure) and the overall percentage of perchloroethylene in the mixture may either increase or decrease the evaporation rates. Consumer products formulated with a high vapor pressure solvent and have high weight fraction of perchloroethylene will vaporize at a faster rate. The nature of the solvent and weight fraction will influence the exposure pathway.

***Inhalation***

EPA expects that inhalation exposure to vapor will be the primary route of exposure for consumer users of perchloroethylene containing products. The magnitude of exposure will depend upon the concentration of perchloroethylene in products, use patterns (including frequency, duration, amount of product used, room of use) and application methods. Several product types and scenarios will be analyzed including spray adhesives, spray degreasers (engine cleaning and electronics cleaning), and aerosol spot removers. Information regarding use patterns and application methods will be needed to build exposure scenarios for other products identified during scoping (e.g., liquid cleaners, adhesive accelerants, building and construction materials, cutting oils). Any products which are spray applied are likely to result in some level of inhalation exposure to the consumer user and also to a bystander in the room of use. Products used in the liquid form are also likely to result in some level of inhalation exposure to the consumer given the high vapor pressure of perchloroethylene. Consumer exposures are expected to be acute in nature, however, there may be a subset of consumers who use products on a frequent or regular basis resulting in sub-chronic or chronic exposures.

Exposures routes for consumers using perchloroethylene-containing products primarily include direct inhalation of vapors, mists and aerosols (e.g., aerosols from spray applications), indirect inhalation exposures after application and dermal exposure to products. Bystanders may be exposed through inhalation of vapors and mists that deposit in the upper respiratory tract; EPA assumes mists will be absorbed via inhalation.

***Dermal***

There is the potential for dermal exposures to perchloroethylene in consumer uses. Exposure to perchloroethylene may also occur via dermal contact with dry-cleaned fabrics or other articles treated with products containing perchloroethylene (U.S. EPA, 2012e). Perchloroethylene is absorbed dermally, and potential exposures will depend on exposure characteristics such as skin surface area, product volume and exposure duration. The potential for dermal absorption is limited based on high vapor pressure, and perchloroethylene is expected to volatilize quickly from surfaces (see Section 2.5.2). However, the nature of the product or article containing perchloroethylene, chemical loading, other

components present in product mixtures and the weight fraction of perchloroethylene in the product will affect dermal absorption.

***Oral***
Consumers may be exposed to perchloroethylene via transfer of chemical from hand to mouth. However, this exposure pathway is expected to be limited by a combination of dermal absorption and volatilization of perchloroethylene from skin. Due to the expected very low magnitude of accidental hand to mouth exposure, EPA does not plan to further assess this pathway.

***Exposures from Disposal***
EPA does not expect exposure to consumers from disposal of consumer products. It is anticipated that most products will be disposed of in original containers, particularly those products that are purchased as aerosol cans.

#### 2.3.5.3 General Population Exposures

Wastewater/liquid wastes, solid wastes or air emissions of perchloroethylene could result in potential pathways for oral, dermal or inhalation exposure to the general population.

***Inhalation***
General population inhalation exposure to perchloroethylene in air may result from industrial manufacturing and processing plant fugitive and stack emissions. Perchloroethylene volatilizes from contaminated soil and shallow ground water, possibly resulting in elevated outdoor inhalation exposure. Through a process known as vapor intrusion, volatilized perchloroethylene may also infiltrate residential and commercial buildings through cracks in floors, crawl spaces, pipe fittings and toilet and sewer junctions, leading to elevated indoor concentrations of perchloroethylene and greater inhalation exposure (ATSDR, 2014; U.S. EPA, 2012f). In addition, inhalation exposures to perchloroethylene may occur due to volatilization of perchloroethylene from contaminated water (municipal or well water) during showering and bathing (U.S. EPA, 2012e).

Families of workers with occupational perchloroethylene exposure are exposed secondarily by perchloroethylene volatilization from workers clothing, and from exhaled breath, as un-metabolized perchloroethylene is exhaled on the breath as the primary excretion mechanism in humans (ATSDR, 2014; U.S. EPA, 2012e).

Indoor emissions, from the use of perchloroethylene containing products and articles (e.g., degreasers; recently dry-cleaned clothing), may also be sources of perchloroethylene in indoor air (ATSDR, 2014; U.S. EPA, 2012e).

***Oral***
The general population may ingest perchloroethylene via contaminated drinking water, ground water and/or surface water (ATSDR, 2014; U.S. EPA, 2012e). Perchloroethylene enters water supplies through industrial and commercial wastewater and liquid waste streams, sewage sludge land application, wet deposition (rain) and leaching from contaminated soils (U.S. EPA, 2009). Oral ingestion pathways may include exposure to contaminated drinking water or breast milk, or incidental ingestion of contaminated water while swimming or bathing. Infants and young children may also be exposed to perchloroethylene via mouthing of treated products and articles (e.g., spot treatment of carpets; dry cleaned blanket).

The EU Risk Assessment Report (ECB, 2005a) indicates that perchloroethylene may be present in fish, although EPA does not anticipate fish ingestion to be a significant general population exposure pathway, as perchloroethylene has a low bioaccumulation potential in aquatic organisms (BCF 40 50`, Kow < 3)(WHO, 2006).

***Dermal***

General population dermal exposure to perchloroethylene is possible from showering, bathing and swimming in contaminated water (U.S. EPA, 2012e). Perchloroethylene is absorbed dermally, and potential exposures will depend on exposure characteristics such as skin surface area, exposure media concentration and exposure duration. The potential for dermal absorption is limited based on high vapor pressure, and perchloroethylene is expected to volatilize quickly from surfaces (see Section 2.5.2). However, the nature of the environmental media containing perchloroethylene and chemical loading will affect dermal absorption.

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#### 2.3.5.4 Potentially Exposed or Susceptible Subpopulations

TSCA requires the determination of whether a chemical substance presents an unreasonable risk to "a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation" by EPA. TSCA § 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." General population is "the total of individuals inhabiting an area or making up a whole group" and refers here to the U.S. general population (U.S. EPA, 2011).

As part of the Problem Formulation, EPA identified potentially exposed and susceptible subpopulations for further analysis during the development and refinement of the life cycle, conceptual models, exposure scenarios, and analysis plan. In this section, EPA addresses the potentially exposed or susceptible subpopulations identified as relevant based on greater exposure. EPA will address the subpopulations identified as relevant based on greater susceptibility in the hazard section.

EPA identifies the following as potentially exposed or susceptible subpopulations that EPA plans to analyze in the risk evaluation due to their *greater exposure*:

- Workers and occupational non-users.
- Consumers and bystanders associated with consumer use. Perchloroethylene has been identified in products available to consumers; however, only some individuals within the general population may use these products. Therefore, those who do use these products are a potentially exposed or susceptible subpopulation due to greater exposure.
- Other groups of individuals within the general population who may experience greater exposures due to their proximity to conditions of use identified in Section 2.2 that result in releases to the environment and subsequent exposures (e.g., individuals who live or work near manufacturing, processing, distribution or use sites).

Perchloroethylene is lipophilic, and accumulates in fatty fluids and tissues in the human body. Subpopulations that may have higher body fat composition, and may be more highly exposed include pubescent and adult women, including women of child-bearing age. The EPA IRIS Assessment for perchloroethylene (U.S. EPA, 2012e) also identified the developing fetus as potentially exposed, as well as infants consuming breastmilk, particularly for mothers with occupational exposure to

perchloroethylene or exposure due to proximity to industrial or commercial sources (U.S. EPA, 2012e). Infants fed by formula may also experience increased perchloroethylene exposure if perchloroethylene is present in drinking water supplies (U.S. EPA, 2012e).

In developing exposure scenarios, EPA will analyze available data to ascertain whether some human receptor groups may be exposed via exposure pathways that may be distinct to a particular subpopulation or lifestage and whether some human receptor groups may have higher exposure via identified pathways of exposure due to unique characteristics (e.g., activities, duration or location of exposure) when compared with the general population (U.S. EPA, 2006b).

The behavior of children may put them in closer contact with some sources of perchloroethylene, such as carpet cleaners. Children may be exposed via inhalation as bystanders, during consumer use in the home. Children tend to consume more water and food per body weight relative to adults, and have greater skin surface area and skin permeability than adults, relative to weight, which can result in proportionally higher ingestion and dermal exposures. Children's exposure to perchloroethylene via ingestion of contaminated food is likely to be low. Perchloroethylene has low bioaccumulation potential and, if present, would have low concentrations in fish or seafood. The half-life of perchloroethylene in soil is short, and is unlikely to be found in food crops. Perchloroethylene has been measured in fatty foods (butter, oils and meats) when stored in proximity to indoor perchloroethylene sources (U.S. EPA, 2012d). Drinking water could be a significant source of perchloroethylene ingestion exposure for children, who drink roughly four times as much water as adults (U.S. EPA, 2011).

EPA will continue to analyze available data to ascertain whether some human receptor groups may be exposed via pathways that may be distinct to a particular subpopulation or lifestage (e.g., children's crawling, mouthing or hand-to-mouth behaviors).

In summary, in the risk evaluation for perchloroethylene, EPA expects to analyze the following potentially exposed groups of human receptors: workers, occupational non-users, consumers, bystanders associated with consumer use, and other groups of individuals within the general population who may experience greater exposure. EPA may also identify additional potentially exposed or susceptible subpopulations that will be considered based on greater exposure.

## 2.4 Hazards

For scoping, EPA conducted comprehensive searches for data on hazards of perchloroethylene, as described in the supplemental document: *Strategy for Conducting Literature Searches for Perchloroethylene: Supplemental File for the TSCA Scope Document*. Based on initial screening, EPA expects to analyze the hazards of perchloroethylene identified in this problem formulation document. However, when conducting the risk evaluation, the relevance of each hazard within the context of a specific exposure scenario will be judged for appropriateness. For example, hazards that occur only as a result of chronic exposures may not be applicable for acute exposure scenarios. This means that it is unlikely that every hazard identified will be analyzed for every exposure scenario.

### 2.4.1 Environmental Hazards

EPA identified the following existing sources of environmental hazard data for perchloroethylene: European Chemicals Bureau (ECB) EU Risk Assessment Report Tetrachloroethylene, Part 1 - environment (ECB, 2005a) and World Health Organization (WHO) Concise International Chemical Assessment Document 68; Tetrachloroethylene WHO (WHO, 2006). Only the *on-topic* references listed in the Ecological Hazard Literature Search Results were considered as potentially relevant

data/information sources for the risk evaluation. Inclusion criteria were used to screen the results of the ECOTOX literature search (as explained in the *Strategy for Conducting Literature Searches for Perchloroethylene: Supplemental Document to the TSCA Scope Document, CASRN:127-18-4*. Data from the screened literature are summarized below (Table 2-9) as ranges (min-max). EPA expects to review these data/information sources during risk evaluation using the data quality review evaluation metrics and the rating criteria described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a).

***Toxicity to Aquatic Organisms***

The acute 96-hour LC50 values for fish range from 4 mg/L for Flagfish (*Jordanella floridae*) to 28.1 mg/L for Indian Silverside (*Menidia berylina*). With aquatic invertebrates, the LC/EC50 values ranged from 2.85 – 30.8 mg/L. For algal toxicity 72/96-hr EC50 values were 3.64 – 500 mg/L based on biomass and abundance (Table 2-9).

Chronic aquatic toxicity data for perchloroethylene are available. Chronic toxicity to fish values range from 0.5- 1.4 mg/L. A 28-day Daphnia magna study reported NOEC value of 0.505 mg/L based on reproduction using measured concentrations. Another 28-day Opossum Shrimp (*Americanmysis bahia*) study reported NOEC value of 0.370 mg/L. For the most conservative chronic toxicity values were reported as algal 72-h NOEC= 0.01 – 0.02 mg/L and LOEC= 0.02– 0.05 mg/L. Based on these NOEC and LOEC, the chronic toxicity values are calculated as 0. 0.014 – 0.032 mg/L (Table 2-9).

***Toxicity to Soil/Sediment and Terrestrial Organisms***

An earthworm (*Eisenia foetida*) toxicity study of perchloroethylene has been tested using OECD Guideline No. 207. The 14-day LC50 was 100–320 mg/kg, the 28-day NOEC (based upon cocoons) was ≤18 mg/kg, and the 28-day NOEC (based upon appearance) was 18–32 mg/kg. Another perchloroethylene study using the carabid beetle (*Poecilus cupreus*) was conducted. No mortality or behavioral changes were observed in this study (Table 2-9).

For terrestrial plants, a 21-day study of lettuce (*Lactuca sativa*) showed EC50 of 12 mg/L based on biomass. Another study looked at the effects on the early developmental stage of lettuce (*Avena sativa*), germinated plants, the 16-day EC50 (growth) was 861 mg/kg based on the converted standard organic matter content.

**Table 2-9: Ecological Hazard Characterization of Perchloroethylene**

| Duration | Test organism | Endpoint | Hazard value* | Units | Effect Endpoint | References |
|---|---|---|---|---|---|---|
| **Aquatic Organisms** | | | | | | |
| Acute | Fish | $LC_{50}$ | 4 – 28.1 | mg/L | Mortality | Smith (1991); Horne (1983) |
| | Aquatic invertebrates | $LC/EC_{50}$ | 2.85 – 30.8 | mg/L | Immobilization | Hollister (1968); Call (1983) as cited in WHO (2006) |
| | Algae | $EC_{50}$ | 3.64 - 500 | mg/L | Biomass/ Abundance | Brack (1994) as cited in ECB (2005); U.S. EPA (1980a) as cited in WHO (2006) |
| | Amphibians | $EC_{50}$ | 2.5 -20.0 | mg/L | Mortality | McDaniel (2004) |
| | Acute COC | 0.80 mg/L | | | | |
| Chronic | Fish | ChV | 0.5-1.4 | mg/L | Growth | Ahmad (1984); Smith (1991) as cited in ECB (2005) |
| | Aquatic invertebrates | ChV | 0.37 – 1.11 (NOEC) | mg/L | Mortality/ Reproduction | Hollister (1968); Richter et al. (1983) as cited in ECB (2005); Call (1983) as cited in WHO (2006) |
| | Algae | NOEC<br>LOEC<br>ChV | 0.01-0.02<br>0.02-0.05<br>0.014-0.032 | mg/L | Abundance | Labra (2010); |
| | Chronic COC | 0.001 mg/L | | | | |
| **Terrestrial Organisms** | | | | | | |
| Acute | Terrestrial invertebrates | $LC_{50}$ | 100 - 320 | mg/Kg | Cocoons appearance | (Vonk et al., 1986) as cited in WHO (2006) |
| | Terrestrial plants | $EC_{50}$ | 861 | mg/Kg | Growth | (Bauer and Dietze, 1992) as cited in WHO (2006) |
| Chronic | Terrestrial plants | $EC_{50}$ | 12 | mg/L | Biomass | Hulzebos, 1993 |

*** Values in the tables are presented as reported by the study authors**

***Concentrations of Concern***

The screening-level acute and chronic concentrations of concern (COCs) for perchloroethylene were derived based on the lowest or most toxic ecological toxicity values (e.g., L/EC50). The information below describes how the acute and chronic COC's were calculated for environmental toxicity of perchloroethylene using assessment factors.

The application of assessment factors is based on established EPA/OPPT methods (U.S. EPA, 2013, 2012c) and were used in this hazard assessment to calculate lower bound effect levels (referred to as the concentration of concern; COC) that would likely encompass more sensitive species not specifically

represented by the available experimental data. Also, assessment factors are included in the COC calculation to account for differences in inter- and intra-species variability, as well as laboratory-to-field variability. It should be noted that these assessment factors are dependent upon the availability of datasets that can be used to characterize relative sensitivities across multiple species within a given taxa or species group, but are often standardized in risk assessments conducted under TSCA, due to limited data availability.

The concentrations of concern for each endpoint were derived based on the ecological hazard data for perchloroethylene. The information below describes how the acute and chronic COCs were calculated for aquatic toxicity.

The acute COC is derived by dividing acute aquatic invertebrates LC50 of 2.85 mg/L (the lowest acute value in the dataset) by an assessment factor (AF) of 5:

- Lowest value for aquatic invertebrates LC50 (2.85 mg/L) / AF of 5 = 0.57 mg/L or 570 µg/L.

The acute COC of 570 µg/L, derived from experimental aquatic invertebrate's endpoint, is used as a conservative hazard level in this problem formulation for perchloroethylene.

The chronic COC was determined based on the lowest chronic toxicity value divided by an assessment factor of 10.

- Lowest chronic value for 72-h algal ChV = 0.014 mg/L / 10 = 0.0014 mg/L or 1.4 µg/L.

The chronic COC of 1.4 µg/L, derived from experimental algae endpoint, is used as the lower bound hazard level in this problem formulation for perchloroethylene.

### 2.4.2 Human Health Hazards

Perchloroethylene has an existing EPA IRIS Assessment U.S. EPA (2012e) and a draft ATSDR Toxicological Profile (ATSDR, 2014); hence, many of the hazards of perchloroethylene have been previously compiled. EPA expects to use these previous analyses as a starting point for identifying key and supporting studies to inform the human health hazard assessment, including dose-response analysis. The relevant studies will be evaluated using the data quality criteria in the *Application of Systematic Review in TSCA Risk Evaluations* document. EPA also expects to consider other studies (e.g., more recently published, alternative test data) that have been published since these reviews, as identified in the literature search conducted by the Agency for perchloroethylene (*Perchloroethylene (CASRN 127-18-4) Bibliography: Supplemental File for the TSCA Scope Document*). EPA expects to consider potential human health hazards associated with perchloroethylene. Based on reasonably available information, the following sections describe the potential hazards associated with perchloroethylene.

#### 2.4.2.1 Non-Cancer Hazards

The EPA IRIS Assessment on perchloroethylene (U.S. EPA, 2012e) evaluated the following non-cancer hazards that may be associated with perchloroethylene exposures: the central nervous system (neurotoxicity), kidney, liver and development and reproduction. In general, neurological effects were found to be associated with lower perchloroethylene inhalation exposures. According to the EPA IRIS Assessment (U.S. EPA, 2012e), support for an association with immune and blood effects were less well characterized. In their draft Toxicological Profile for perchloroethylene, ATSDR (2014) identified similar hazard concerns. The National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances (NAC/AEGL, 2009) also identified irritation as a hazard concern.

***Acute Toxicity***
Data from acute exposure studies in animals and human incidents indicate that short term exposure to perchloroethylene may cause irritation and neurotoxicity and can impair cognitive function in humans (U.S. EPA, 2012e). An Acute Exposure Guidance Limit (AEGL) values, established by the National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances (NAC/AEGL, 2009), has been developed based on irritation to humans (AEGL-1), ataxia in rodents (AEGL-2), and lethality in mice (AEGL-3) (NAC/AEGL, 2009).

***Neurotoxicity***
Evidence in humans and animals show that chronic exposure to perchloroethylene can cause neurotoxicity, resulting in decrements in color vision, visuospatial memory and possibly other aspects of cognition and neuropsychological function (U.S. EPA, 2012e). Neurotoxic effects have been characterized in human controlled exposure, occupational exposure and residential studies, as well as in experimental animal studies, providing evidence of an association between perchloroethylene exposure and neurological deficits (U.S. EPA, 2012e). The EPA IRIS assessment for perchloroethylene (U.S. EPA, 2012e) further notes that the nervous system is an expected target with oral perchloroethylene exposures because perchloroethylene and metabolites produced from inhalation exposures will also reach the target tissue via oral exposure.

***Kidney Toxicity***
Evidence for kidney toxicity in humans is based on studies of kidney biomarkers, which provide information on nephron integrity and tubule damage. Epidemiologic studies support an association between perchloroethylene and chronic kidney disease (U.S. EPA, 2012e). Animal evidence supports an association between perchloroethylene exposure and chronic kidney disease. Adverse effects on the kidney (e.g., kidney-to-body weight ratios, hyaline droplet formation, glomerular "nephrosis," karyomegaly (enlarged nuclei), cast formation, and other lesions or indicators of renal toxicity) have been observed in studies of rodents exposed to high concentrations of perchloroethylene by inhalation, oral and intraperitoneal (i.p.) injection of perchloroethylene metabolites (U.S. EPA, 2012e).

***Liver Toxicity***
Liver toxicity (i.e., necrosis, vacuolation, etc) has been reported in multiple animal species by inhalation and oral exposures to perchloroethylene, with the mouse typically being more sensitive than the rat (U.S. EPA, 2012e). The liver effects are characterized by increased liver weight, necrosis, inflammatory cell infiltration, triglyceride increases proliferation, cytoplasmic vacuolation (fatty changes), pigment in cells, oval cell hyperplasia and regenerative cellular foci. The EPA IRIS Assessment for perchloroethylene (U.S. EPA, 2012e) found suggestive evidence that perchloroethylene is a liver toxicant in humans.

***Reproductive/Developmental Toxicity***
The EPA IRIS Assessment for perchloroethylene (U.S. EPA, 2012e) evaluated the developmental and reproductive toxicity of perchloroethylene in humans and animals. Studies of tetrachloroethylene exposure in humans have evaluated several reproductive outcomes including effects on menstrual disorders, semen quality, fertility, time to pregnancy, and risk of adverse pregnancy outcomes including spontaneous abortion, low birth weight or gestational age, birth anomalies, and stillbirth (U.S. EPA, 2012e). Data from animal studies identified various manifestations of developmental toxicity including, increased mortality and decreased body weight in the offspring of rodents exposed via inhalation.

***Irritation***

U.S. EPA (2012e) and ATSDR (2014) indicate perchloroethylene is irritating. Irritation data for perchloroethylene have also been reviewed outside the EPA IRIS Assessment. Controlled exposures in humans and case reports have identified eye and nose irritation (NAC/AEGL, 2009).

#### 2.4.2.2 Genotoxicity and Cancer Hazards

Epidemiologic data provide evidence associating perchloroethylene with several cancer types, including non-Hodgkin lymphoma, multiple myeloma and bladder cancer, with more limited evidence for esophageal, kidney, lung, cervical and breast cancer (U.S. EPA, 2012e). Perchloroethylene is generally considered to be non-genotoxic, however several metabolites exhibit mutagenic and/or genotoxic properties and may contribute to potential genotoxic mode of action (MOA) (U.S. EPA, 2012e). In 2012, EPA released the outcome of the weight-of-evidence cancer assessment, which described the weight-of-evidence judgment of the likelihood that perchloroethylene is a human carcinogen, and quantitative estimates of risk from oral and inhalation exposure (U.S. EPA, 2012e). Following U.S. EPA (2005a) Guidelines for Carcinogen Risk Assessment, EPA concluded that perchloroethylene is "likely to be carcinogenic in humans by all routes of exposure" (U.S. EPA, 2012e).

#### 2.4.2.3 Potentially Exposed or Susceptible Subpopulations

TSCA requires that the determination of whether a chemical substance presents an unreasonable risk include consideration of unreasonable risk to "a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation" by EPA. TSCA § 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly."

In developing the hazard assessment, EPA will analyze available data to ascertain whether some human receptor groups may show greater susceptibility to the chemical's hazards due to intrinsic factors. EPA plans to analyze the susceptibility factors identified in the EPA IRIS assessment for perchloroethylene U.S. EPA (2012e) and ATSDR (2014) evaluations. These assessments both identified the following subpopulations as possibly more susceptible to adverse effects associated with perchloroethylene exposures: early and later lifestages and groups defined by health and nutrition status, gender, race/ethnicity, genetics and multiple exposures and cumulative risk. However U.S. EPA (2012e) also determined that the available data was insufficient to allow for a quantitative assessment of the impact of susceptibility on risk.

The California Office of Environmental Health Hazard Assessment OEHHA (2016) derived an inhalation cancer unit risk factor for perchloroethylene based on the same physiologically based pharmacokinetic (PBPK) model (Chiu and Ginsberg, 2011) used in the EPA IRIS assessment (U.S. EPA, 2012e). The model included both oxidative metabolism and glutathione conjugation metabolism; the latter varies greatly within the human population, with some variation representing sensitive subpopulations (Spearow et al., 2017; OEHHA, 2016). EPA will consider this information during the risk evaluation phase.

## 2.5 Conceptual Models

EPA risk assessment guidance (U.S. EPA, 2014d), defines Problem Formulation as the part of the risk assessment framework that identifies the major factors to be considered in the assessment. It draws from the regulatory, decision-making and policy context of the assessment and informs the assessment's technical approach.

A conceptual model describes the actual or predicted relationships between the chemical substance and receptors, either human or environmental. These conceptual models are integrated depictions of the conditions of use, exposures (pathways and routes), hazards and receptors. The initial conceptual models describing the scope of the assessment for perchloroethylene, have been refined during problem formulation. The changes to the conceptual models in this problem formulation are described along with the rationales.

In this section EPA outlines those pathways that will be included and further analyzed in the TSCA risk evaluation; will be included but will not be further analyzed in risk evaluation; and will not be included in the TSCA risk evaluation and the underlying rationale for these decisions.

EPA determined as part of problem formulation that it is not necessary to conduct further analysis on certain exposure pathways that were identified in the perchloroethylene scope document and that remain in the risk evaluation. Each risk evaluation will be "fit-for-purpose," meaning not all conditions of use will warrant the same level of evaluation and the Agency may be able to reach some conclusions without extensive or quantitative risk evaluations. 82 FR 33726, 33734, 33739 (July 20, 2017).

As part of this problem formulation, EPA also identified exposure pathways under regulatory programs of other environmental statutes, administered by EPA, which adequately assess and effectively manage exposures and for which long-standing regulatory and analytical processes already exist, i.e., the Clean Air Act (CAA), the Safe Drinking Water Act (SDWA), the Clean Water Act (CWA) and the Resource Conservation and Recovery Act (RCRA). OPPT worked closely with the offices within EPA that administer and implement the regulatory programs under these statutes. In some cases, EPA has determined that chemicals present in various media pathways (i.e., air, water, land) fall under the jurisdiction of existing regulatory programs and associated analytical processes carried out under other EPA-administered statutes and have been assessed and effectively managed under those programs. EPA believes that the TSCA risk evaluation should generally focus on those exposure pathways associated with TSCA conditions of use that are not adequately assessed and effectively managed under the regulatory regimes discussed above because these pathways are likely to represent the greatest areas of risk concern. As a result, EPA does not expect to include in the risk evaluation certain exposure pathways identified in the perchloroethylene scope document.

### 2.5.1 Conceptual Model for Industrial and Commercial Activities and Uses: Potential Exposures and Hazards

The revised conceptual model (Figure 2-2) describes the pathways of exposure from industrial and commercial activities and uses of perchloroethylene that EPA expects to include in the risk evaluation. There are exposures to workers and/or occupational non-users via inhalation routes and/or exposures to workers via dermal routes for all conditions of use identified in this problem formulation. In addition to the pathways illustrated in the figure, EPA will evaluate activities resulting in exposures associated with distribution in commerce (e.g. loading, unloading) throughout the various lifecycle stages and conditions of use (e.g. manufacturing, processing, industrial use, commercial use, disposal) rather than a single distribution scenario.

***Inhalation***

Inhalation exposures for workers are regulated by OSHA's occupational safety and health standards for perchloroethylene which include a PEL of 100 ppm TWA, exposure monitoring, control measures and respiratory protection (29 CFR 1910.134). EPA expects that for workers and occupational non-users exposure via inhalation will be the most significant route of exposure for most exposure scenarios. EPA

expects to further analyze inhalation exposures to vapors and mists for workers and occupational non-users in the risk evaluation.

***Dermal***

There is the potential for dermal exposures to perchloroethylene in many worker scenarios. Where workers may be exposed to perchloroethylene, the OSHA standard requires that workers are protected from contact (e.g. gloves) (29 CFR 1910.132). Dermal exposures would be concurrent with inhalation exposures and the overall contribution of dermal exposure to the total exposure is expected to be small however there may be exceptions for occluded scenarios. Occupational non-users are not directly handling perchloroethylene; therefore, skin contact with liquid perchloroethylene is not expected for occupational non-users and EPA does not expect to further analyze this pathway in the risk evaluation. EPA expects to further analyze dermal exposures for skin contact with liquids.

The parameters determining the absorption of perchloroethylene vapor are based on the concentration of the vapor, the duration of exposure and absorption. As described by ATSDR, a human study comparing absorption of perchloroethylene vapor via the dermal and inhalation routes (*i.e.*, exposure to vapor with and without respiratory protection) found that absorption via the dermal route is only 1% of the combined dermal and inhalation routes (ATSDR, 2014). Therefore, EPA will not further analyze worker or occupational non-user exposure via vapor-to-dermal contact, because the contribution to overall exposure will be orders of magnitude lower than direct inhalation of vapors.

***Waste Handling, Treatment and Disposal***

Figure 2-2 shows that waste handling, treatment and disposal is expected to lead to the same pathways as other industrial and commercial activities and uses. The path leading from the "Waste Handling, Treatment and Disposal" box to the "Hazards Potentially Associated with Acute and/or Chronic Exposures See Section 2.4.2" box was re-routed to accurately reflect the expected exposure pathways, routes, and receptors associated with these conditions of use of perchloroethylene.

For each condition of use identified in Table 2-3, a determination was made as to whether or not each unique combination of exposure pathway, route, and receptor will be further analyzed in the risk evaluation. The results of that analysis along with the supporting rationale are presented in Appendix C and Appendix E.

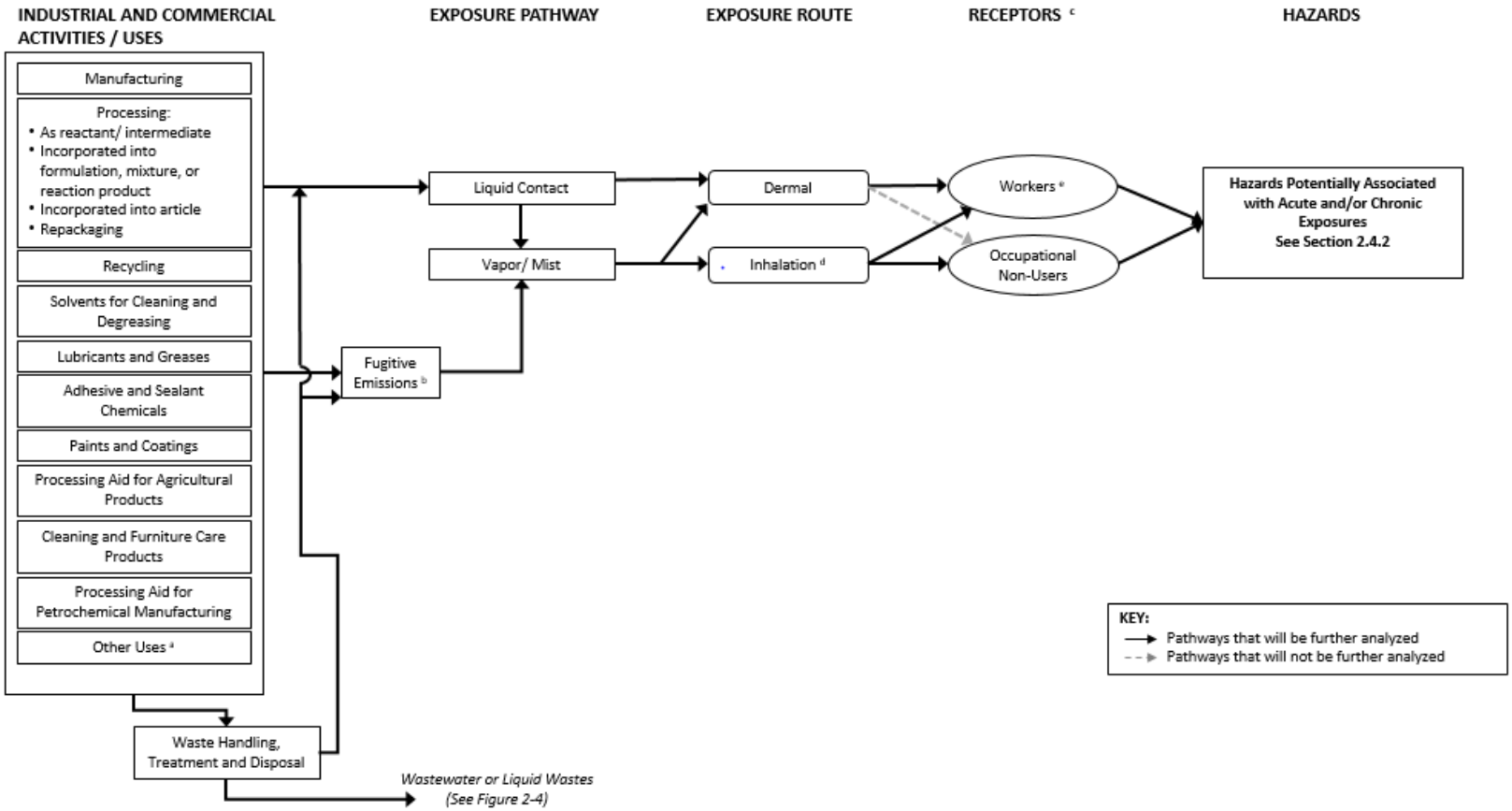


**Figure 2-2. Perchloroethylene Conceptual Model for Industrial and Commercial Activities and Uses: Potential Exposures and Hazards**

The conceptual model presents the exposure pathways, exposure routes and hazards to human receptors from industrial and commercial activities and uses of perchloroethylene.

[a] Some products are used in both commercial and consumer applications such adhesives and sealants. Additional uses of perchloroethylene are included in Table 2-3.

[b] Fugitive air emissions are those that are not stack emissions and include fugitive equipment leaks from valves, pump seals, flanges, compressors, sampling connections and open-ended lines; evaporative losses from surface impoundment and spills; and releases from building ventilation systems.

[c] Receptors include potentially exposed or susceptible subpopulations.

[d] Exposure may occur through mists that deposit in the upper respiratory tract however, based on physical chemical properties, mists of perchloroethylene will likely be rapidly absorbed in the respiratory tract or evaporate and will be considered as an inhalation exposure.

[e] When data and information are available to support the analysis, EPA also considers the effect that engineering controls and/or personal protective equipment have on occupational exposure levels.

### 2.5.2 Conceptual Model for Consumer Activities and Uses: Potential Exposures and Hazards

The revised conceptual model (Figure 2-3) illustrates the pathways of exposure from consumer uses of perchloroethylene that EPA expects to include in the risk evaluation. It should be noted that some consumers may purchase and use products primarily intended for commercial use.

***Inhalation***

EPA expects inhalation to be the primary route of exposure and plans to further analyze inhalation exposures to perchloroethylene vapor and mist for consumers and bystanders.

***Dermal***

There is potential for dermal exposures to perchloroethylene from consumer uses. Dermal exposure may occur via direct liquid contact during use. Direct contact with liquid perchloroethylene would be concurrent with inhalation exposures and dermal exposures to consumers in occluded and non-occluded scenarios are expected. Bystanders will not have direct dermal contact with liquid perchloroethylene. EPA expects to further analyze direct dermal contact with liquid perchloroethylene for consumers.

Consumers and bystanders can have skin contact with perchloroethylene vapor concurrently with inhalation exposures. Similar to workers (see Section 2.5.1) the parameters determining the absorption of perchloroethylene vapor are based on the concentration of the vapor, the duration of exposure and absorption. The concentration of the vapor and the duration of exposure are the same for concurrent dermal and inhalation exposures. Therefore, the differences between dermal and inhalation exposures depend on the absorption. As described by ATSDR, a human study comparing absorption of perchloroethylene vapor via the dermal and inhalation routes (*i.e.*, exposure to vapor with and without respiratory protection) found that absorption via the dermal route is only 1% of the combined dermal and inhalation routes (ATSDR, 2014). Therefore, EPA will not further analyze consumer or bystander exposure via vapor-to-dermal contact, because the contribution to overall exposure will be orders of magnitude lower than direct inhalation of vapors.

***Oral***

Consumers may be exposed to perchloroethylene via transfer of chemical from hand to mouth. This exposure pathway will be limited by a combination of dermal absorption and volatilization; therefore, this pathway will not be further evaluated.

Furthermore, based on available toxicological data, EPA does not expect that considering separate oral routes of exposure for mists or for incidental ingestion would have significantly different toxicity, rather mists will be included as part of consumer inhalation exposures and skin contact will be included as part of consumer dermal exposures. Bystanders are not directly handling perchloroethylene; therefore, inhalation exposure to mists and incidental ingestion via contact with perchloroethylene are not expected for bystanders. EPA plans no further analysis of this pathway for consumers or bystanders.

***Disposal***

EPA does not expect to further analyze exposure to consumers from disposal of consumer products. It is anticipated that most products will be disposed of in original containers, particularly those products that are purchased as aerosol cans.

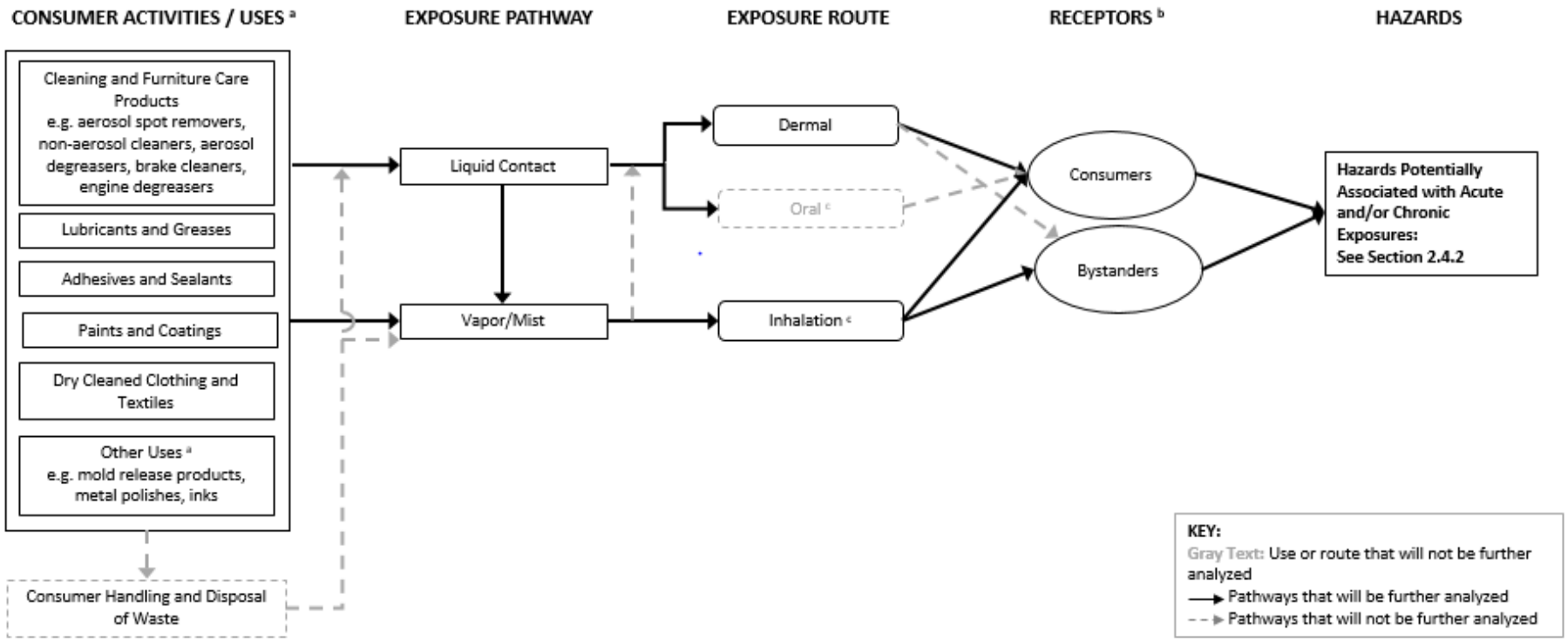


**Figure 2-3. Perchloroethylene Conceptual Model for Consumer Activities and Uses: Potential Exposures and Hazards**

The conceptual model presents the exposure pathways, exposure routes and hazards to human receptors from consumer activities and uses of perchloroethylene.

[a] Some products are used in both commercial and consumer applications. Additional uses of perchloroethylene are included in Table 2.3.

[b] Receptors include potentially exposed or susceptible subpopulations

[c] .Consumers may be exposed to perchloroethylene via transfer of chemical from hand to mouth. This exposure pathway will be limited by a combination of dermal absorption and volatilization; therefore, this pathway will not be further evaluated.

### 2.5.3 Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards

The revised conceptual model (Figure 2-4) illustrates the expected exposure pathways to human (i.e., general population) and ecological receptors (i.e., aquatic and terrestrial) from environmental releases and waste streams associated with industrial and commercial activities for perchloroethylene that EPA expects to include in the risk evaluation. The pathways that EPA expects to include and analyze further in the risk evaluation is described in Section 2.5.3.1 and shown in the conceptual model Figure 2-4. The pathways that EPA does not expect to include in the risk evaluation s are described in Section 2.5.3.2.

#### 2.5.3.1 Pathways That EPA Expects to Include and Further Analyze in the Risk Evaluation

EPA plans to analyze aquatic organisms exposed via contaminated surface water.

There are no national recommended water quality criteria for the protection of aquatic life for perchloroethylene and as a result EPA does not believe that perchloroethylene exposure to aquatic organisms in surface water has been adequately assessed or effectively managed under other EPA statutory authorities (see Section 2.5.3.2). EPA identified and reviewed national scale monitoring data to support this problem formulation. EPA and the USGS National Water Quality Assessment Program (Cycle 1, 1992-2001) reported perchloroethylene contamination in U.S. surface water and ground water in 19.6% of samples (n=5,911) and at 13.2% of sites (n=4,295), with detection in surface water occurring more frequently than in ground water (U.S. EPA, 2009). More recently measured, national-scale monitoring data was from EPA's STOrage and RETreival (STORET) and National Water Information System (NWIS). Based on STORET query for perchloroethylene for the past ten years, perchloroethylene is detected in surface water in the United States. The data showed a detection rate (above quantification limit and/or above reporting limit) of approximately 15% for surface water, with detections ranging from 0.02 µg/L to 26.7 µg/L. As summarized in Section 2.4.1 perchloroethylene showed hazard at concentrations as low as 14 µg/L for aquatic plants. The chronic COC value of 1 µg/L is not sufficiently below the range of monitored concentrations to eliminate risk concerns. Therefore, EPA plans to evaluate risks to aquatic organisms from exposures to perchloroethylene in surface waters.

#### 2.5.3.2 Pathways That EPA Does Not Expect to Include in the Risk Evaluation

Exposures to receptors may occur from industrial and/or commercial uses, industrial releases to air, water or land; and other conditions of use. As described in section 2.5, pathways under other environmental statutes, administered by EPA, which adequately assess and effectively manage exposures and for which long-standing regulatory and analytical processes already exist will not be included in the risk evaluation. These pathways are described below.

**Ambient Air Pathway**

The Clean Air Act (CAA) contains a list of hazardous air pollutants (HAP) and provides EPA with the authority to add to that list pollutants that present, or may present, a threat of adverse human health effects or adverse environmental effects. For stationary source categories emitting HAP, the CAA requires issuance of technology-based standards and, if necessary, additions or revisions to address developments in practices, processes, and control technologies, and to ensure the standards adequately protect public health and the environment. The CAA thereby provides EPA with comprehensive authority to regulate emissions to ambient air of any hazardous air pollutant.

Perchloroethylene is a HAP. EPA has issued a number of technology-based standards for source categories that emit perchloroethylene to ambient air and, as appropriate, has reviewed, or is in the process of reviewing remaining risks. Because stationary source releases of perchloroethylene to ambient air are adequately assessed and any risks effectively managed when under the jurisdiction of the CAA, EPA does not plan to evaluate emission pathways to ambient air from commercial and industrial stationary sources or associated inhalation exposure of the general population or terrestrial species in this TSCA evaluation.

**Drinking Water Pathway**

EPA has regular analytical processes to identify and evaluate drinking water contaminants of potential regulatory concern for public water systems under the Safe Drinking Water Act (SDWA). Under SDWA, EPA must also review and revise "as appropriate" existing drinking water regulations every 6 years.

EPA has promulgated National Primary Drinking Water Regulations (NPDWRs) for perchloroethylene under the Safe Drinking Water Act. EPA has set an enforceable Maximum Contaminant Level (MCL) as close as feasible to a health based, non-enforceable Maximum Contaminant Level Goal (MCLG). Feasibility refers to both the ability to treat water to meet the MCL and the ability to monitor water quality at the MCL, SDWA Section 1412(b)(4)(D), and public water systems are required to monitor for the regulated chemical based on a standardized monitoring schedule to ensure compliance with the (MCL).

Hence, because the drinking water exposure pathway for perchloroethylene is currently addressed in the SDWA regulatory analytical process for public water systems, EPA does not plan to include this pathway in the risk evaluation for perchloroethylene under TSCA. EPA's Office of Water and Office of Pollution Prevention and Toxics will continue to work together providing understanding and analysis of the SDWA regulatory analytical processes and to exchange information related to toxicity and occurrence data on chemicals undergoing risk evaluation under TSCA.

**Ambient Water Pathways**

EPA develops recommended water quality criteria under section 304(a) of the CWA for pollutants in surface water that are protective of aquatic life or human health designated uses. EPA develops and publishes water quality criteria based on priorities of states and others that reflect the latest scientific knowledge. A subset of these chemicals are identified as "priority pollutants" (103 human health and 27 aquatic life). The CWA requires states adopt numeric criteria for priority pollutants for which EPA has published recommended criteria under section 304(a), the discharge or presence of which in the affected waters could reasonably be expected to interfere with designated uses adopted the state. When states adopt criteria that EPA approves as part of state's regulatory water quality standards, exposure is considered when state permit writers determine if permit limits are needed and at what level for a specific discharger of a pollutant to ensure protection of the designated uses of the receiving water. Once states adopt criteria as water quality standards, the CWA requires National Pollutant Discharge Elimination System (NPDES) discharge permits include effluent limits as stringent as necessary to meet standards. CWA section 301(b)(1)(C). This is the process used under the CWA to address risk to human health and aquatic life from exposure to a pollutant in ambient waters.

EPA has identified perchloroethylene as a priority pollutant and EPA has developed recommended water quality criteria for protection of human health for perchloroethylene which are available for adoption into state water quality standards for the protection of human health and are available for use by NPDES permitting authorities in deriving effluent limits to meet state narrative criteria. As such,

EPA does not expect to include this pathway in the risk evaluation under TSCA. EPA's Office of Water and Office of Pollution Prevention and Toxics will continue to work together providing understanding and analysis of the CWA water quality criteria development process and to exchange information related to toxicity of chemicals undergoing risk evaluation under TSCA. EPA may update its CWA section 304(a) water quality criteria for perchloroethylene in the future under the CWA.

EPA has not developed CWA section 304(a) recommended water quality criteria for the protection of aquatic life for perchloroethylene, so there are no national recommended criteria for this use available for adoption into state water quality standards and available for use in NPDES permits. As a result, this pathway will undergo aquatic life risk evaluation under TSCA (see Section 2.4.1). EPA may publish CWA section 304(a) aquatic life criteria for perchloroethylene in the future if it is identified as a priority under the CWA.

**Biosolids Pathways**

CWA Section 405(d) requires EPA to 1) promulgate regulations that establish numeric criteria and management practices that are adequate to protect public health and the environment from any reasonably anticipated adverse effects of toxic pollutants during the use or disposal of sewage sludge, and 2) review such regulations at least every two years to identify additional toxic pollutants that occur in biosolids (i.e., "Biennial Reviews") and regulate those pollutants if sufficient scientific evidence shows they may be present in sewage sludge in concentrations which may adversely affect public health or the environment. EPA also periodically conducts surveys to determine what may be present in sewage sludge. EPA has conducted four sewage sludge surveys and identified compounds that occur in biosolids in seven Biennial Reviews. EPA has regulated 10 chemicals in biosolids under CWA 405(d).

EPA has identified perchloroethylene in biosolids biennial reviews. The purpose of such reviews is to identify additional toxic pollutants in biosolids. EPA can potentially regulate those pollutants under CWA 405(d), based on a subsequent assessment of risk. EPA's Office of Water is currently developing modeling tools in order to conduct risk assessments for chemicals in biosolids. Because the biosolids pathway for perchloroethylene is currently being addressed in the CWA regulatory analytical process, this pathway will not be further analyzed in the risk evaluation for perchloroethylene under TSCA. EPA's Office of Water and Office of Pollution Prevention and Toxics will continue to work together to discuss significant data gaps and exchange information related to exposure and toxicity of this chemical as OW conducts the risk assessment under the CWA.

**Disposal Pathways**

Perchloroethylene is included on the list of hazardous wastes pursuant to RCRA 3001 (40 CFR §§ 261.33) as a listed waste on the F, K and U lists. The general RCRA standard in Section RCRA 3004(a) for the technical criteria that govern the management (treatment, storage, and disposal) of hazardous waste are those "necessary to protect human health and the environment," RCRA 3004(a). The regulatory criteria for identifying "characteristic" hazardous wastes and for "listing" a waste as hazardous also relate solely to the potential risks to human health or the environment. 40 C.F.R. §§ 261.11, 261.21-261.24. RCRA statutory criteria for identifying hazardous wastes require EPA to "tak[e] into account toxicity, persistence, and degradability in nature, potential for accumulation in tissue, and other related factors such as flammability, corrosiveness, and other hazardous characteristics." Subtitle C control cover not only hazardous wastes that are landfilled, but also hazardous wastes that are incinerated (subject to joint control under RCRA Subtitle C and the Clean Air Act (CAA) hazardous waste combustion MACT) or injected into UIC Class I hazardous waste wells (subject to joint control under Subtitle C and the Safe Drinking Water Act (SDWA)).

EPA does not expect to include emissions to ambient air from municipal and industrial waste incineration and energy recovery units in the risk evaluation, as they are regulated under section 129 of the Clean Air Act. CAA section 129 also requires EPA to review and, if necessary, add provisions to ensure the standards adequately protect public health and the environment. Thus, combustion by-products from incineration treatment of perchloroethylene wastes (the majority of the 1.1 million lbs identified as treated in Tables 2-6 – 2-8) would be subject to these regulations, as would perchloroethylene burned for energy recovery (2.3 million lbs).

EPA does not expect to include on-site releases to land that go to underground injection in its risk evaluation. TRI reporting in 2016 indicated 272 pounds released to underground injection to a Class I well and no releases to underground injection wells of Classes II-VI. Environmental disposal of perchloroethylene injected into Class I well types managed and prevented from further environmental release by RCRA and SDWA regulations. Therefore, disposal of perchloroethylene via underground injection is not likely to result in environmental and general population exposures.

EPA does not expect to include on-site releases to land from RCRA Subtitle C hazardous waste landfills or exposures of the general population (including susceptible populations) or terrestrial species from such releases in the TSCA evaluation. Based on 2015 reporting to TRI, the majority of the land disposals occur in Subtitle C landfills (78,120 lbs). Design standards for Subtitle C landfills require double liner, double leachate collection and removal systems, leak detection system, run on, runoff, and wind dispersal controls, and a construction quality assurance program. They are also subject to closure and post-closure care requirements including installing and maintaining a final cover, continuing operation of the leachate collection and removal system until leachate is no longer detected, maintaining and monitoring the leak detection and groundwater monitoring system. Bulk liquids may not be disposed in Subtitle C landfills. Subtitle C landfill operators are required to implement an analysis and testing program to ensure adequate knowledge of waste being managed, and to train personnel on routine and emergency operations at the facility. Hazardous waste being disposed in Subtitle C landfills must also meet RCRA waste treatment standards before disposal. Given these controls, general population exposure to perchloroethylene in groundwater from Subtitle C landfill leachate is not expected to be a significant pathway.

EPA does not expect to include on-site releases to land from RCRA Subtitle D municipal solid waste landfills or exposures of the general population (including susceptible populations) or terrestrial species from such releases in the TSCA evaluation. While permitted and managed by the individual states, municipal solid waste (MSW) landfills are required by federal regulations to implement some of the same requirements as Subtitle C landfills. MSW landfills generally must have a liner system with leachate collection and conduct groundwater monitoring and corrective action when releases are detected. MSW landfills are also subject to closure and post-closure care requirements, and must have financial assurance for funding of any needed corrective actions. MSW landfills have also been designed to allow for the small amounts of hazardous waste generated by households and very small quantity waste generators (less than 220 lbs per month). Bulk liquids may not be disposed in Subtitle C landfills.

EPA does not expect to include on-site releases to land from industrial non-hazardous waste and construction/demolition waste landfills in the perchloroethylene risk evaluation. Industrial non-hazardous and construction/demolition waste landfills are primarily regulated under state regulatory programs. States must also implement limited federal regulatory requirements for siting, groundwater monitoring and corrective action and a prohibition on open dumping and disposal of bulk liquids. States

may also establish additional requirements such as for liners, post-closure and financial assurance, but are not required to do so. Therefore, EPA does not expect to include this pathway in the risk evaluation.

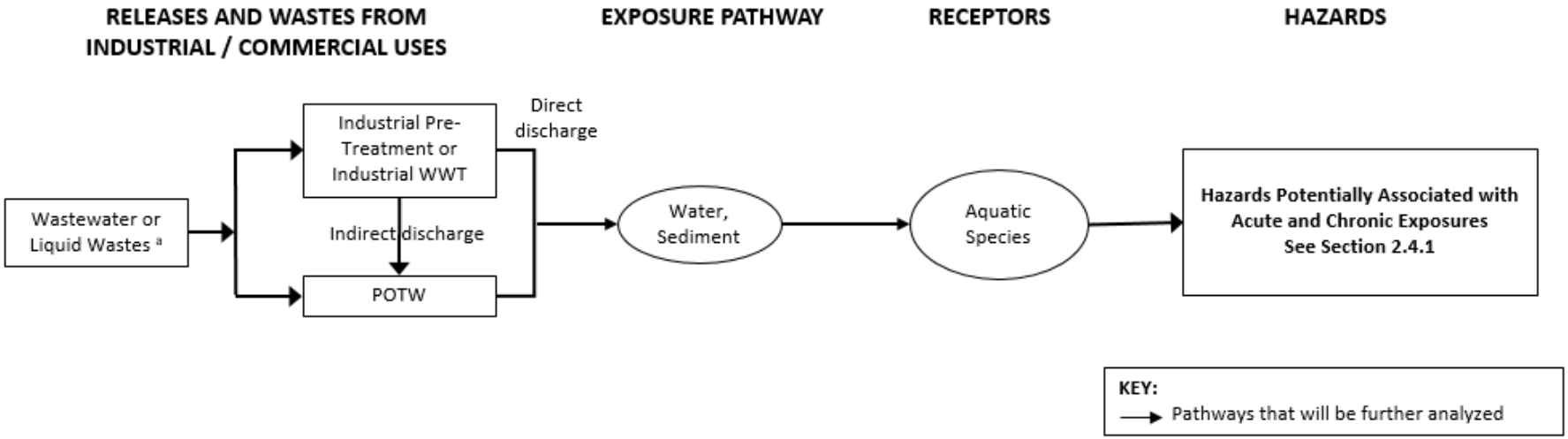


**Figure 2-4. Perchloroethylene Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards**
The conceptual model presents the exposure pathways, exposure routes and hazards to human and environmental receptors from environmental releases and wastes of perchloroethylene that will be analyzed.

[a] Industrial wastewater or liquid wastes may be treated on-site and then released to surface water (direct discharge) or pre-treated and released to POTW (indirect discharge).

## 2.6 Analysis Plan

The analysis plan presented in the problem formulation elaborates on the initial analysis plan that was published in the *Scope of the Risk Evaluation for Perchloroethylene (*U.S. EPA, 2017c*)*.

The analysis plan outlined here is based on the conditions of use for perchloroethylene, as described in Section 2.2 of this problem formulation. EPA is implementing systematic review approaches to identify, select, assess, integrate and summarize the findings of studies supporting the TSCA risk evaluation. The analytical approaches and considerations in the analysis plan are used to frame the scope of the systematic review activities for this assessment. The supplemental document, *Application of Systematic Review in TSCA Risk Evaluations,* provides additional information about criteria and methods that have been and will be applied to the first 10 chemical risk evaluations.

While EPA has conducted a comprehensive search for reasonably available data, as described in the Scope of the Risk Evaluation for Perchloroethylene (U.S. EPA, 2017c), EPA encourages submission of additional existing data, such as full study reports or workplace monitoring from industry sources, that may be relevant for refining conditions of use, exposures, hazards and potentially exposed or susceptible subpopulations during risk evaluation. EPA will continue to consider new information submitted by the public.

During risk evaluation, EPA will rely on the comprehensive literature results [*Perchloroethylene (CASRN 127-18-4) Bibliography: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0732)] or supplemental literature searches to address specific questions. Further, EPA may consider any relevant confidential business information (CBI) in the risk evaluation in a manner that protects the confidentiality of the information from public disclosure. The analysis plan is based on EPA's knowledge of perchloroethylene to date, which includes partial, but not complete review of identified literature. If additional data or approaches become available, EPA may refine its analysis plan based on this information.

### 2.6.1 Exposure

Based on their physical-chemical properties, expected sources, and transport and transformation within the outdoor and indoor environment chemical substances are more likely to be present in some media and less likely to be present in others. Media-specific levels will vary based on the chemical substance of interest. For most chemical substances level(s) can be characterized through a combination of available monitoring data and modeling approaches.

#### 2.6.1.1 Environmental Releases

EPA expects to consider and analyze releases to relevant environmental media as follows:

1) Review reasonably available published literature or information on processes and activities associated with the conditions of use to evaluate the types of releases and wastes generated. EPA has reviewed some key data sources containing information on processes and activities resulting in releases, and the information found is shown in Appendix B-1. EPA will continue to review potentially relevant data sources identified in Table Apx B-3.1 in Appendix B during risk evaluation.

   EPA plans to review the following key data sources in Table 2-10 for additional information on activities resulting in environmental releases. The evaluation strategy for engineering and

occupational data sources discussed in the *Application of Systematic Review in TSCA Risk Evaluations* describes how data, information, and studies will be reviewed.

**Table 2-10. Potential Sources of Environmental Release Data**

| |
|---|
| U.S. EPA TRI Data (Reporting Year 2016 only) |
| U.S. EPA Generic Scenarios |
| OECD Emission Scenario Documents |
| EU Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) Specific Environmental Release Categories (SpERC) factsheets |
| Discharge Monitoring Report (DMR) surface water discharge data for perchloroethylene from NPDES-permitted facilities |

2) Review reasonably available chemical-specific release data, including measured or estimated release data (e.g., data collected under the TRI program). EPA has reviewed key release data sources including the Toxics Release Inventory (TRI), and the data from this source is summarized in Section 2.3.2 above and also in Appendix B. EPA will continue to review relevant data sources as identified in Table Apx B-3.2 in Appendix B during risk evaluation. EPA will match identified data to applicable conditions of use and identify data gaps where no data are found for particular conditions of use. EPA will attempt to address data gaps identified as described in steps 3 and 4 below by considering potential surrogate data and models.

3) Review reasonably available measured or estimated release data for surrogate chemicals that have similar uses and chemical and physical properties. Data for solvents that are used in the same types of applications may be considered as surrogate data for perchloroethylene. As with perchloroethylene, trichloroethylene is used in paints and coatings, in adhesives and sealants, and as solvents for cleaning and degreasing. EPA will evaluate the use of data for solvents such as trichloroethylene as surrogates to fill data gaps where uses of perchloroethylene and other solvents align. If surrogate data are used, EPA normally converts air concentrations using the ratio of the vapor pressures of the two chemicals. EPA will review literature sources identified and if surrogate data are found, EPA will match these data to applicable conditions of use for potentially filling data gaps.

4) Understand and consider regulatory limits that may inform estimation of environmental releases. EPA has identified information from various EPA statutes (including, for example, regulatory limits, reporting thresholds or disposal requirements) that may be relevant to release estimation. Some of the information has informed revision of the conceptual models during problem formulation. EPA will further consider relevant regulatory requirements in estimating releases during risk evaluation.

5) Review and determine applicability of OECD Emission Scenario Documents (ESDs) and EPA Generic Scenarios to estimation of environmental releases. Potentially relevant OECD Emission Scenario Documents (ESDs) and EPA Generic Scenarios (GS) have been identified that correspond to some conditions of use. For example, the ESD on Industrial Use of Adhesives for Substrate Bonding, the ESD on the Coating Industry (Paints, Lacquers and Varnishes), and the GS on the Use of Vapor Degreasers are some of the ESDs and GSs that EPA may use to assess potential releases. EPA will need to critically review these generic scenarios and ESDs to determine their applicability to the conditions of use assessed. EPA was not able to identify ESDs or GSs corresponding to several conditions of use, including use of perchloroethylene as

an intermediate, recycling of perchloroethylene, use of perchloroethylene as an industrial processing aid, and use of perchloroethylene in commercial carpet cleaning. EPA will perform additional targeted research to understand those conditions of use which may inform identification of release scenarios. EPA may also need to perform targeted research for applicable models and associated parameters that EPA may use to estimate releases for certain conditions of use. If ESDs and GSs are not available, other methods may be considered. Additionally, for conditions of use where no measured data on releases are available, EPA may use a variety of methods including the application of default assumptions such as standard loss fractions associated with drum cleaning (3%) or single process vessel cleanout (1%).

6) Map or group each condition(s) of use to a release assessment scenario. EPA has identified release scenarios and mapped them to some conditions of use. For example, some scenario groupings include Contractor Adhesive Removal and Industrial In-line Vapor Degreasing. EPA grouped similar conditions of use (based on factors including process equipment and handling, release sources and usage rates of perchloroethylene and formulations containing perchloroethylene, or professional judgment) into scenario groupings but may further refine these groupings as additional information becomes available during risk evaluation.
   EPA was not able to identify release scenarios corresponding to several conditions of use due to a lack of general knowledge of those conditions of use. EPA will perform additional targeted research to understand those uses which may inform identification of release scenarios.
7) Complete the weight of the evidence of environmental release data.
   EPA will rely on the weight of the scientific evidence when evaluating and integrating environmental release data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

#### 2.6.1.2 Environmental Fate

EPA expects to consider and analyze fate and transport in environmental media as follows:

1) Review reasonably available measured or estimated environmental fate endpoint data collected through the literature search.

   Key environmental fate characteristics were included in assessments conducted by the EPA Integrated Risk Information System (U.S. EPA, 2012d), EPA Office of Water (U.S. EPA, 2015b), US Agency for Toxic Substances and Disease Registry (ATSDR, 2014) and European Chemicals Bureau (ECB, 2005b). These information sources will be used as a starting point for the environmental fate assessment. Other sources that will be consulted include those that are identified through the systematic review process. Studies will be evaluated using the evaluation strategies laid out in *Application of Systematic Review in TSCA Risk Evaluations*.

   If measured values resulting from sufficiently high-quality studies are not available (to be determined through the systematic review process), chemical properties will be estimated using

EPI Suite, SPARC, and other chemical parameter estimation models. Estimated fate properties will be reviewed for applicability and quality.

2) Using measured environmental fate data and/or environmental fate modeling, determine the influence of environmental fate endpoints (e.g., persistence, bioaccumulation, partitioning, transport) on exposure pathways and routes of exposure to environmental receptors.

   Measured fate data including volatilization from water, sorption to organic matter in soil and sediments, aqueous and atmospheric photolysis rates, and aerobic and anaerobic biodegradation rates, along with physical-chemical properties and models such as the EPI Suite™ STP model (which estimates removal in wastewater treatment due to adsorption to sludge and volatilization to air) and volatility model (which estimates half-life from volatilization from a model river and model lake), will be used to characterize the movement of perchloroethylene within and among environmental media and the persistence of perchloroethylene in media.

3) Evaluate the weight of the evidence of environmental fate data.
   EPA will rely on the weight of the scientific evidence when evaluating and integrating environmental fate data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

#### 2.6.1.3 Environmental Exposures

EPA expects to consider the following in developing its environmental exposure assessment of perchloroethylene:

1) Refine and finalize exposure scenarios for environmental receptors by considering unique combinations of sources (use descriptors), exposure pathways, exposure settings, populations exposed, and exposure routes. For perchloroethylene, exposure scenarios for environmental receptors include exposures from surface water.

2) Review reasonably available environmental and biological monitoring data for environmental exposure to surface water. EPA will rely on databases (see examples below) and literature obtained during systematic review to include ranges and trends of chemical in surface water, including any trends seen in concentrations and spatial trends.
   - STORET and NWIS (USGS/EPS): https://www.epa.gov/waterdata/storage-and-retrieval-and-water-quality-exchange#portal
   - OPPT monitoring database

3) Review reasonably available information on releases to determine how modeled estimates of concentrations near industrial point sources compare with available monitoring data. Available exposure models that estimate surface water (e.g. E-FAST) will be evaluated and considered alongside available surface water data to characterize environmental exposures. Modeling approaches to estimate surface water concentrations generally consider the following inputs: direct release into surface water and transport (partitioning within media) and characteristics of the environment (river flow, volume of pond, meteorological data).

4) Determine applicability of existing additional contextualizing information for any monitored data or modeled estimates during risk evaluation. For example, site/location, time period, and conditions under which monitored data were collected will be evaluated to determine relevance and applicability to wider scenario development. Any studies which relate levels of perchloroethylene in the environment or biota with specific sources or groups of sources will be evaluated.

5) Evaluate the weight of evidence of environmental occurrence data and modeled estimates. EPA will rely on the weight of the scientific evidence when evaluating and integrating environmental exposure data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence. Refer to the supplemental document, Application of Systematic Review in TSCA Risk Evaluations, for more information on the general process for data integration.

#### 2.6.1.4 Occupational Exposures

EPA expects to consider and analyze both worker and occupational non-user exposures as follows:

1) Review reasonably available exposure monitoring data for specific condition(s) of use. EPA expects to review exposure data including workplace monitoring data collected by government agencies such as the Occupational Safety and Health Administration (OSHA) and the National Institute of Occupational Safety and Health (NIOSH), and monitoring data found in published literature. These workplace monitoring data include personal exposure monitoring data (direct exposures) and area monitoring data (indirect exposures).

   EPA has reviewed available monitoring data collected by OSHA and NIOSH and will match these data to applicable conditions of use. EPA has also identified additional data sources that may contain relevant monitoring data for the various conditions of use. EPA will review these sources (identified in Table 2-11 and in Table Apx-B-3.3) and extract relevant data for consideration and analysis during risk evaluation.

   OSHA has established a permissible exposure limit (PEL) of 100 ppm 8-hour time-weighted average (TWA). The American Conference of Government Industrial Hygienists (ACGIH) has established a Threshold Limit Value (TLV) of 25 ppm 8-hour TWA. Also, NIOSH has established an immediately dangerous to life or health (IDLH) value of 150 ppm. EPA will consider the influence of these regulatory limits and recommended exposure guidelines on occupational exposures in the occupational exposure assessment.

   Table 2-11. Potential Sources of Occupational Exposure Data

| |
|---|
| 2014 Draft ATSDR Toxicological Profile for Perchloroethylene |
| U.S. OSHA Chemical Exposure Health Data (CEHD) program data |
| U.S. NIOSH Health Hazard Evaluation (HHE) Program reports |
| 1985 EPA Occupational Exposure and Release Assessment for Tetrachloroethylene |

2) Review reasonably available exposure data for surrogate chemicals that have uses, volatility and chemical and physical properties similar to perchloroethylene. EPA will review literature sources identified and if surrogate data are found, these data will be matched to applicable conditions of use for potentially filling data gaps. For several conditions of use (e.g., vapor degreasing, cold cleaning, coating applications, adhesive applications), EPA believes trichloroethylene and other

similar solvents that share the same conditions of use may serve as surrogate for perchloroethylene.

3) For conditions of use where data is limited or not available, review existing exposure models that may be applicable in estimating exposure levels. EPA has identified potentially relevant OECD ESDs and EPA GS corresponding to some conditions of use. For example, the ESD on Industrial Use of Adhesives for Substrate Bonding, the ESD on Metalworking Fluids, and the GS for Textile Finishing are some of the ESDs and GS's that EPA may use to estimate occupational exposures. EPA will need to critically review these generic scenarios and ESDs to determine their applicability to the conditions of use assessed. EPA was not able to identify ESDs or GS's corresponding to several conditions of use, including use of perchloroethylene as an intermediate, recycling of perchloroethylene, use as an industrial processing aid, and commercial carpet cleaning. EPA will perform additional targeted research to understand those conditions of use, which may inform identification of exposure scenarios. EPA may also need to perform targeted research to identify applicable models that EPA may use to estimate exposures for certain conditions of use.

   EPA was not able to identify release scenarios corresponding to several conditions of use. EPA may conduct industry outreach efforts or perform supplemental, targeted literature searches to better understand the process steps involved in that condition of use before occupational exposure assessment can be made. EPA will perform additional targeted research to understand those conditions of use, which may inform identification of exposure scenarios. EPA will consider exposure models in the Chemical Screening Tool For Exposure and Environmental Releases (ChemSTEER) Tool that are routinely used for assessing new chemicals. EPA may also need to perform targeted research to identify other applicable models that EPA could use to estimate exposures for certain conditions of use.

4) Review reasonably available data that may be used in developing, adapting or applying exposure models to the particular risk evaluation. This step will be performed after Steps #2 and #3 above. Based on information developed from Step #2 and Step #3, EPA will evaluate relevant data to determine whether the data can be used to develop, adapt, or apply models for specific conditions of use (and corresponding exposure scenarios). EPA may utilize existing, peer-reviewed exposure models developed by EPA/OPPT, other government agencies, or available in the scientific literature, or EPA may elect to develop additional models to assess specific condition(s) of use. Inhalation exposure models may be simple box models or two-zone (near-field/far-field) models. In two-zone models, the near-field exposure represents potential inhalation exposures to workers, and the far-field exposure represents potential inhalation exposures to occupational non-users.

   As part of the 2014 risk assessment (RA) and subsequent Section 6 rulemaking for TCE and the 2016 draft RA for 1-BP, EPA developed models to assess inhalation exposures to workers and occupational non-users during the use of these chemicals in dry cleaning, spot cleaning, vapor degreasing, cold cleaning, and aerosol degreasing. During risk evaluation, EPA will evaluate the applicability of these models to perchloroethylene, and adapt and refine these models as necessary for evaluating exposure to perchloroethylene in these scenarios.

   EPA will consider the effect of evaporation when evaluating options for dermal exposure assessment. In addition, EPA will consider the impact of occluded exposure or repeated dermal

contacts. EPA anticipates that existing EPA/OPPT dermal exposure models would not be suitable for quantifying dermal exposure to semi-volatile chemicals such as perchloroethylene.

5) Consider and incorporate applicable engineering controls and/or personal protective equipment into exposure scenarios. EPA will review potentially relevant data sources on engineering controls and personal protective equipment as identified in Table_Apx B-3.4 in the Appendix and to determine their applicability and incorporation into exposure scenarios during risk evaluation. EPA will assess worker exposure pre- and post-implementation of engineering controls, using available information on available control technologies and control effectiveness. For example, EPA may assess worker exposure in industrial use scenarios before and after implementation of local exhaust ventilation.

6) Map or group each condition of use to occupational exposure assessment scenario(s). EPA has identified exposure scenarios and mapped them to some (or most) conditions of use. EPA was not able to identify occupational exposure scenarios corresponding to several conditions of use due generally to a lack of understanding of those conditions of use (e.g., use of perchloroethylene metal and stone polishes). EPA will perform targeted research to understand those uses which may inform identification of occupational exposure scenarios. EPA grouped similar conditions of use (based on factors including process equipment and handling, usage rates of perchloroethylene and formulations containing perchloroethylene, exposure/release sources) into scenario groupings but may further refine these groupings as additional information is identified during risk evaluation.

7) Evaluate the weight of the evidence of occupational exposure data. EPA will rely on the weight of the scientific evidence when evaluating and integrating occupational data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence. Refer to the *Application of Systematic Review in TSCA Risk Evaluations* document for more information on the general process for data integration.

#### 2.6.1.5 Consumer Exposures

EPA expects to consider and analyze both consumers using a consumer product and bystanders associated with the consumer using the product as follows:

1) Refine and finalize exposure scenarios for consumers by mapping sources of exposure (i.e., consumer products), exposure pathways, exposure settings, exposure routes, and populations exposed. Considerations for constructing exposure scenarios for consumers:
    - Reasonably available data on consumer products or products available for consumer use including the weight fraction of perchloroethylene in products;
    - Information characterizing the use patterns of consumer products containing perchloroethylene including the following: intended or likely consumer activity, method of application (e.g., spray-applied, brush-applied, dip), formulation type, amount of product used, frequency and duration of individual use events, and room or setting of use;
    - The associated route of exposure for consumers; and
    - Populations who may be exposed to products as users or bystanders in the home, including potentially exposed and susceptible subpopulations such as children or women

of child bearing age and subsets of consumers who may use commercially-available products or those who may use products more frequently than typical consumers.

During consumer exposure modeling, these factors determine the resulting exposure route and magnitude. For example, while the product with the highest weight fraction in a given consumer product scenario could be run early on to indicate preliminary levels of exposure, that product may not actually result in the highest potential exposure due to having a lower frequency of use.

2) Evaluate the potential and magnitude of exposure routes based on available data. perchloroethylene, inhalation of vapor is expected to result in higher exposure to consumers and bystanders in the home compared to dermal absorption through direct contact due to fate and exposure properties. The data sources associated with these respective pathways have not been comprehensively evaluated, therefore quantitative comparisons across exposure pathways or in relation to toxicity thresholds are not yet possible.

3) Review and use existing indoor exposure models that may be applicable in estimating inhalation and dermal exposure. For example, the Consumer Exposure Model (CEM version 2.0) and the Multi-Chamber Concentration and Exposure Model (MCCEM) to estimate and evaluate indoor exposures to perchloroethylene in consumer and commercial products.

4) Review reasonably available empirical data that may be used in developing, adapting or applying exposure models to the particular risk evaluation. For example, existing models developed for a chemical assessment may be applicable to another chemical assessment if model parameter data are available.

5) Review reasonably available consumer product-specific sources to determine how those exposure estimates compare with each other and with indoor air and product use monitoring data for perchloroethylene.

6) Review reasonably available population- or subpopulation-specific exposure factors and activity patterns to determine if potentially exposed or susceptible subpopulations need be further refined. Based on hazard concerns, certain subpopulations such as pregnant women may be included for any consumer use scenarios, as a user or bystander. For a small subset of uses (e.g. craft glues and adhesives) children may be users of perchloroethylene containing products. For other uses of perchloroethylene containing products children and/or infants would generally not considered “users”, but may be assessed as bystanders of consumer uses in the home. Other subpopulations may be subject to greater exposure, such as DIY users or those in the business of arts and crafts. Considerations will include:
    - Age-specific differences (exposure factors and activity patterns) for populations defined in the exposure scenarios. Exposure factors and activities patterns will be sourced from EPA’s 2011 Exposure Factors Handbook.
    - Characteristics of the user of the consumer product and the bystander in the room, including for example, women of child bearing age and children.
    - Subpopulations that may have greater exposure due to magnitude, frequency or duration of exposure.

7) Evaluate the weight of evidence of consumer exposure estimates based on different approaches. EPA will rely on the weight of the scientific evidence when evaluating and integrating consumer exposure data. The data integration strategy will be designed to be fit-for-purpose in which EPA

will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence. Refer to the supplemental document, *Application of Systematic Review in TSCA Risk Evaluations* for more information on the general process for data evaluation. Map or group each condition of use to consumer exposure assessment scenario(s). Refine and finalize exposure scenarios for consumers by mapping sources of exposure (i.e., consumer products), exposure pathways, exposure settings, exposure routes, and populations exposed. Considerations for constructing exposure scenarios for consumers:

#### 2.6.1.6 General Population

EPA does not expect to consider and analyze general population exposures in the risk evaluation for perchloroethylene EPA has determined that the existing regulatory programs and associated analytical processes have addressed or are in the process of addressing potential risks of perchloroethylene that may be present in various media pathways (e.g., air, water, land) for the general population. For these cases, EPA believes that the TSCA risk evaluation should focus not on those exposure pathways, but rather on exposure pathways associated with TSCA uses that are not subject to those regulatory processes.

### 2.6.2 Hazards (Effects)

#### 2.6.2.1 Environmental Hazards

EPA will conduct an environmental hazard assessment of perchloroethylene as follows:

1) Review reasonably available environmental hazard data, including data from alternative test methods (e.g., computational toxicology and bioinformatics; high-throughput screening methods; data on categories and read-across; in vitro studies).

   Environmental hazard data will be evaluated using the ecological toxicity data quality criteria outlined in the Application of Systematic Review in TSCA Risk Evaluations document. The study evaluation results will be documented in the risk evaluation phase and data from suitable studies will be extracted and integrated in the risk evaluation process.

   Conduct hazard identification (the qualitative process of identifying acute and chronic endpoints) and concentration-response assessment (the quantitative relationship between hazard and exposure) for all identified environmental hazard endpoints. Suitable environmental hazard data will be reviewed for acute and chronic endpoints for mortality and other effects (e.g. growth, immobility, reproduction, etc.). EPA will evaluate the character of the concentration-response relationship (i.e. positive, negative or no response) as part of the review.
   Sufficient environmental hazard studies are available to assess the hazards of environmental concentrations of perchloroethylene to aquatic species.

2) Derive aquatic concentrations of concern (COC) for acute and, where possible, chronic endpoints. The aquatic environmental hazard studies may be used to derive acute and chronic concentrations of concern (COC) for mortality, behavioral, developmental and reproductive or other endpoints determined to be detrimental to environmental populations. Depending on the robustness of the evaluated data for a particular organism (e.g. aquatic invertebrates), environmental hazard values (e.g. ECx/LCx/NOEC/LOEC, etc.) may be derived and used to further understand the hazard characteristics of perchloroethylene to aquatic species.

3) Evaluate the weight of the evidence of environmental hazard data. EPA will rely on the weight of the scientific evidence when evaluating and integrating environmental hazard data. The data integration strategy will be designed to be fit-for-purpose. EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence. Refer to the supplemental document, Application of Systematic Review in TSCA Risk Evaluations, for more information on the general process for data integration.

4) Consider the route(s) of exposure, available biomonitoring data and available approaches to integrate exposure and hazard assessments. EPA believes there is sufficient information to evaluate the potential risks to aquatic organisms from exposures to perchloroethylene in ground water and surface water.

#### 2.6.2.2 Human Health Hazards

EPA expects to consider and analyze human health hazards as follows:

1) Review reasonably available human health hazard data, including data from alternative test methods as needed (e.g., computational toxicology and bioinformatics; high-throughput screening methods; data on categories and read-across; *in vitro* studies; systems biology).

   For the perchloroethylene risk evaluation, EPA will evaluate information in the IRIS assessment and human health studies using OPPT's structured process described in the document, *Application of Systematic Review in TSCA Risk Evaluations*. Human and animal data will be identified and included as described in the inclusion and exclusion criteria in Appendix F. EPA expects to prioritize the evaluation of mechanistic evidence. Specifically, EPA does not plan to evaluate mechanistic studies unless needed to clarify questions about associations between perchloroethylene and health effects and its relevance to humans. The *Applications of Systematic Review* document describes the process of how studies will be evaluated using specific data evaluation criteria and a predetermined approach. Study results will be extracted and presented in evidence tables by hazard endpoint. EPA expects to evaluate relevant studies identified in the Integrated Risk Information System (IRIS) *Toxicological Review of Tetrachloroethylene* (U.S. EPA, 2012e). In addition, EPA intends to review studies published after the acute reference values were published (e.g. AEGLs) from January 1, 2010 to March 2, 2017 that were captured in the comprehensive literature search conducted by the Agency for perchloroethylene (see *Perchloroethylene (CASRN 127-18-4) Bibliography: Supplemental File for the TSCA Scope Document*) using the approaches described in *Application of Systematic Review in TSCA Risk Evaluations*. To more fully understand circumstances related to deaths by individuals using perchloroethylene, EPA/OPPT will review case reports, case series and ecological studies related to deaths and effects that may imminently lead to death (respiratory distress). EPA/OPPT will not be evaluating case reports and series or ecological studies for endpoints that appear to be less severe endpoints (e.g., nausea).

2) In evaluating reasonably available data, determine whether particular human receptor groups may have greater susceptibility to the chemical's hazard(s) than the general population. Reasonably available human health hazard data will be evaluated to ascertain whether some human receptor groups may have greater susceptibility than the general population to perchloroethylene hazard(s).

3) Conduct hazard identification (the qualitative process of identifying non-cancer and cancer endpoints) and dose-response assessment (the quantitative relationship between hazard and exposure) for all identified human health hazard endpoints.

   Human health hazards from acute and chronic exposures will be identified by evaluating the human and animal data that meet the data quality criteria described in *Application of Systematic Review in TSCA Risk Evaluations*. Data quality evaluation will be performed on relevant studies identified in the IRIS assessment (U.S. EPA, 2012e), and assessments of the effects of acute exposures in the (NAC/AEGL). Data quality evaluation will also be performed on studies that were identified in the comprehensive literature search and that met the inclusion criteria for full-text screening (see *Application of Systematic Review in TSCA Risk Evaluations*. Hazards identified by studies meeting data quality criteria will be grouped by routes of exposure relevant to humans (oral, inhalation) and by cancer and noncancer endpoints.

   Dose-response assessment will be performed in accordance with EPA guidance (U.S. EPA, 2012a, 2011, 1994). Dose-response analyses performed to support the IRIS oral and inhalation reference dose determinations and for the cancer unit risk and slope factor (U.S. EPA, 2012e) may be used if the data meet data quality criteria and if additional information on the identified hazard endpoints or additional hazard endpoints would not alter the analysis.

4) Derive points of departure (PODs) where appropriate; conduct benchmark dose modeling depending on the available data. Adjust the PODs as appropriate to conform (e.g., adjust for duration of exposure) to the specific exposure scenarios evaluated.

   Hazard data will be evaluated to determine the type of dose-response modeling that is applicable, if the dose-response modeling requires updating. Where modeling is feasible, a set of dose-response models that are consistent with a variety of potentially underlying biological processes will be applied to empirically model the dose-response relationships in the range of the observed data consistent with the EPA *Benchmark Dose Technical Guidance Document*. Where dose-response modeling is not feasible, NOAELs or LOAELs will be identified.

   EPA will evaluate whether the available PBPK and empirical kinetic models are adequate for route-to-route and interspecies extrapolation of the POD, or for extrapolation of the POD to appropriate exposure durations for the risk evaluation.

5) Consider the route(s) of exposure (oral, inhalation, dermal), available route-to-route extrapolation approaches, available biomonitoring data and available approaches to correlate internal and external exposures to integrate exposure and hazard assessment.

   EPA believes there are sufficient data to conduct dose-response analysis with benchmark dose modeling or NOAELs or LOAELs for both inhalation and oral routes of exposure.

   A route-to-route extrapolation from the inhalation and oral toxicity studies is needed to assess systemic risks from dermal exposures. Without an adequate PBPK model, the approaches described in the EPA guidance document *Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part E, Supplemental Guidance for Dermal Risk Assessment)* could be applied. These approaches may be able to further inform the relative importance of dermal exposures compared with other routes of exposure.

6) Evaluate the weight of the evidence of human health hazard data. EPA will rely on the weight of the scientific evidence when evaluating and integrating human health hazard data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence. Refer to the S*ystematic Review Approaches and Methods Applied to TSCA Risk Evaluations* document for more information on the general process for data evaluation.

### 2.6.3 Risk Characterization

Risk characterization is an integral component of the risk assessment process for both ecological and human health risks. EPA will derive the risk characterization in accordance with EPA's *Risk Characterization Handbook* (U.S. EPA, 2000a). As defined in EPA's *Risk Characterization Policy*, "the risk characterization integrates information from the preceding components of the risk evaluation and synthesizes an overall conclusion about risk that is complete, informative and useful for decision makers." Risk characterization is considered to be a conscious and deliberate process to bring all important considerations about risk, not only the likelihood of the risk, but also the strengths and limitations of the assessment, and a description of how others have assessed the risk into an integrated picture.

Risk characterization at EPA assumes different levels of complexity depending on the nature of the risk assessment being characterized. The level of information contained in each risk characterization varies according to the type of assessment for which the characterization is written. Regardless of the level of complexity or information, the risk characterization for TSCA risk evaluations will be prepared in a manner that is transparent, clear, consistent, and reasonable (TCCR) (U.S. EPA, 2000a). EPA will also present information in this section consistent with approaches described in the Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act Risk Evaluation Framework Rule (82 FR 33726). For instance, in the risk characterization summary, EPA will further carry out the obligations under TSCA section 26; for example, by identifying and assessing uncertainty and variability in each step of the risk evaluation, discussing considerations of data quality such as the reliability, relevance and whether the methods utilized were reasonable and consistent, explaining any assumptions used, and discussing information generated from independent peer review. EPA will also be guided by EPA's Information Quality Guidelines (U.S. EPA, 2002) as it provides guidance for presenting risk information. Consistent with those guidelines, in the risk characterization, EPA will also identify: (1) Each population addressed by an estimate of applicable risk effects; (2) the expected risk or central estimate of risk for the potentially exposed or susceptible subpopulations affected; (3) each appropriate upper-bound or lower bound estimate of risk; (4) each significant uncertainty identified in the process of the assessment of risk effects and the studies that would assist in resolving the uncertainty; and (5) peer reviewed studies known to the Agency that support, are directly relevant to, or fail to support any estimate of risk effects and the methodology used to reconcile inconsistencies in the scientific information.

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# APPENDICES

# Appendix A REGULATORY HISTORY

## A.1 Federal Laws and Regulations

**Table_Apx A-1. Federal Laws and Regulations**

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| **EPA Regulations** | | |
| Toxics Substances Control Act (TSCA) – Section 6(b) | EPA is directed to identify and begin risk evaluations on 10 chemical substances drawn from the 2014 update of the TSCA Work Plan for Chemical Assessments. | Perchloroethylene is on the initial list of chemicals to be evaluated for unreasonable risk under TSCA (81 FR 91927, December 19, 2016). |
| Toxics Substances Control Act (TSCA) – Section 8(a) | The TSCA Section 8(a) Chemical Data Reporting (CDR) Rule requires manufacturers (including importers) to give EPA basic exposure-related information on the types, quantities and uses of chemical substances produced domestically and imported into the United States. | Perchloroethylene manufacturing (including importing), processing, and use information is reported under the Chemical Data Reporting (CDR) rule (76 FR 50816, August 16, 2011). |
| Toxics Substances Control Act (TSCA) – Section 8(b) | EPA must compile, keep current, and publish a list (the TSCA Inventory) of each chemical substance manufactured, processed or imported in the United States. | Perchloroethylene was on the initial TSCA Inventory and therefore was not subject to EPA's new chemicals review process (76 FR 50816, August 16, 2011). |
| Toxics Substances Control Act (TSCA) – Section 8(e) | Manufacturers (including imports), processors, and distributors must immediately notify EPA if they obtain information that supports the conclusion that a chemical substance or mixture presents a substantial risk of injury to health or the environment. | Eleven risk reports received for perchloroethylene (1978-2010) (US EPA, ChemView. Accessed April 13, 2017). |
| Toxics Substances Control Act (TSCA) – Section 4 | Provides EPA with authority to issue rules and orders requiring manufacturers (including importers) and processors to test chemical substances and mixtures. | Nine chemical data submissions from test rules received for perchloroethylene (1978-1980) (US EPA, ChemView. Accessed April 13, 2017). |
| Emergency Planning and Community Right-to-Know Act (EPCRA) – Section 313 | Requires annual reporting from facilities in specific industry sectors that employ 10 or more full time equivalent employees and that manufacture, process or otherwise use a | Perchloroethylene is a listed substance subject to reporting requirements under 40 CFR 372.65 effective as of January 1, 1987. |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | TRI-listed chemical in quantities above threshold levels. | |
| Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) - Sections 3 and 6 | FIFRA governs the sale, distribution and use of pesticides. Section 3 of FIFRA generally requires that pesticide products be registered by EPA prior to distribution or sale. Pesticides may only be registered if, among other things, they do not cause "unreasonable adverse effects on the environment." Section 6 of FIFRA provides EPA with the authority to cancel pesticide registrations if either (1) the pesticide, labeling or other material does not comply with FIFRA; or (2) when used in accordance with widespread and commonly recognized practice, the pesticide generally causes unreasonable adverse effects on the environment. | EPA removed perchloroethylene and other chemical substances from its list of pesticide product inert ingredients used in pesticide products (63 FR 34384, June 24, 1998). |
| Clean Air Act (CAA) – Section 112(b) | Defines the original list of 189 hazardous air pollutants (HAP). Under 112(c) of the CAA, EPA must identify and list source categories that emit HAP and then set emission standards for those listed source categories under CAA section 112(d). CAA section 112(b)(3)(A) specifies that any person may petition the Administrator to modify the list of HAP by adding or deleting a substance. Since 1990 EPA has removed two pollutants from the original list leaving 187 at present. | Lists perchloroethylene as a Hazardous Air Pollutant (42 U.S. Code § 7412), and is considered an "urban air toxic" (CAA Section 112(k)). |
| Clean Air Act (CAA) – Section 112(d) | Section 112(d) states that the EPA must establish national emission standards for HAP (NESHAP) for each category or subcategory of major sources and area sources of HAPs [listed pursuant to Section 112(c)]. The standards must require the maximum degree of emission reduction that the EPA determines to be achievable by each particular source category. Different criteria for maximum achievable control technology (MACT) apply for new and existing sources. Less stringent | There are a number of source-specific CAA, Section 112, NESHAPs for perchloroethylene, including:<br>Dry cleaners (73 FR 39871, July 11, 2008)<br>Organic liquids distribution (non-gasoline) (69 FR 5038, February 3, 2004)<br>Off-site waste and recovery operations (64 FR 38950, July 20, 1999)<br>Rubber Tire Manufacturing (67 FR 45588, July 9, 2002) |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | standards, known as generally available control technology (GACT) standards, are allowed at the Administrator's discretion for area sources. | Wood furniture manufacturing (60 FR 62930, December 7, 1995)<br>Synthetic organic chemical manufacturing (59 FR 19402, April 22,1994)<br>Chemical Manufacturing Area Source Categories (74 FR 56008, October 29, 2009)<br>Publicly Owned Treatment Works (64 FR 57572, October 26, 1999)<br>Site Remediation includes perchloroethylene (68 FR 58172, October 8, 2003) |
| Clean Air Act (CAA) – Section 112(d) and 112(f) | Risk and technology review (RTR) of section 112(d) MACT standards. Section 112(f)(2) requires EPA to conduct risk assessments for each source category subject to section 112(d) MACT standards, and to determine if additional standards are needed to reduce remaining risks. Section 112(d)(6) requires EPA to review and revise the MACT standards, as necessary, taking into account developments in practices, processes and control technologies." | EPA has promulgated a number of RTR NESHAP (e.g., the RTR NESHAP for Perchloroethylene Dry Cleaning (71 FR 42724; July 27, 2006) and the RTR NESHAP for Halogenated Solvent Cleaning (72 FR 25138; May 3, 2007) and will do so, as required, for the remaining source categories with NESHAP |
| Clean Air Act (CAA) – Section 183(e) | Section 183(e) requires EPA to list the categories of consumer and commercial products that account for at least 80 percent of all VOC emissions in areas that violate the National Ambient Air Quality Standards (NAAQS) for ozone and to issue standards for these categories that require "best available controls." In lieu of regulations, EPA may issue control techniques guidelines if the guidelines are determined to be substantially as effective as regulations. | Perchloroethylene is listed under the National Volatile Organic Compound Emission Standards for Aerosol Coatings (40 CFR part 59, subpart E). Perchloroethylene has a reactivity factor of 0.04g O3/g VOC. |
| Clean Air Act (CAA) – Section 612 | Under Section 612 of the Clean Air Act (CAA), EPA's Significant New Alternatives Policy (SNAP) program reviews substitutes for ozone depleting substances within a comparative risk framework. EPA publishes lists of acceptable and unacceptable alternatives. A determination that an | Under the SNAP program, EPA listed perchloroethylene as an acceptable substitute in cleaning solvent for metal cleaning, electronics cleaning and precision cleaning (59 FR 13044, March 18, 1994). Perchloroethylene is cited as an alternative to methyl chloroform and CFC-113 for metals, |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | alternative is unacceptable or acceptable only with conditions, is made through rulemaking. | electronics and precision cleaning. Perchloroethylene was also noted to have no ozone depletion potential and cited as a VOC-exempt solvent and acceptable ozone-depleting substance substitute (72 FR 30142, May 30, 2007). |
| Clean Water Act (CWA) – Section 301(b), 304(b), 306, and 307(b) | Requires establishment of Effluent Limitations Guidelines and Standards for conventional, toxic, and non-conventional pollutants. For toxic and non-conventional pollutants, EPA identifies the best available technology that is economically achievable for that industry after considering statutorily prescribed factors and sets regulatory requirements based on the performance of that technology. | Perchloroethylene is designated as a toxic pollutant under section 307(a)(1) of CWA and as such is subject to effluent limitations. Also under section 304, perchloroethylene is included in the list of total toxic organics (TTO) (40 CFR 413.02(i)). |
| Clean Water Act (CWA) 304(a) | Section 304(a)(1) of the Clean Water Act (CWA) requires EPA to develop and publish, and from time to time revise, recommended criteria for the protection of water quality that accurately reflect the latest scientific knowledge. Water quality criteria developed under section 304(a) are based solely on data and scientific judgments on the relationship between pollutant concentrations and environmental and human health effects. | |
| Clean Water Act (CWA) – Section 307(a) | Establishes a list of toxic pollutants or combination of pollutants under the CWA. The statute specifies a list of families of toxic pollutants also listed in the Code of Federal Regulations at 40 CFR 401.15. The "priority pollutants" specified by those families are listed in 40 CFR part 423, Appendix A. These are pollutants for which best available technology effluent limitations must be established on either a national basis through rules (Sections 301(b), 304(b), 307(b), 306), or on a case-by-case best professional judgement basis in NPDES permits (Section 402(a)(1)(B)). | |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| Safe Drinking Water Act (SDWA) – Section 1412 | Requires EPA to publish a non-enforceable maximum contaminant level goals (MCLGs) for contaminants which 1. may have an adverse effect on the health of persons; 2. are known to occur or there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern; and 3. in the sole judgment of the Administrator, regulation of the contaminant presents a meaningful opportunity for health risk reductions for persons served by public water systems. When EPA publishes an MCLG, EPA must also promulgate a National Primary Drinking Water Regulation (NPDWR) which includes either an enforceable maximum contaminant level (MCL) or a required treatment technique. Public water systems are required to comply with NPDWRs | Perchloroethylene is subject to National Primary Drinking Water Regulations (NPDWR) under SDWA with a MCLG of zero and an enforceable maximum contaminant level (MCL) of 0.005 mg/L (40 CFR 141.61). On January 11, 2017, EPA announced a review of the eight existing NPDWRs (82 FR 3518). Perchloroethylene is one of the eight NPDWRs. EPA requested comment on the eight NPDWRs identified as candidates for revision. |
| Comprehensive Environmental Response, Compensation and Liability Act (CERCLA) – Section 102(a) and 103 | Authorizes EPA to promulgate regulations designating as hazardous substances those substances which, when released into the environment, may present substantial danger to the public health or welfare or the environment. EPA must also promulgate regulations establishing the quantity of any hazardous substance the release of which must be reported under Section 103.<br><br>Section 103 requires persons in charge of vessels or facilities to report to the National Response Center if they have knowledge of a release of a hazardous substance above the reportable quantity threshold. | Perchloroethylene is a hazardous substance under CERCLA. Releases of perchloroethylene in excess of 100 pounds must be reported (40 CFR 302.4). |
| Resource Conservation and Recovery Act (RCRA) – Section 3001 | Directs EPA to develop and promulgate criteria for identifying the characteristics of hazardous waste, and for listing hazardous waste, taking into account toxicity, persistence, and | Perchloroethylene is included on the list of hazardous wastes pursuant to RCRA 3001. RCRA Hazardous Waste Code: D039 at 0.7 mg/L; F001, F002; U210. |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | degradability in nature, potential for accumulation in tissue, and other related factors such as flammability, corrosiveness, and other hazardous characteristics. | In 2013, EPA modified its hazardous waste management regulations to conditionally exclude solvent-contaminated wipes that have been cleaned and reused from the definition of solid waste under RCRA (78 FR 46447, July 31, 2013). |
| Superfund Amendments and Reauthorization Act (SARA) – | Requires the Agency to revise the hazardous ranking system and update the National Priorities List of hazardous waste sites, increases state and citizen involvement in the superfund program and provides new enforcement authorities and settlement tools. | Perchloroethylene is listed on SARA, an amendment to CERCLA and the CERCLA Priority List of Hazardous Substances. This list includes substances most commonly found at facilities on the CERCLA National Priorities List (NPL) that have been deemed to pose the greatest threat to public health. |
| **Other Federal Regulations** | | |
| Federal Hazardous Substance Act (FHSA) | Allows the Consumer Product Safety Commission (CPSC) to (1) require precautionary labeling on the immediate container of hazardous household products or (2) to ban certain products that are so dangerous or the nature of the hazard is such that required labeling is not adequate to protect consumers. | Under the Federal Hazardous Substance Act, section 1500.83(a)(31), visual novelty devices containing perchloroethylene are regulated by CPSC. |
| Federal Food, Drug, and Cosmetic Act (FFDCA) | Provides the U.S. FDA (Food and Drug Administration) with authority to oversee the safety of food, drugs and cosmetics. | The FDA regulates perchloroethylene in bottled water. The maximum permissible level of perchloroethylene in bottled water is 0.005 mg/L (21 CFR 165.110). |
| Occupational Safety and Health Act (OSH Act) | Requires employers to provide their workers with a place of employment free from recognized hazards to safety and health, such as exposure to toxic chemicals, excessive noise levels, mechanical dangers, heat or cold stress or unsanitary conditions. Under the Act, the Occupational Safety and Health Administration can issue occupational safety and health standards including such provisions as Permissible Exposure Limits (PELs), exposure | In 1970, OSHA issued occupational safety and health standards for perchloroethylene that included a Permissible Exposure Limit (PEL) of 100 ppm TWA, exposure monitoring, control measures and respiratory protection (29 CFR 1910.1000). |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | monitoring, engineering and administrative control measures and respiratory protection. | |
| Atomic Energy Act Department of Energy (DOE) | The Atomic Energy Act authorizes DOE to regulate the health and safety of its contractor employees | 10 CFR 851.23, Worker Safety and Health Program, requires the use of the 2005 ACGIH TLVs if they are more protective than the OSHA PEL. The 2005 TLV for perchloroethylene is 25 ppm (8hr Time Weighted Average) and 100 ppm Short Term Exposure Limit(STEL). |

## A.2 State Laws and Regulations

**Table_Apx A-2. State Laws and Regulations**

| State Actions | Description of Action |
|---|---|
| **State actions** | |
| State Permissible Exposure Limits | California has a workplace PEL of 25 ppm (California, OEHHA, 1988) |
| State Right-to-Know Acts | Massachusetts (454 CMR 21.00), New Jersey (42 N.J.R 1709(a)), Pennsylvania (Chapter 323, Hazardous Substance List), Rhode Island (RI Gen. Laws Sec. 28-21-1et seq). |
| Volatile Organic Compound (VOC) Regulations for Consumer Products | Many states regulate perchloroethylene as a VOC. These regulations may set VOC limits for consumer products and/or ban the sale of certain consumer products as an ingredient and/or impurity. Regulated products vary from state to state, and could include contact and aerosol adhesives, aerosols, electronic cleaners, footwear or leather care products, and general degreasers, among other products. California (Title 17, California Code of Regulations, Division 3, Chapter 1, Subchapter 8.5, Articles 1, 2, 3 and 4), Connecticut (R.C.S.A Sections 22a-174-40, 22a-174-41, and 22a-174-44), Delaware (Adm. Code Title 7, 1141), District of Columbia (Rules 20-720, 20-721, 20-735, 20-736, 20737), Illinois (35 Adm Code 223), Indiana ( 326 IAC 8-15), Maine (Chapter 152 of the Maine Department of Environmental Protection Regulations), Maryland (COMAR 26.11.32.00 to 26.11.32.26), Michigan (R 336.1660 and R 336. 1661), New Hampshire (Env--A 4100) New Jersey (Title 7, Chapter 27, Subchapter 24), New York (6 CRR-NY III A 235), Rhode Island (Air Pollution Control Regulation No. 31), and Virginia (9VAC5 CHAPTER 45) all have VOC regulations or limits for consumer products. Some of these states also require emissions reporting. |
| Other | There are several state level NESHAPs for dry cleaning and restrictions or phase outs of perchloroethylene (e.g. California, Maine, Massachusetts). Numerous states list perchloroethylene on a list of chemical substances of high concern to children (e.g. Oregon, Vermont, Washington). Under the California Proposition 65 list |

| State Actions | Description of Action |
|---|---|
| | (California OEHHA), perchloroethylene is known to the state of California to cause cancer. |

## A.3 International Laws and Regulations

**Table_Apx A-3. Regulatory Actions by Other Governments and Tribes**

| Country/Organization | Requirements and Restrictions |
|---|---|
| Canada | Perchloroethylene is on the Canadian List of Toxic Substances (CEPA 1999 Schedule 1). The use and sale of perchloroethylene in the dry cleaning industry is regulated under *Use in Dry Cleaning and Reporting Requirements Regulations (Canada Gazette*, Part II on March 12, 2003. Perchloroethylene is also regulated for use and sale for solvent degreasing under Solvent Degreasing Regulations (SOR/2003-283) (Canada Gazette, Part II on August 13, 2003). The purpose of the regulation is to reduce releases of perchloroethylene into the environment from solvent degreasing facilities using more than 1,000 kilograms of perchloroethylene per year. The regulation includes a market intervention by establishing tradable allowances for the use of perchloroethylene in solvent degreasing operations that exceed the 1,000 kilograms threshold per year. |
| European Union | Perchloroethylene was evaluated under the 2013 Community Rolling Action Plan (CoRAP). The conclusion was no additional regulatory action was required (European Chemicals Agency (ECHA) database. Accessed April, 18 2017). |
| Australia | In 2011, a preliminary assessment of perchloroethylene was conducted (National Industrial Chemicals Notification and Assessment Scheme, NICNAS, 2016, Tetrachloroethylene. Accessed April, 18 2017). |
| Japan | Perchloroethylene is regulated in Japan under the following legislation:<br>• Act on the Evaluation of Chemical Substances and Regulation of Their Manufacture, etc. (Chemical Substances Control Law; CSCL)<br>• Act on Confirmation, etc. of Release Amounts of Specific Chemical Substances in the Environment and Promotion of Improvements to the Management Thereof<br>• Industrial Safety and Health Act (ISHA)<br>• Air Pollution Control Law<br>• Water Pollution Control Law<br>• Soil Contamination Countermeasures Act<br>• Law for the Control of Household Products Containing Harmful Substances<br>(National Institute of Technology and Evaluation (NITE) Chemical Risk Information Platform (CHIRP). Accessed April 18, 2017) |
| Australia, Austria, Belgium, Canada, Denmark, European Union, Finland, France, | Occupational exposure limits for perchloroethylene (GESTIS International limit values for chemical agents (Occupational exposure limits, OELs) database. Accessed April 18, 2017). |

| Country/Organization | Requirements and Restrictions |
|---|---|
| Germany, Hungary, Ireland, Israel, Japan, Latvia, New Zealand, People's Republic of China, Poland, Singapore, South Korea, Spain, Sweden, Switzerland, United Kingdom | |
| Basel Convention | Halogenated organic solvents (Y41) are listed as a category of waste under the Basel Convention – Annex I. Although the United States is not currently a party to the Basel Convention, this treaty still affects U.S. importers and exporters. |
| OECD Control of Transboundary Movements of Wastes Destined for Recovery Operations | Halogenated organic solvents (A3150) are listed as a category of waste subject to The Amber Control Procedure under Council Decision C (2001) 107/Final. |

# Appendix B PROCESS, RELEASE AND OCCUPATIONAL EXPOSURE INFORMATION

This appendix provides information and data found in preliminary data gathering for perchloroethylene.

## B.1 Process Information

Process-related information potentially relevant to the risk evaluation may include process diagrams, descriptions and equipment. Such information may inform potential release sources and worker exposure activities. EPA will consider this information in combination with available monitoring data and estimation methods and models, as appropriate, to quantify occupational exposure and releases for the various conditions of use in the risk evaluation.

### B.1.1 Manufacture (Including Import)

#### B.1.1.1 Domestic Manufacture

Perchloroethylene was previously produced through chlorination of acetylene to tetrachloroethane, then dehydrochlorination to trichloroethylene (TCE), followed by chlorination of TCE to pentachloroethane and finally dehydrochlorination to perchloroethylene (Snedecor et al., 2004). The last U.S. plant using the acetylene process was shut down in 1978 (Snedecor et al., 2004). Currently, most perchloroethylene is manufactured using one of three methods: chlorination of ethylene dichloride (EDC); chlorination of hydrocarbons containing one to three carbons (C1 to C3) or their partially chlorinated derivatives; or oxychlorination of two-carbon (C2) chlorinated hydrocarbons (ATSDR, 2014; Snedecor et al., 2004; U.S. EPA, 1985b).

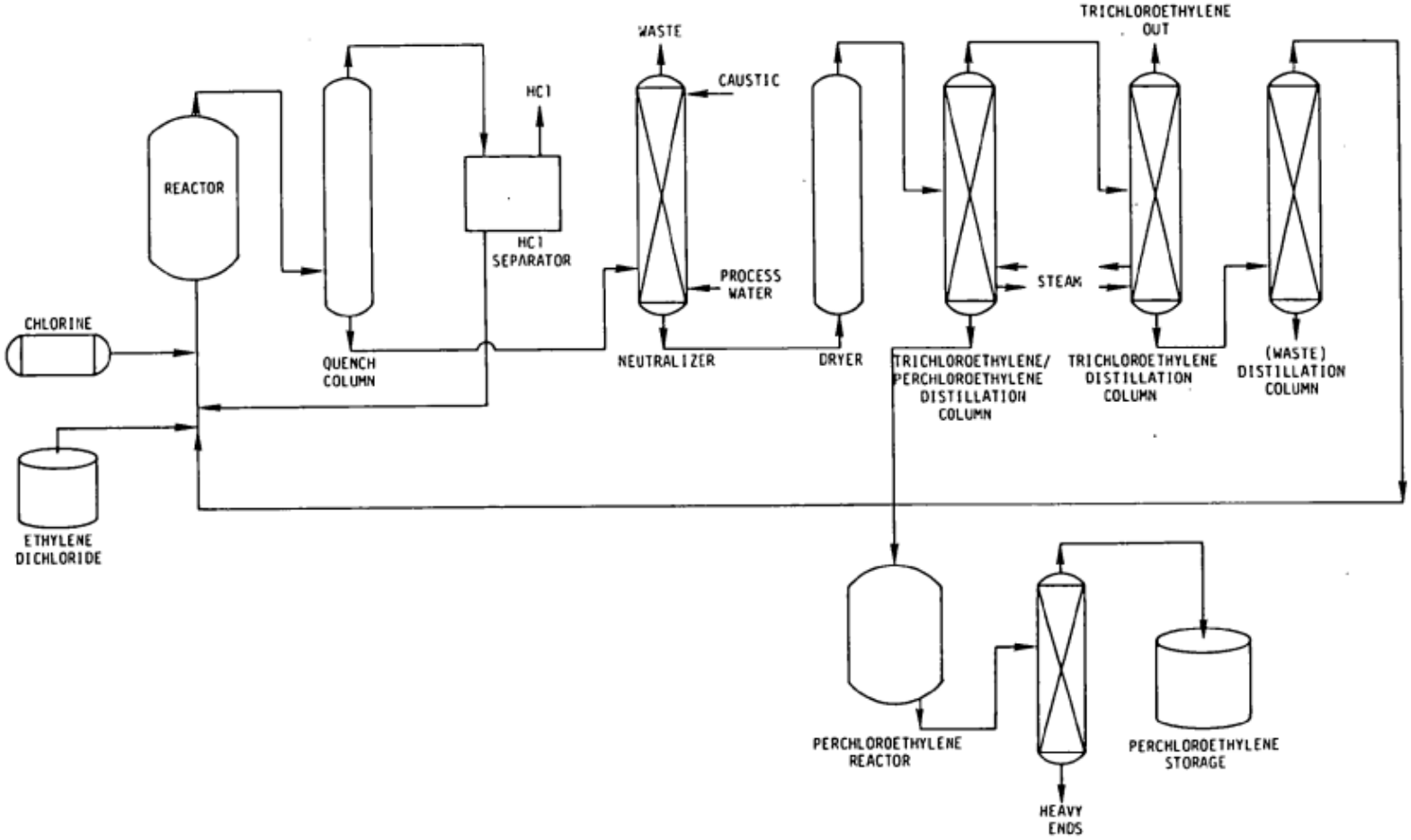
***Chlorination of EDC*** **–** The chlorination of EDC involves a non-catalytic reaction of chlorine and EDC or other C2 chlorinated hydrocarbons to form perchloroethylene and TCE as co-products and hydrochloric acid (HCl) as a byproduct (ATSDR, 2014; Snedecor et al., 2004; U.S. EPA, 1985b). Following reaction, the product undergoes quenching, HCl separation, neutralization, drying and distillation (U.S. EPA, 1985b). This process is advantageous at facilities that have a feedstock source of mixed C2 chlorinated hydrocarbons from other processes and an outlet for the HCl byproduct (Snedecor et al., 2004). Figure_Apx B-1 illustrates a typical process diagram of the production of perchloroethylene via EDC chlorination (U.S. EPA, 1985b).

***Chlorination of C1-C3 hydrocarbons*** **–** The chlorination of C1-C3 hydrocarbons involves the reaction of chlorine with a hydrocarbon such as methane, ethane, propane, propylene or their chlorinated derivatives, at high temperatures (550–700°C), with or without a catalyst, to form perchloroethylene and carbon tetrachloride ($CCl_4$) as co-products and HCl as a byproduct (ATSDR, 2014; Snedecor et al., 2004; U.S. EPA, 1985b). This process is advantageous because mixed chlorinated hydrocarbon wastes from other processes can be used as a feedstock (ATSDR, 2014; (Snedecor et al., 2004)). Due to phase-out of CFC-11 and CFC-12 and most $CCl_4$ uses, most facilities using this method maximize the production of perchloroethylene and minimize or eliminate the production of $CCl_4$ (Snedecor et al., 2004). Figure_Apx B-2 illustrates a typical process diagram of the production of perchloroethylene via C1-C3 hydrocarbon chlorination (U.S. EPA, 1985b).

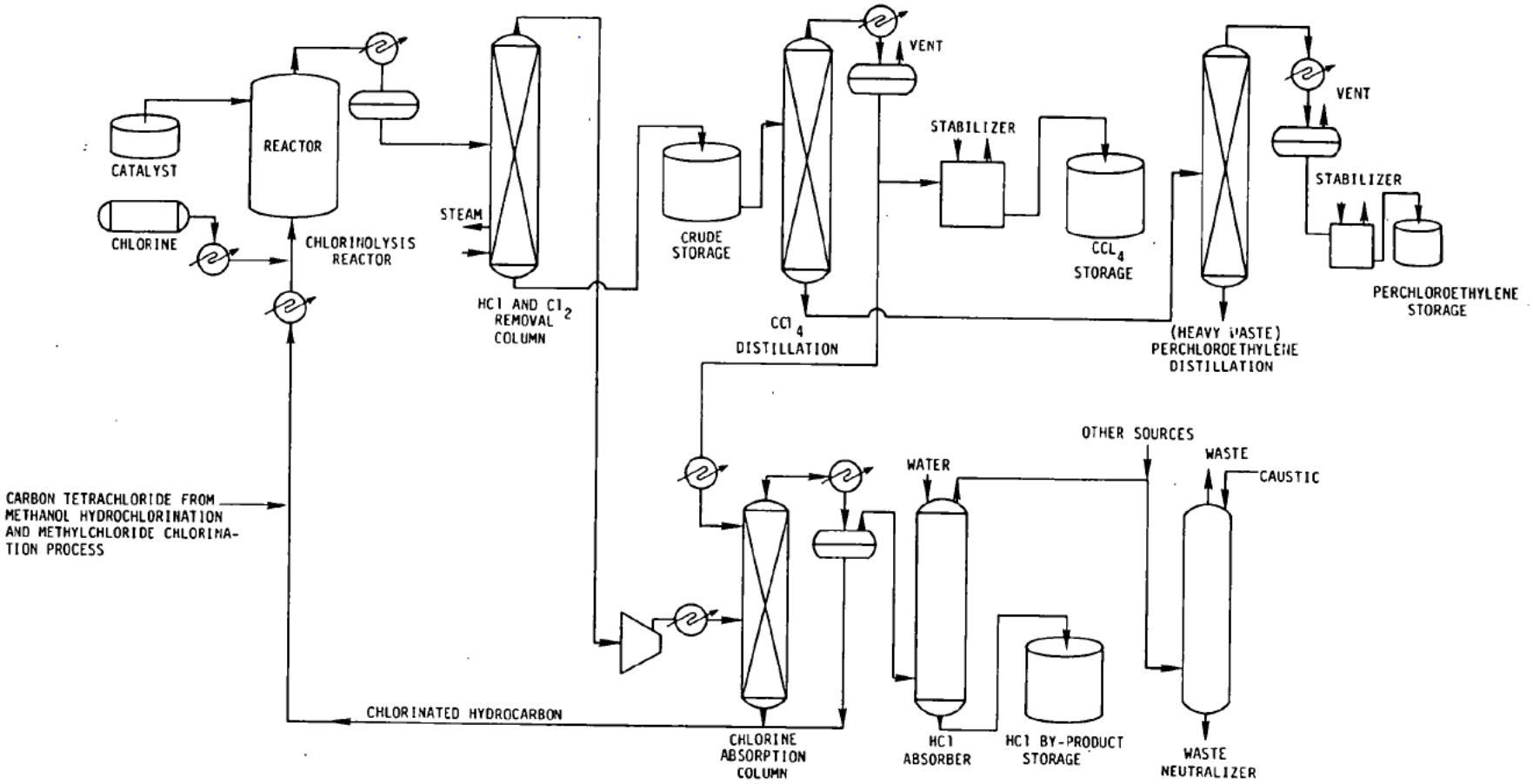
***Oxychlorination of C2 chlorinated hydrocarbons*** **–** The oxychlorination of C2 chlorinated hydrocarbons involves the reaction of either chlorine or HCl and oxygen with EDC in the presence of a catalyst to produce perchloroethylene and TCE as co-products (ATSDR, 2014; Snedecor et al., 2004). Following reaction, the product undergoes HCl separation, drying, distillation, neutralization with ammonia and a final drying step (U.S. EPA, 1985b). The advantage of this process is that no byproduct

HCl is produced and can be combined with other processes as a net HCl consumer (ATSDR, 2014; Snedecor et al., 2004). Figure_Apx B-3 illustrates a typical process diagram of the production of perchloroethylene via oxychlorination of C2 hydrocarbons (U.S. EPA, 1985b).

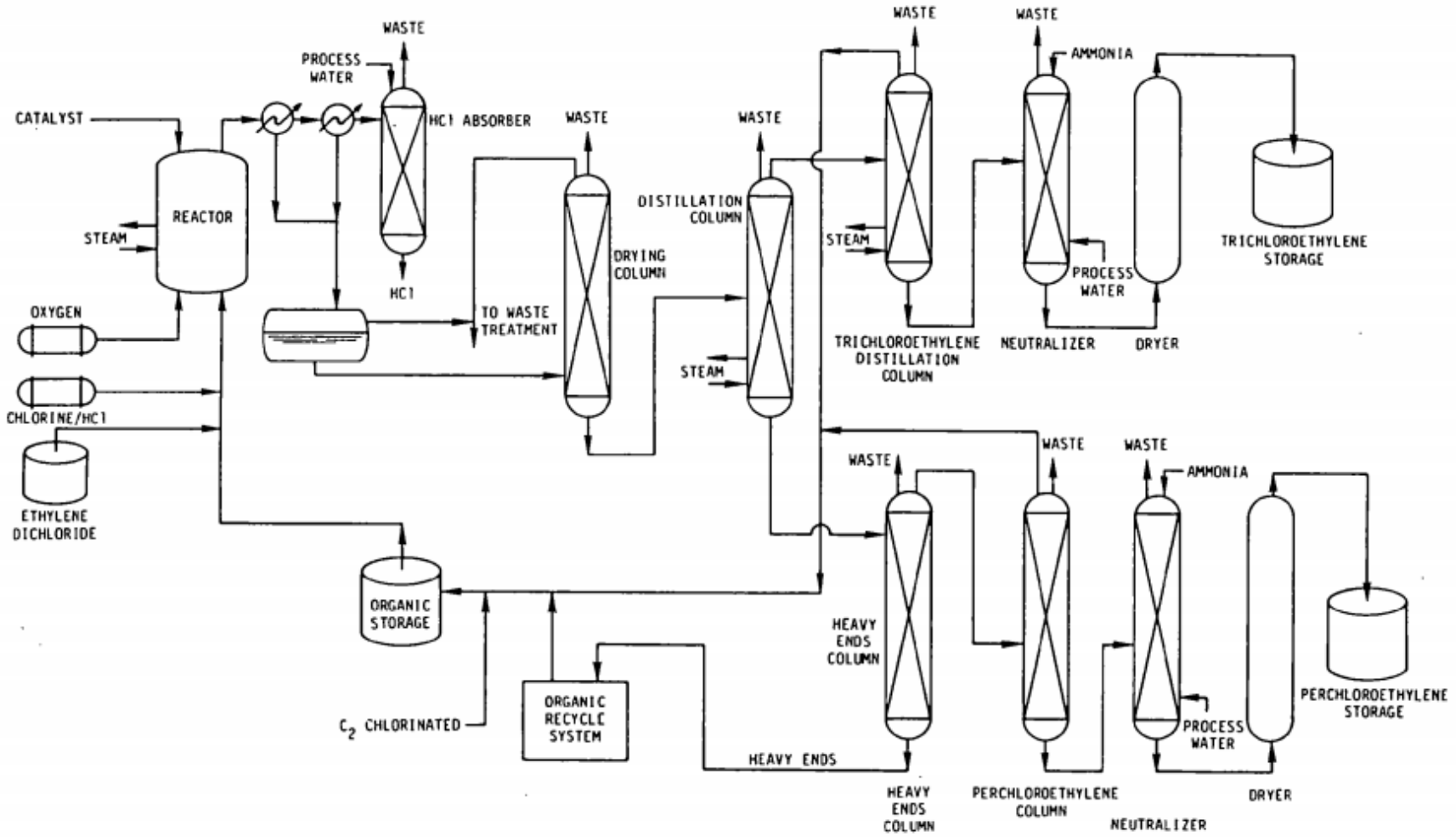
In all three processes the product ratio of perchloroethylene to TCE/$CCl_4$ products are controlled by adjusting the reactant ratios (Snedecor et al., 2004).




**Figure_Apx B-1. Process Flow Diagram for the Manufacture of Perchloroethylene via Chlorination of EDC (EPA, 1985)**




**Figure_Apx B-2. Process Flow Diagram for the Manufacture of Perchloroethylene via Chlorination of Hydrocarbons (EPA, 1985)**




**Figure_Apx B-3. Process Flow Diagram for the Manufacture of Perchloroethylene via Oxychlorination of C2 Chlorinated Hydrocarbons (EPA, 1985)**

### B.1.1.2 Import

According to Snedecor et al. (2004), perchloroethylene may be shipped by barge, tank car, tank truck or 55-gallon steel drums. Perchloroethylene may be stored in steel tanks that are dry, free of rust and equipped with a chemical vent dryer and controlled evaporation vent (Snedecor et al., 2004).

## B.1.2 Processing and Distribution

Based on the reported industrial processing operations in the 2016 CDR, perchloroethylene may be incorporated into a variety of formulations, products and articles, or used industrially as a chemical intermediate (U.S. EPA, 2016b). Some industrial or commercial products may also be repackaged into appropriately-sized containers to meet specific customer demands (U.S. EPA, 2016b).

### B.1.2.1 Reactant or Intermediate

Processing as a reactant or intermediate is the use of perchloroethylene as a feedstock in the production of another chemical product via a chemical reaction in which perchloroethylene is consumed to form the product. In the past, perchloroethylene was used as feedstock (with chlorine) for the manufacture of one- and two-carbon (C1 and C2) CFCs (Smart and Fernandez, 2000). However, due to discovery that CFCs contribute to stratospheric ozone depletion, the use of CFCs was phased-out by the year 2000 to comply with the Montreal Protocol (Smart and Fernandez, 2000). Since the phase-out of CFCs, perchloroethylene has been used to manufacture the CFC alternatives, HCFCs, specifically the HCFC-123 alternative to CFC-11 (Smart and Fernandez, 2000). Perchloroethylene is also used as a feedstock in the production of trichloroacetyl chloride (Smart and Fernandez, 2000).

HCFC-123 is produced by fluorination of perchloroethylene with liquid or gaseous hydrofluoric acid (HF). The manufacture of HCFC is more complex than the manufacture of CFCs due to potential byproduct formation or catalyst inactivation caused by the extra hydrogen atom in the HCFCs (Smart and Fernandez, 2000). Therefore, the process involved in the manufacture of HCFCs requires additional reaction and distillation steps as compared to the CFC manufacturing process (Smart and Fernandez, 2000).

Perchloroethylene is also used by Honeywell International Inc. in the manufacture of HFC-125 (R-125), HCFC-124 (R-124), and CFC-113 (R-113) (Honeywell, 2017). In 2016, Honeywell used approximately 65 million pounds of perchloroethylene to manufacture R-125 and R-124 and approximately 20 million pounds to manufacture R-113 (Honeywell, 2017). The majority of the R-113 is used as an intermediate for manufacture of chlorotrifluoroethylene (CTFE) monomer; however, a small portion is used in exempted applications vital to U.S. security (Honeywell, 2017). Perchloroethylene is received at the Honeywell facilities in railcars and trucks and is transferred into storage vessels with a pump and vapor balance (Honeywell, 2017). Some perchloroethylene is lost when disconnecting the hose; however, the storage tank is pressurized so there are no point emissions or breathing losses (Honeywell, 2017). The primary emission of perchloroethylene at Honeywell facilities are from fugitive emissions. The facilities utilize a fugitive emissions monitoring program and leak detection program to reduce fugitive emissions (Honeywell, 2017).

Honeywell representatives indicated that the R-125/R-124 processes achieve a once through perchloroethylene conversion of 95% and the remaining 5% is recovered and recycled back into the process (Honeywell, 2017). For the R-113 process, the once through conversion rate is 99% and the remaining 1% is recovered and recycled back into the process (Honeywell, 2017). The ultimate conversion from both processes is 100%. Honeywell indicated they do not detect any perchloroethylene in their products (Honeywell, 2017).

Perchloroethylene is also used in catalyst regeneration at petroleum refineries (Dow Chemical Co., 2008; Public Comment, EPA-HQ-OPPT-2016-0732-0018). Perchloroethylene is consumed in the catalyst regeneration process; therefore, EPA considers this use as a reactant/intermediate. According to public comments from the American Fuel and Petrochemical Manufacturers (AFPM) (Public Comment, EPA-HQ-OPPT-2016-0732-0018), perchloroethylene is used in both the reforming and isomerization processes at refineries. In the reforming process, perchloroethylene is added directly to a regenerator in a Continuous Catalytic Regeneration reforming unit, and in the isomerization process, perchloroethylene is added to the hydrocarbon feed (Public Comment, EPA-HQ-OPPT-2016-0732-0018). In both processes, perchloroethylene provides chlorine ions to regenerate the catalysts and is consumed in the process (Public Comment, EPA-HQ-OPPT-2016-0732-0018).

### B.1.2.2 Incorporating into a Formulation, Mixture or Reaction Product

Incorporation into a formulation, mixture or reaction product refers to the process of mixing or blending of several raw materials to obtain a single product or preparation. The uses of perchloroethylene that may require incorporation into a formulation include adhesives, sealants, coatings, inks, lubricants and plastic and rubber manufacturing. Perchloroethylene specific formulation processes were not identified; however, several ESDs published by the OECD and Generic Scenarios published by EPA have been identified that provide general process descriptions for these types of products.

The formulation of coatings and inks typically involves dispersion, milling, finishing and filling into final packages (OECD, 2009c; U.S. EPA, 2001b). Adhesive formulation involves mixing together volatile and non-volatile chemical components in sealed, unsealed or heated processes (OECD, 2009a). Sealed processes are most common for adhesive formulation because many adhesives are designed to set or react when exposed to ambient conditions (OECD, 2009a). Lubricant formulation typically involves the blending of two or more components, including liquid and solid additives, together in a blending vessel (OECD, 2004a). In plastics and rubber manufacturing the formulation step usually involves the compounding of the polymer resin with additives and other raw materials to form a masterbatch in either open or closed blending processes (U.S. EPA, 2014b; OECD, 2009b). After compounding, the resin is fed to an extruder where is it converted into pellets, sheets, films or pipes (U.S. EPA, 2014b).

### B.1.2.3 Incorporating into an Article

Incorporation into an article typically refers to a process in which a chemical becomes an integral component of an article (as defined at 40 CFR 704.3) that is distributed for industrial, trade or consumer use. The use of perchloroethylene in plastic and rubber manufacturing and the use in textile processing (as a finishing agent) are the only uses that would incorporate perchloroethylene into an article. Perchloroethylene may also be used in the plastics and rubber product manufacturing as a degreasing solvent (NIOSH, 1994b). For descriptions of degreaser uses see Appendix B.1.3.2.

***Plastics and Rubber Product Manufacturing***

In plastic manufacturing, the final plastic article is produced in a conversion process that forms the compounded plastic into the finished products (U.S. EPA, 2014c; OECD, 2009b). The converting process is different depending on whether the plastic is a thermoplastic or a thermosetting material (OECD, 2009b). Thermoplastics converting involves the melting of the plastic material, forming it into a new shape and then cooling it (U.S. EPA, 2014c; OECD, 2009b). The converting of thermoplastics may involve extrusion, injection molding, blow molding, rotational molding or thermoforming (U.S. EPA, 2014c; OECD, 2009b).

Conversion of thermosetting materials involves using heat and pressure to promote curing, typically through cross-linking (OECD, 2009b). The primary conversion process for thermosetting materials is compression molding; however, fiber reinforced thermosetting plastics are converted using hand layup, spray molding and filament winding (OECD, 2009b). After the forming process, finishing operations such as filing, grinding, sanding, polishing, painting, bonding, coating and engraving are performed to complete the process (U.S. EPA, 2014c).

***Textile Processing***

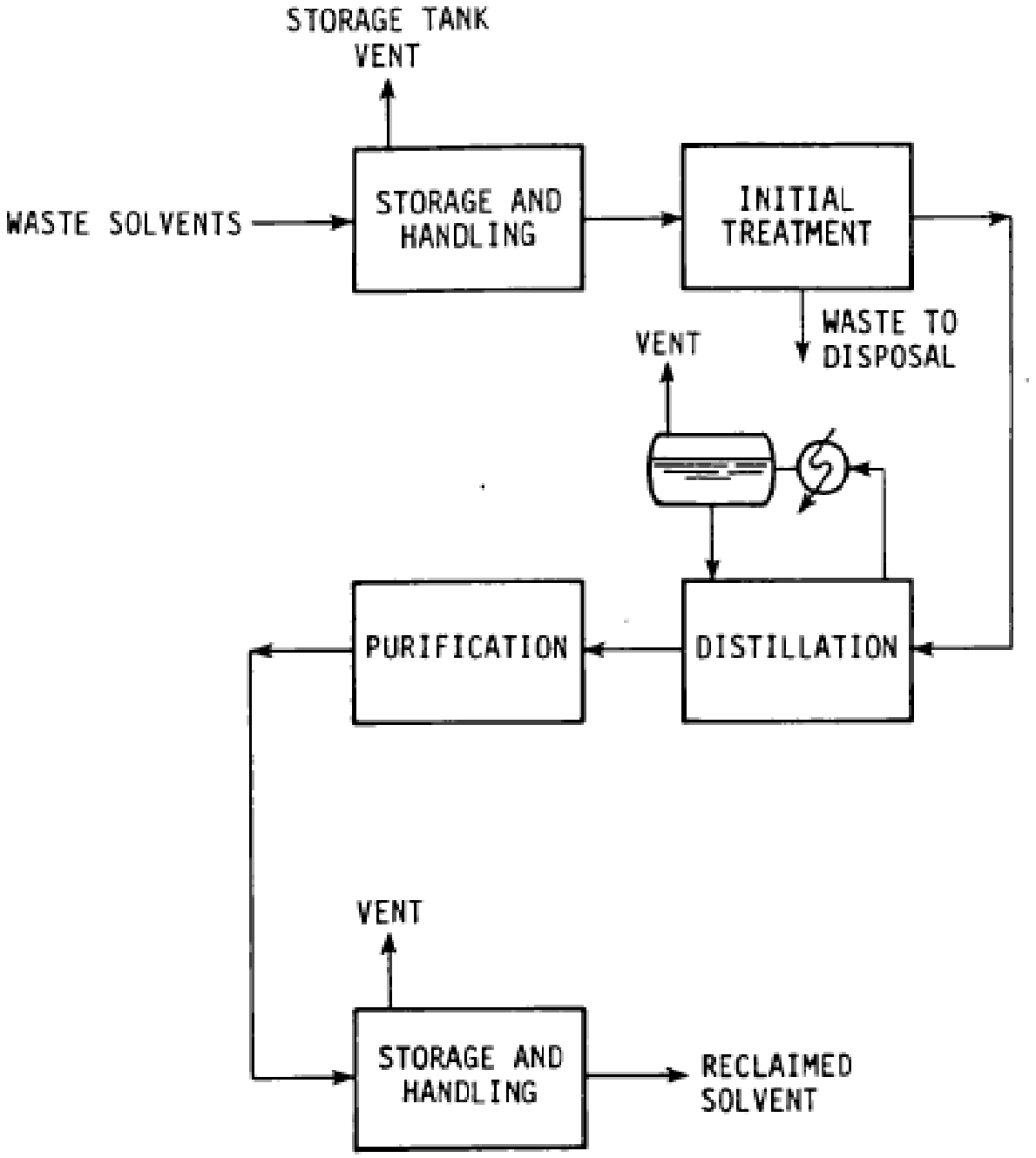
In textile processing, the purpose of the finishing stage is to impart special qualities to the textile (i.e. article). Perchloroethylene may be used as a water and stain repellant or as a fabric protector during textile finishing [cite market report]. Finishes may include mechanical treatments (e.g., calendaring and napping) or chemical treatments (e.g. stiffening, softening, water and soil repellents, antimicrobials, and fire retardants) (OECD, 2004b). The finishing process occurs after the textile is pre-treated and/or dyed/printed (OECD, 2004b). Chemical finishes are applied from aqueous solution/dispersions using the pad/dry/cure process (OECD, 2004b). In this process, the fabric is immersed in the aqueous finishing solution and then squeezed between metal rolls to remove excess solution and evenly distribute the finishing agent (OECD, 2004b). The fabric is then passed over a series of heated metal rolls for drying and cured using an oven (OECD, 2004b).

#### B.1.2.4 Repackaging

Typical repackaging sites receive the chemical in bulk containers and transfer the chemical from the bulk container into another smaller container in preparation for distribution in commerce.

#### B.1.2.5 Recycling

Waste perchloroethylene solvent is generated when it becomes contaminated with suspended and dissolved solids, organics, water or other substance (U.S. EPA, 1980c). Waste solvents can be restored to a condition that permits reuse via solvent reclamation/recycling (U.S. EPA, 1985a, 1980c). Waste perchloroethylene is shopped to a solvent recovery site where it is piped or manually loaded into process equipment (U.S. EPA, 1985a). The waste solvent then undergoes a vapor recovery (e.g., condensation, adsorption and absorption) or mechanical separation (e.g., decanting, filtering, draining, setline and centrifuging) step followed by distillation, purification and final packaging (U.S. EPA, 1985a, 1980c). Figure_Apx B-4 illustrates a typical perchloroethylene solvent recovery process flow diagram (U.S. EPA, 1985a).




**Figure_Apx B-4. Process Flow Diagram of Perchloroethylene Solvent Recovery (U.S. EPA, 1985b)**

### B.1.3 Uses

In this document, EPA has grouped uses based on CDR categories, and identified examples within these categories as subcategories of use. Note that some subcategories of use may be grouped under multiple CDR categories. The differences between these uses will be further investigated and defined later during risk evaluation.

#### B.1.3.1 Cleaning and Furniture Care Products

The "Cleaning and Furniture Care Products" category encompasses chemical substances contained in products that are used to remove dirt, grease, stains and foreign matter from furniture and furnishings or to cleanse, sanitize, bleach, scour, polish, protect or improve the appearance of surfaces. Products designed to clean wood floors or other substrates which contain perchloroethylene are used in industrial or commercial settings and are primarily formulated as liquids.

***Dry Cleaning Solvent and Spot Cleaner***

Perchloroethylene can be used as a solvent in dry cleaning machines and is found in products used to spot clean garments. Spot cleaning products can be applied to the garment either before or after the garment is dry cleaned. The process and worker activities associated with commercial dry cleaning and spot cleaning have been previously described in EPA's 1-Bromopropane (1-BP) Draft Risk Assessment (U.S. EPA, 2016c). Note: The 1-BP risk assessment focuses on use at commercial dry cleaning facilities; however, according to EPA's *Economic Impact Analysis of the Final Perchloroethylene Dry Cleaning Residual Risk Standard* (U.S. EPA, 2006a), there are seven industrial dry cleaners that use perchloroethylene. Industrial dry cleaners clean heavily stained articles such as work gloves, uniforms, mechanics' overalls, mops and shop rags (U.S. EPA, 2006a). The general worker activities at industrial dry cleaners are not expected to significantly differ from activities at commercial dry cleaners.

***Non-Aerosol Degreasers and Cleaners***

Perchloroethylene can also be used as a solvent in non-aerosol degreasing and cleaning products. Non-aerosol cleaning products typically involve dabbing or soaking a rag with cleaning solution and then using the rag to wipe down surfaces or parts to remove contamination (U.S. EPA, 2014a).The cleaning solvent is usually applied in excess and allowed to air-dry (U.S. EPA, 2014a). Parts may be cleaned in place or removed from the service item for more thorough cleaning (U.S. EPA, 2014a).

***Aerosol Spray Degreasers and Cleaners***

Aerosol degreasing is a process that uses an aerosolized solvent spray, typically applied from a pressurized can, to remove residual contaminants from fabricated parts. Products containing perchloroethylene may be used in aerosol degreasing applications such as brake cleaning, engine degreasing and metal product cleaning. This use has been previously described in EPA's 1-BP Draft Risk Assessment (U.S. EPA, 2016c). Aerosol degreasing may occur at either industrial facilities or at commercial repair shops to remove contaminants on items being serviced. Aerosol degreasing products may also be purchased and used by consumers for various applications.

#### B.1.3.2 Solvents for Cleaning and Degreasing

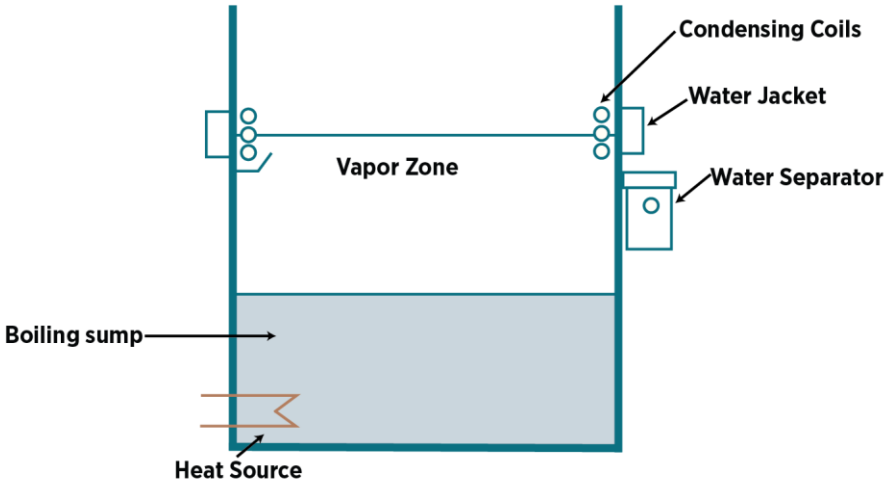
EPA has gathered information on different types of cleaning and degreasing systems from recent TCE risk assessment (U.S. EPA, 2014e) and risk management activities (FR 81(242): 91592-91624. December 16, 2016, and FR 82(12): 7432-7461. January 19, 2017) and 1-BP risk assessment (U.S. EPA, 2016c) activities. Provided below are descriptions of five cleaning and degreasing uses of perchloroethylene.

***Vapor Degreasers***

Vapor degreasing is a process used to remove dirt, grease and surface contaminants in a variety of metal cleaning industries. Vapor degreasing may take place in batches or as part of an in-line (i.e., continuous) system. Vapor degreasing equipment can generally be categorized into one of three degreaser types described below:

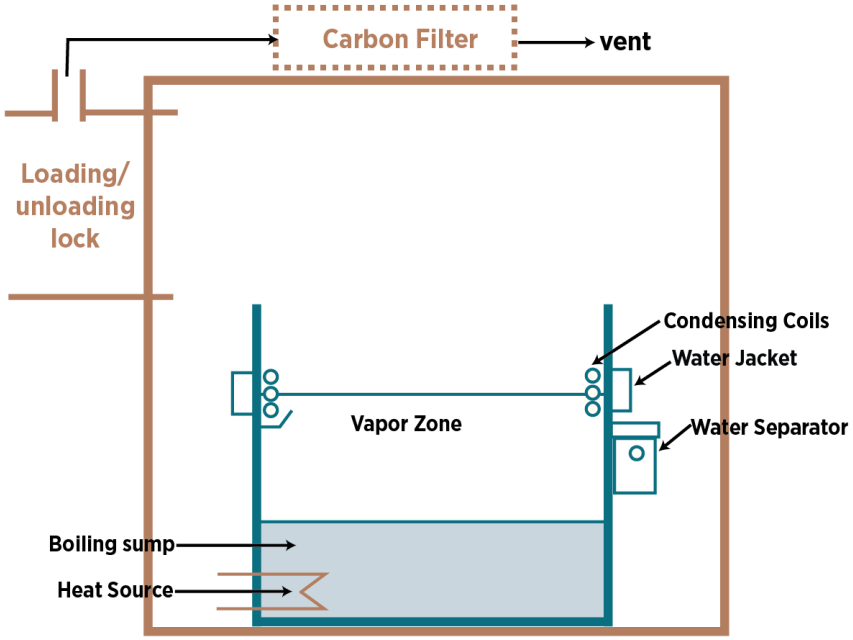
**Batch vapor degreasers:** In batch machines, each load (parts or baskets of parts) is loaded into the machine after the previous load is completed. Individual organizations, regulations and academic studies have classified batch vapor degreasers differently. For the purposes of the scope document, EPA categories the batch vapor degreasers into five types: open top vapor degreasers (OTVDs); OTVDs with enclosures; closed-loop degreasing systems (airtight); airless degreasing systems (vacuum drying); and airless vacuum-to-vacuum degreasing systems.

- Open top vapor degreasers (OTVD) – In OTVDs, a vapor cleaning zone is created by heating the liquid solvent in the OTVD causing it to volatilize. Workers manually load or unload fabricated parts directly into or out of the vapor cleaning zone. The tank usually has chillers along the side of the tank to prevent losses of the solvent to the air. However, these chillers are not able to eliminate emissions, and throughout the degreasing process significant air emissions of the solvent can occur. These air emissions can cause issues with both worker health and safety as well as environmental issues. Additionally, the cost of replacing solvent lost to emissions can be expensive (NEWMOA, 2001). Figure_Apx B-5 illustrates a standard OTVD.



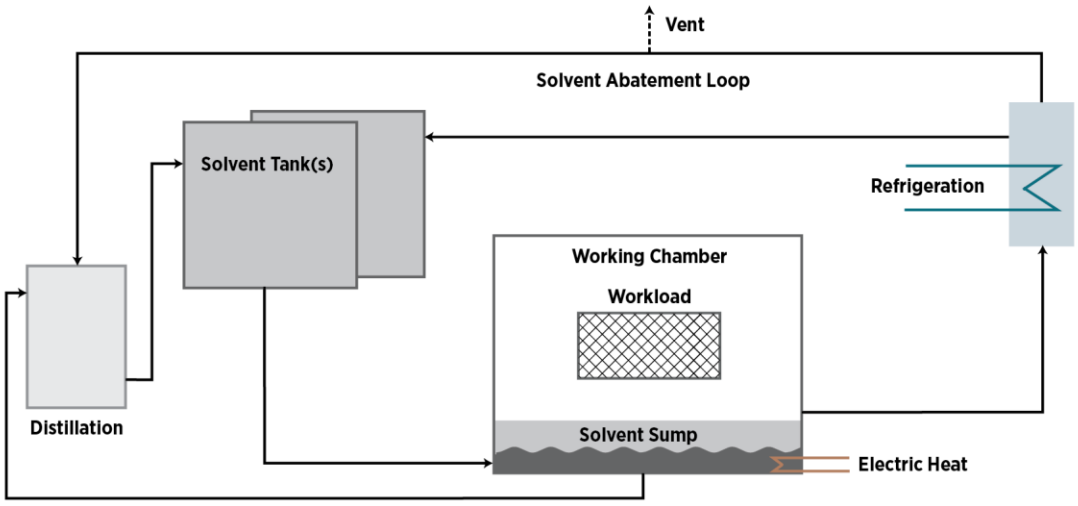

**Figure_Apx B-5. Open Top Vapor Degreaser**

- OTVD with enclosure – OTVDs with enclosures operate the same as standard OTVDs except that the OTVD is enclosed on all sides during degreasing. The enclosure is opened and closed to add or remove parts to/from the machine, and solvent is exposed to the air when the cover is open. Enclosed OTVDs may be vented directly to the atmosphere or first vented to an external carbon filter and then to the atmosphere (U.S. EPA; ICF Consulting, 2004; U.S. EPA). Figure_Apx B-6 illustrates an OTVD with an enclosure. The dotted lines in Figure_Apx B-6 represent the optional carbon filter that may or may not be used with an enclosed OTVD.




**Figure_Apx B-6. Open Top Vapor Degreaser with Enclosure**

- Closed-loop degreasing system (Airtight) – In closed-loop degreasers, parts are placed into a basket, which is then placed into an airtight work chamber. The door is closed and solvent vapors are sprayed onto the parts. Solvent can also be introduced to the parts as a liquid spray or liquid immersion. When cleaning is complete, vapors are exhausted from the chamber and circulated over a cooling coil where the vapors are condensed and recovered. The parts are dried by forced hot air. Air is circulated through the chamber and residual solvent vapors are captured by carbon adsorption. The door is opened when the residual solvent vapor concentration has reached a specified level (Kanegsberg and Kanegsberg, 2011). Figure_Apx B-7 illustrates a standard closed-loop vapor degreasing system.




**Figure_Apx B-7. Closed-loop/Vacuum Vapor Degreaser**

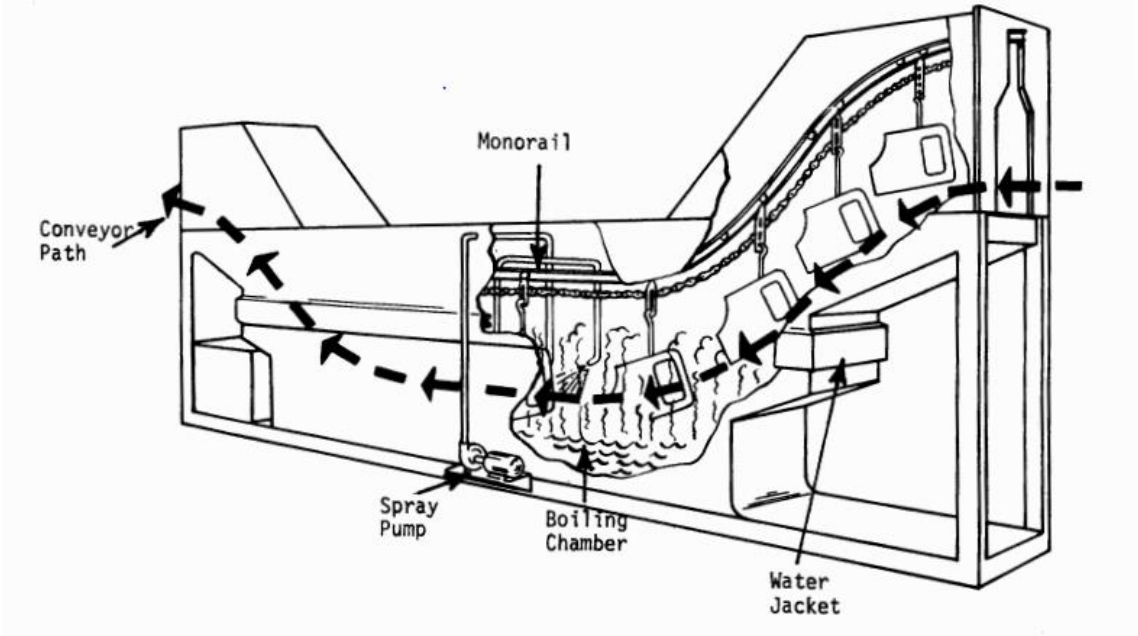
- Airless degreasing system (vacuum drying) – Airless degreasing systems are also sealed, closed-loop systems, but remove air at some point of the degreasing process. Removing air typically takes the form of drawing vacuum, but could also include purging air with nitrogen at some point of the process (in contrast to drawing vacuum, a nitrogen purge operates at a slightly positive pressure). In airless degreasing systems with vacuum drying only, the cleaning stage works similarly as with the airtight closed-loop degreaser. However, a vacuum is generated during the drying stage, typically below 5 torr (5 mmHg). The vacuum dries the parts and a vapor recovery system captures the vapors (Kanegsberg and Kanegsberg, 2011; NEWMOA, 2001; U.S. EPA, 2001a).

- Airless vacuum-to-vacuum degreasing system – Airless vacuum-to-vacuum degreasers are true "airless" systems because the entire cycle is operated under vacuum. Typically, parts are placed into the chamber, the chamber sealed, and then vacuum drawn within the chamber. The typical solvent cleaning process is a hot solvent vapor spray. The introduction of vapors in the vacuum chamber raises the pressure in the chamber. The parts are dried by again drawing vacuum in the chamber. Solvent vapors are recovered through compression and cooling. An air purge then purges residual vapors over an optional carbon adsorber and through a vent. Air is then introduced in the chamber to return the chamber to atmospheric pressure before the chamber is opened (Durkee, 2014; NEWMOA, 2001).

The general design of vacuum vapor degreasers and airless vacuum degreasers is similar as illustrated in Figure_Apx B-7 for closed-loop systems except that the work chamber is under vacuum during various stages of the cleaning process.

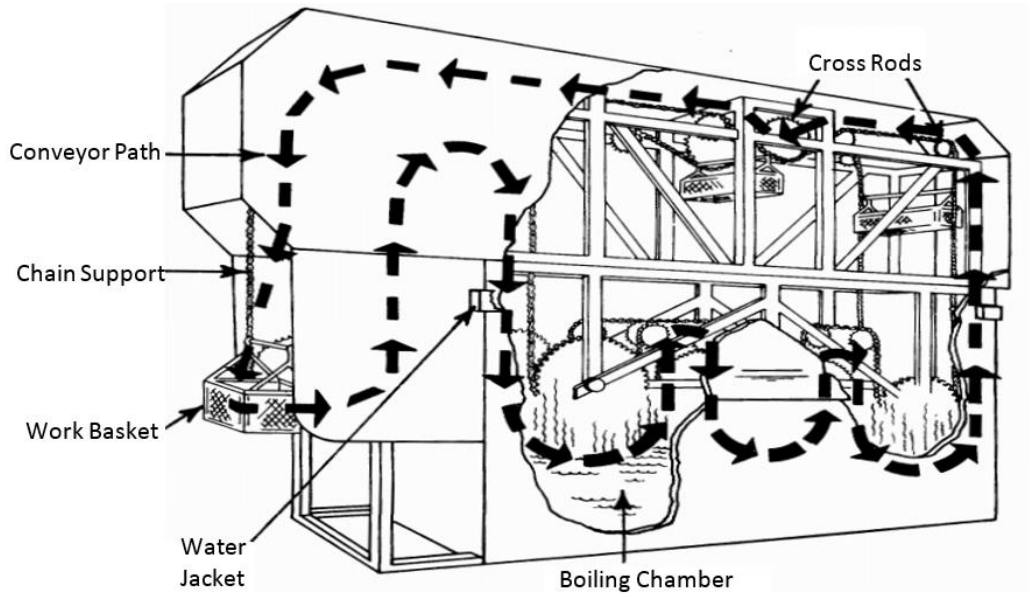
**Conveyorized vapor degreasers:** In conveyorized systems, an automated parts handling system, typically a conveyor, continuously loads parts into and through the vapor degreasing equipment and the subsequent drying steps. Conveyorized degreasing systems are usually fully enclosed except for the conveyor inlet and outlet portals. Conveyorized degreasers are likely used in shops where there are a large number of parts being cleaned. There are seven major types of conveyorized degreasers: monorail degreasers; cross-rod degreasers; vibra degreasers; ferris wheel degreasers; belt degreasers; strip degreasers; and circuit board degreasers (U.S. EPA, 1977).

- Monorail Degreasers – Monorail degreasing systems are typically used when parts are already being transported throughout the manufacturing areas by a conveyor (U.S. EPA, 1976). They use a straight-line conveyor to transport parts into and out of the cleaning zone. The parts may enter one side and exit and the other or may make a 180° turn and exit through a tunnel parallel to the entrance (U.S. EPA, 1976). Figure_Apx B-8 illustrates a typical monorail degreaser (U.S. EPA, 1976).



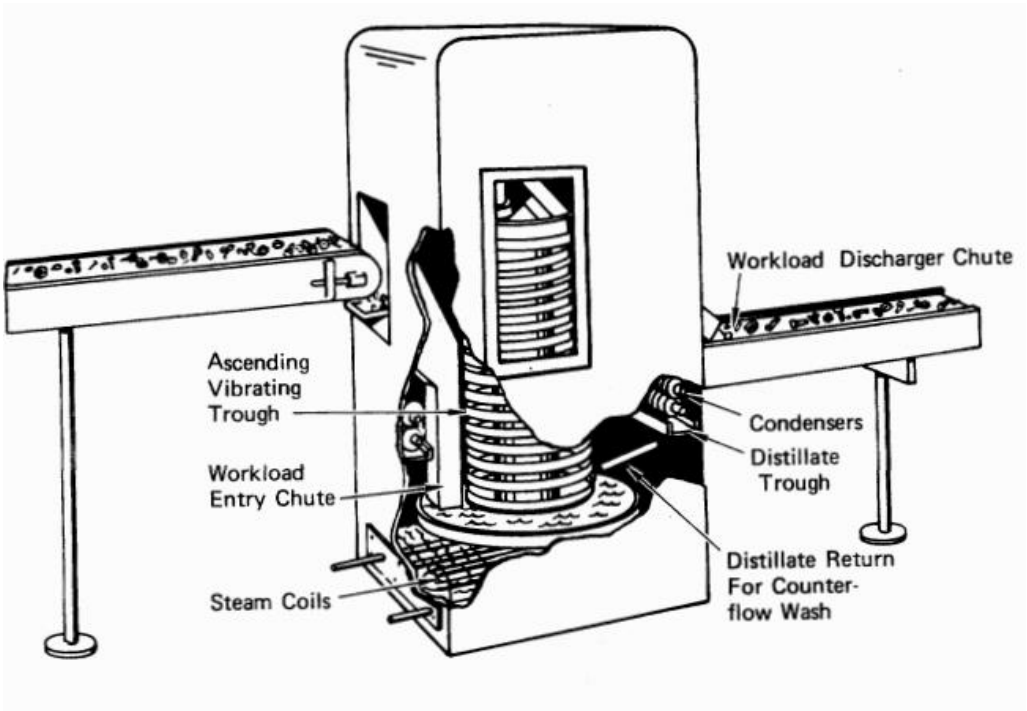

**Figure_Apx B-8. Monorail Conveyorized Vapor Degreasing System (EPA, 1977a)**

- Cross-rod Degreasers – Cross-rod degreasing systems utilize two parallel chains connected by a rod that support the parts throughout the cleaning process. The parts are usually loaded into perforated baskets or cylinders and then transported through the machine by the chain support system. The baskets and cylinders are typically manually loaded and unloaded (U.S. EPA, 1976). Cylinders are used for small parts or parts that need enhanced solvent drainage because of crevices and cavities. The cylinders allow the parts to be tumbled during cleaning and drying and thus increase cleaning and drying efficiency. Figure_Apx B-9 illustrates a typical cross-rod degreaser (U.S. EPA, 1976).



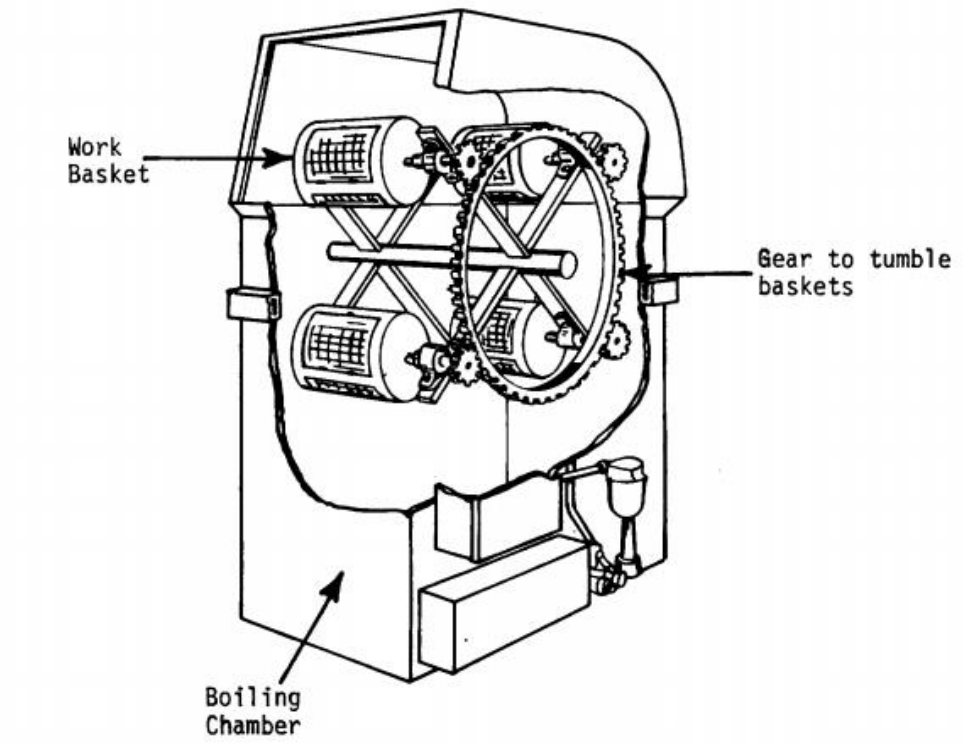

**Figure_Apx B-9. Cross-Rod Conveyorized Vapor Degreasing System (EPA, 1977a)**

- Vibra Degreasers – In vibra degreasing systems, parts are fed by conveyor through a chute that leads to a pan flooded with solvent in the cleaning zone. The pan and the connected spiral elevator are continuously vibrated throughout the process causing the parts to move from the pan and up a spiral elevator to the exit chute. As the parts travel up the elevator, the solvent condenses and the parts are dried before exiting the machine (U.S. EPA, 1976). Figure_Apx B-10 illustrates a typical vibra degreaser (U.S. EPA, 1976).



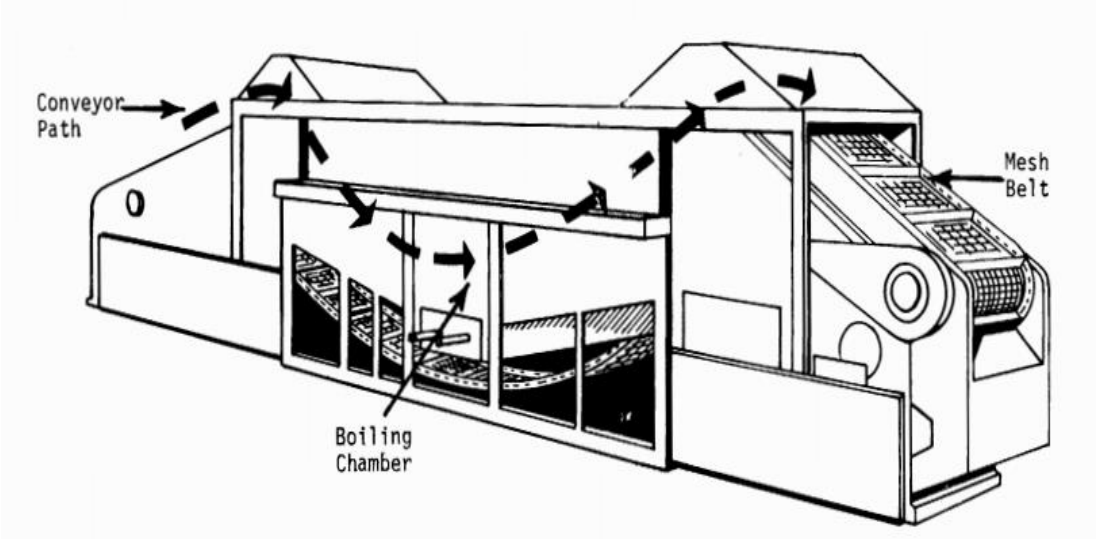

**Figure_Apx B-10. Vibra Conveyorized Vapor Degreasing System (U.S. EPA, 1977)**

- Ferris wheel degreasers – Ferris wheel degreasing systems are generally the smallest of all the conveyorized degreasers (U.S. EPA, 1976). In these systems, parts are manually loaded into perforated baskets or cylinders and then rotated vertically through the cleaning zone and back out. Figure_Apx B-11 illustrates a typical ferris wheel degreaser (U.S. EPA, 1976).




**Figure_Apx B-11. Ferris Wheel Conveyorized Vapor Degreasing System (EPA, 1977a)**

- Belt degreasers – Belt degreasing systems (similar to strip degreasers; see next bullet) are used when simple and rapid loading and unloading of parts is desired (U.S. EPA, 1976). Parts are loaded onto a mesh conveyor belt that transports them through the cleaning zone and out the other side. Figure_Apx B-12 illustrates a typical belt or strip degreaser (U.S. EPA, 1976).

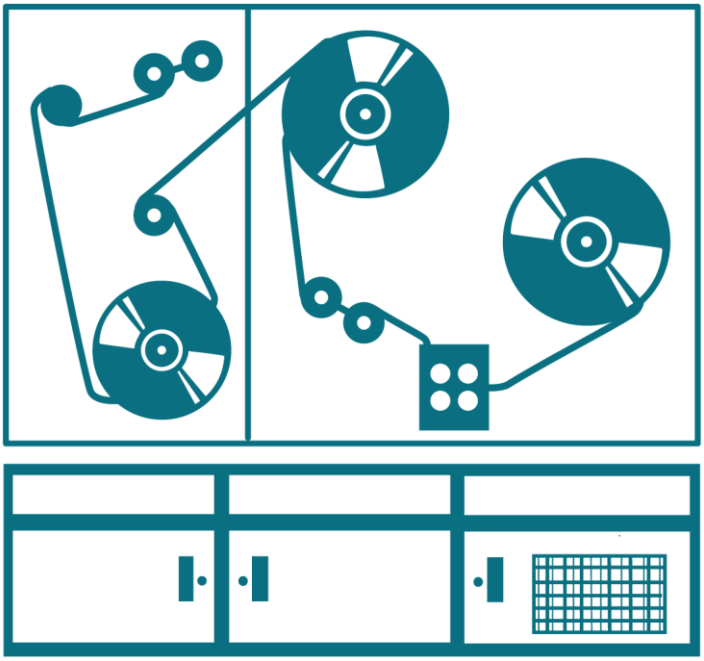



**Figure_Apx B-12. Belt/Strip Conveyorized Vapor Degreasing System (U.S. EPA, 1977)**

- Strip degreasers – Strip degreasing systems operate similar to belt degreasers except that the belt itself is being cleaned rather than parts being loaded onto the belt for cleaning. Figure_Apx B-12 illustrates a typical belt or strip degreaser (U.S. EPA, 1976).

- Circuit board cleaners – Circuit board degreasers use any of the conveyorized designs. However, in circuit board degreasing, parts are cleaned in three different steps due to the manufacturing processes involved in circuit board production (U.S. EPA, 1976).

**Continuous web vapor degreasers:** Continuous web cleaning machines are a subset of conveyorized degreasers but differ in that they are specifically designed for cleaning parts that are coiled or on spools such as films, wires and metal strips (Kanegsberg and Kanegsberg, 2011; U.S. EPA, 2006b). In continuous web degreasers, parts are uncoiled and loaded onto rollers that transport the parts through the cleaning and drying zones at speeds greater than 11 feet per minute (U.S. EPA, 2006b). The parts are then recoiled or cut after exiting the cleaning machine (Kanegsberg and Kanegsberg, 2011; U.S. EPA, 2006b). Figure_Apx B-13 illustrates a typical continuous web cleaning machine.



**Figure_Apx B-13. Continuous Web Vapor Degreasing System**

***Cold Cleaners***

Perchloroethylene can also be used as a solvent in cold cleaners, which are non-boiling solvent degreasing units. Cold cleaning operations include spraying, brushing, flushing and immersion. In a typical batch-loaded, maintenance cold cleaner, dirty parts are cleaned manually by spraying and then soaking in the tank. After cleaning, the parts are either suspended over the tank to drain or are placed on an external rack that routes the drained solvent back into the cleaner. Batch manufacturing cold cleaners could vary widely, but have two basic equipment designs: the simple spray sink and the dip tank. The dip tank design typically provides better cleaning through immersion, and often involves an immersion tank equipped with agitation (U.S. EPA, 1981). Emissions from batch cold cleaning machines typically result from (1) evaporation of the solvent from the solvent-to-air interface, (2) “carry out” of excess solvent on cleaned parts and (3) evaporative losses of the solvent during filling and draining of the machine (U.S. EPA, 2006b).

***Non-Aerosol Degreasers and Cleaners***

Perchloroethylene can also be used as a solvent in non-aerosol degreasing and cleaning products. Non-aerosol cleaning products typically involve dabbing or soaking a rag with cleaning solution and then using the rag to wipe down surfaces or parts to remove contamination (U.S. EPA, 2014a). The cleaning solvent is usually applied in excess and allowed to air-dry (U.S. EPA, 2014a). Parts may be cleaned in place or removed from the service item for more thorough cleaning (U.S. EPA, 2014a).

***Aerosol Spray Degreasers and Cleaners***

Aerosol degreasing is a process that uses an aerosolized solvent spray, typically applied from a pressurized can, to remove residual contaminants from fabricated parts. Products containing perchloroethylene may be used in aerosol degreasing applications such as brake cleaning, engine degreasing and metal product cleaning. This use has been previously described in EPA's 1-BP Draft Risk Assessment(U.S. EPA, 2016c). Aerosol degreasing may occur at either industrial facilities or at commercial repair shops to remove contaminants on items being serviced. Aerosol degreasing products may also be purchased and used by consumers for various applications.

#### B.1.3.3 Lubricant and Greases

In the 2016 CDR (U.S. EPA, 2016b), two companies reported commercial use of perchloroethylene in lubricants and greases. The *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: Tetrachloroethylene (Perchloroethylene)* [EPA-HQ-OPPT-2016-0732-0003 ] identified perchloroethylene in penetrating lubricants, cutting oils, aerosol lubricants, red greases, white lithium greases, silicone lubricants and greases and chain and cable lubricants. Most of the products identified by EPA are applied by either aerosol or non-aerosol spray applications.

#### B.1.3.4 Adhesives and Sealants

Based on products identified in *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: Tetrachloroethylene (Perchloroethylene)* [EPA-HQ-OPPT-2016-0732-0003 ] and 2016 CDR reporting, perchloroethylene may be used in adhesive and sealants for industrial, commercial and consumer applications (U.S. EPA, 2016b). The OECD ESD for Use of Adhesives (OECD, 2013) provides general process descriptions and worker activities for industrial adhesive uses.

Liquid adhesives are unloaded from containers into the coating reservoir, applied to a flat or three-dimensional substrate and the substrates are then joined and allowed to cure (OECD, 2013). The majority of adhesive applications include spray, roll, curtain, syringe or bead application (OECD, 2013). For solvent-based adhesives, the volatile solvent (in this case perchloroethylene) evaporates during the curing stage (OECD, 2013). Worker activities include unloading activities, container and equipment cleaning activities and manual applications of adhesive (OECD, 2013). Based on EPA's knowledge of the industry, overlap in process descriptions, worker activities and application methods are expected for sealant products.

EPA's *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: Tetrachloroethylene (Perchloroethylene)* (EPA-HQ-OPPT-2016-0732-0003) states that the use of perchloroethylene in consumer adhesives is especially prevalent with uses in arts and crafts and light repairs. EPA has also identified several sealants and adhesives that contain perchloroethylene and are marketed for commercial uses, such as construction applications. Based on EPA's knowledge of the industry, the likely application methods for commercial and consumer uses include spray, brush, syringe, eyedropper, roller and bead applications.

### B.1.3.5 Paints and Coatings

Based on products identified in *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: Tetrachloroethylene (Perchloroethylene)* (EPA-HQ-OPPT-2016-0732-0003) ] and 2016 CDR reporting (U.S. EPA, 2016b), perchloroethylene may be used in various paints and coatings for industrial, commercial and consumer applications. Several OECD ESDs and EPA generic scenarios provide general process descriptions and worker activities for industrial and commercial uses.

Typical coating applications include manual application with roller or brush, air spray systems, airless and air-assisted airless spray systems, electrostatic spray systems, electrodeposition/electrocoating and autodeposition, dip coating, curtain coating systems, roll coating systems and supercritical carbon dioxide systems (OECD, 2009c). After application, solvent-based coatings typically undergo a drying stage in which the solvent evaporates from the coating (OECD, 2009c).

### B.1.3.6 Processing Aid for Pesticide, Fertilizer and Other Agricultural Manufacturing

In the 2016 CDR (U.S. EPA, 2016b), two sites owned by Olin Corporation reported use of perchloroethylene as a "processing aid, not otherwise listed" for use in the "pesticide, fertilizer, and other agricultural chemical manufacturing" industry.

### B.1.3.7 Processing Aid, Specific to Petroleum Production

In the 2016 CDR (U.S. EPA, 2016b), two sites owned by Olin Corporation reported use of perchloroethylene as a "processing aid, specific to petroleum production" for use in the "Petrochemical Manufacturing" industry. A Dow Product Safety Assessment (Dow Chemical Co, 2008) for perchloroethylene describes a use at oil refineries for catalyst regeneration. However, a public comment from AFPM (Public Comment, EPA-HQ-OPPT-2016-0732-0018) indicates that perchloroethylene is consumed in the catalyst regeneration process and therefore would be considered an "intermediate" (see Appendix B.1.2.1 for description). It is unclear if this CDR reporting code is related to the use in catalyst regeneration or another processing aid use.

### B.1.3.8 Other Uses

***Other Industrial Uses***

Based on products identified in *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: Tetrachloroethylene (Perchloroethylene)* (EPA-HQ-OPPT-2016-0732-0003) , a variety of other industrial uses may exist for perchloroethylene, including textile processing, laboratory applications, foundry applications and wood furniture manufacturing. It is unclear at this time the total volume of perchloroethylene used in any of these applications. More information on these uses will be gathered through expanded literature searches in subsequent phases of the risk evaluation process.

***Other Commercial/Consumer Uses***

Based on products identified in EPA's *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: Tetrachloroethylene (Perchloroethylene)* (EPA-HQ-OPPT-2016-0732-0003) , a variety of other commercial and consumer uses may exist for perchloroethylene including carpet cleaning; laboratory applications; metal and stone polishes; inks and ink removal products; welding applications; photographic film applications; mold cleaning, release and protectant products. Similar to the "Other" industrial uses, more information on these uses will be gathered through expanded literature searches in subsequent phases of the risk evaluation process.

## B.1.4 Disposal

Perchloroethylene is listed as a hazardous waste under RCRA and federal regulations prevent land disposal of various chlorinated solvents that may contain perchloroethylene (ATSDR, 2014).

Perchloroethylene may be disposed of by absorption in vermiculite, dry sand, earth or other similar material and then buried in a secured sanitary landfill or incineration (HSDB, 2012). In incineration, complete combustion is necessary to prevent phosgene formation and acid scrubbers must be used to remove any haloacids produced (ATSDR, 2014). Perchloroethylene may also be discharged to waterways if proper permits are held (ATSDR, 2014).

## B.2 Occupational Exposure Data

EPA presents below an example of occupational exposure-related information from the preliminary data gathering. EPA will consider this information and data in combination with other data and methods for use in the risk evaluation.

Table_Apx B-1 summarizes personal monitoring OSHA CEHD data by NAICS code (OSHA, 2017a) and Table_Apx B-2 summarizes NIOSH HHE data.

**Table_Apx B-1. Summary of Perchloroethylene Personal Monitoring Air Samples Obtained from OSHA Inspections Conducted Between 2011 and 2016**

| Release/Exposure Scenario | NAICS | NAICS Description | 8-hr TWA Concentration (ppm)[a] | | | | | STEL, Peak, or Ceiling Concentration (ppm) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Number of Data Points | Minimum | Maximum | Average | Number of Zero Values[b] | Number of Data Points | Minimum | Maximum | Average | Number of Zero Values[b] |
| Unknown, company inspected is an excavation contractor, possibly from contact with soil contaminated with perchloroethylene | 236220 | Commercial and Institutional Building Construction | 2 | 0 | 0 | 0 | 2 | 2 | 0 | 0 | 0 | 2 |
| Unknown, likely impurity in refrigerant | 238220 | Plumbing, Heating, and Air-Conditioning Contractors | 1 | 5.2 | | | 0 | No Data Available | | | | |
| Textile pre-treatment or textile finishing | 313310 | Textile and Fabric Finishing Mills | 1 | 0 | | | 1 | 1 | 0 | | | 1 |
| Textile pre-treatment or textile finishing | 313312 | Textile and Fabric Finishing (except Broadwoven Fabric) Mills[c] | 1 | 0 | | | 1 | 1 | 0 | | | 1 |
| Other uses (ink and ink removal products), wipe cleaning, or aerosol degreasing | 323113 | Commercial Screen Printing | 1 | 0 | | | 1 | 1 | 0 | | | 1 |
| Plastics converting (possibly as a degreaser/cleaner, mold release agent, or paint/coating) | 326199 | All Other Plastics Product Manufacturing | 2 | 0.2 | 0.3 | 0.2 | 0 | 1 | 0.9 | | | 0 |
| Vapor degreasing or cold cleaning | 331512 | Steel Investment Foundries | 3 | 0.02 | 0.03 | 0.02 | 0 | No Data Available | | | | |
| Vapor degreasing or cold cleaning | 332439 | Other Metal Container Manufacturing | 2 | 0.03 | 0.03 | 0.03 | 0 | No Data Available | | | | |
| Vapor degreasing or cold cleaning | 332991 | Ball and Roller Bearing Manufacturing | 3 | 0 | 0 | 0 | 3 | 3 | 0 | 0 | 0 | 3 |
| Vapor degreasing or cold cleaning | 332996 | Fabricated Pipe and Pipe Fitting Manufacturing | 3 | 0 | 0 | 0 | 3 | 3 | 0 | 0 | 0 | 3 |

| Release/Exposure Scenario | NAICS | NAICS Description | 8-hr TWA Concentration (ppm)[a] | | | | | STEL, Peak, or Ceiling Concentration (ppm) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Number of Data Points | Minimum | Maximum | Average | Number of Zero Values[b] | Number of Data Points | Minimum | Maximum | Average | Number of Zero Values[b] |
| Vapor degreasing or cold cleaning | 334511 | Search, Detection, Navigation, Guidance, Aeronautical, and Nautical System and Instrument Manufacturing | 1 | 0.3 | | | 0 | 1 | 0.3 | | | 0 |
| Vapor degreasing or cold cleaning | 335999 | All Other Miscellaneous Electrical Equipment and Component Manufacturing | 1 | 2.1 | | | 0 | 1 | 19 | | | 0 |
| Unknown, likely impurity in refrigerant | 445110 | Supermarkets and Other Grocery (except Convenience) Stores | 2 | 0 | 0 | 0 | 2 | 2 | 0 | 0 | 0 | 2 |
| Industrial and commercial dry cleaning | 448110 | Men's Clothing Stores | 1 | 7.8 | | | 0 | 1 | 8.6 | | | 0 |
| Commercial auto repair/servicing | 485410 | School and Employee Bus Transportation | 1 | 63 | | | 0 | 1 | 100 | | | 0 |
| Commercial auto repair/servicing | 811198 | All Other Automotive Repair and Maintenance | 1 | 110 | | | 0 | 1 | 120 | | | 0 |
| Industrial and commercial dry cleaning | 812310 | Coin-Operated Laundries and Drycleaners | 1 | 2.3 | | | 0 | 1 | 9.1 | | | 0 |
| Industrial and commercial dry cleaning | 812320 | Drycleaning and Laundry Services (except Coin-Operated) | 30 | 0.1 | 390 | 27.8 | 0 | 22 | 0.5 | 480 | 55.4 | 0 |
| Unknown – this seems to be for OSHA inspectors which could have been collected during site inspections | 926150 | Regulation, Licensing, and Inspection of Miscellaneous Commercial Sectors | 6 | 0 | 7.2 | 1.4 | 3 | 6 | 0 | 7.2 | 1.6 | 3 |
| Vapor degreasing, cold cleaning, aerosol degreasing, wipe cleaning or other uses (laboratory chemical) | 927110 | Space Research and Technology | 1 | 0 | | | 1 | 1 | 0 | | | 1 |

[a] Assumes all TWA data are 8-hr TWA.

[b] For facilities where all samples are measured as zero, it is unclear if perchloroethylene is present at the facility. For facilities where the samples are zero and other samples are greater than zero, the zero values likely represent non-detects.

[c] This is a 2007 NAICS code, the corresponding 2012 and 2017 NAICS code is 313310 for "Textile and Fabric Finishing Mills."

Note: The data set also includes samples for a facility classified using the 2012/2017 NAICS code as a separate line item. All data for both NAICS codes were zero values.

**Table_Apx B-2. Summary of Monitoring Data from NIOSH Health Hazard Evaluations Conducted since 1990**

| Data Source | Report Number | Exposure/Release Scenario | Facility Description | Number of Exposure Samples | Minimum of Exposure Values (ppm) | Maximum of Exposure Values (ppm) | Comments |
|---|---|---|---|---|---|---|---|
| NIOSH, 1992 | HETA 91-351-2252 | Industrial and commercial dry cleaning | Office co-located with a dry cleaner | 0 | No exposure data provided. | | |
| NIOSH, 1994 | HETA 91-377-2383 | Plastics converting (as a degreaser) | Molded rubber parts manufacturer | PBZ: 15<br>Area: 2 | PBZ: ND<br>Area: 0.76 | PBZ: 5.3<br>Area: 1.2 | PBZ: Full-shift TWA<br>Area: 2-hr Measurement |
| NIOSH, 1999 | HETA 98-0249-2773 | Industrial and commercial dry cleaning | Dry cleaning facility in a hotel | PBZ: 5<br>Area: 2 | PBZ: 0.17<br>Area: 5.6 | PBZ: 5.8<br>Area: 7.4 | All full-shift measurements. Study also took "real-time" peak measurements ranging from 377 to >2,000 ppm. |
| NIOSH, 2008 | HETA 07-0055-3073 | Commercial auto repair/ servicing | School bus maintenance shop | 0 | No exposure data provided. | | |

ND – Non-detect

## B.3 References related to Risk Evaluation – Environmental Release and Occupational Exposure

**Table_Apx B-3. Potentially Relevant Data Sources for Process Description Related Information for Perchloroethylene[3]**

| Bibliography | url |
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| Johansen, K.,Tinnerberg, H.,Lynge, E. (2005). Use of history science methods in exposure assessment for occupational health studies Occupational and Environmental Medicine, 62(7), 434-441 | Johansen et al. (2005) |
| Stefaniak, A. B.,Breysse, P. N.,Murray, M. P. M.,Rooney, B. C.,Schaefer, J. (2000). An evaluation of employee exposure to volatile organic compounds in three photocopy centers Environmental Research, 83(2), 162-173 | Stefaniak et al. (2000) |

[3] The data sources identified are based on preliminary results to date of the full-text screening step of the Systematic Review process. Further screening and quality control are on-going.

| | |
|---|---|
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| Hsia, (2008). Chlorinated solvents - The key to surface cleaning performance #journal#, #volume#(#issue#), #Pages# | HSIA (2008) |
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| Ec, (2009). Recommendation of the scientific committee on occupational exposure limits for tetrachloroethylene (perchloroethylene) #journal#, #volume#(#issue#), #Pages# | EC (2009) |
| Erm, (2017). Life cycle assessment of used oil management #journal#, #volume#(#issue#), #Pages# | ERM (2017) |
| Japanese Ministry of, Environment (2004). Manual for PRTR release estimation models: 1. Examples of calculation in typical processes #journal#, #volume#(#issue#), #Pages# | Japanese Ministry of Environment (2004a) |

**Table_Apx B-4. Potentially Relevant Data Sources for Estimated or Measured Release Data for Perchloroethylene[4]**

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| Tsai, W. enT (2012). An Analysis of Reducing Perchloroethylene Emissions in the Urban Environment: A Case Study of Taiwan CLEAN - Soil, Air, Water, 40(2), 123-126 | Tsai (2012) |

[4] The data sources identified are based on preliminary results to date of the full-text screening step of the Systematic Review process. Further screening and quality control are on-going.

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| U.S, E. P. A. (1995). EPA office of compliance sector notebook project. Profile of the dry cleaning industry #journal#, #volume#(#issue#), #Pages# | U.S. EPA (1995a) |
| Oecd, (2009). Emission scenario document on adhesive formulation #journal#, #volume#(#issue#), #Pages# | OECD (2009a) |
| Oecd, (2013). Emission scenario document on the industrial use of adhesives for substrate bonding #journal#, #volume#(#issue#), #Pages# | OECD (2013) |
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| Oecd, (2015). Emission scenario documents on coating industry (paints, lacquers and varnishes) #journal#, #volume#(#issue#), #Pages# | OECD (2009c) |
| (1978). Control of volatile organic emissions from perchloroethylene dry cleaning systems #journal#, #volume#(#issue#), #Pages# | 1978) |
| U.S, E. P. A. (1980). Compilation of Air Pollutant Emission Factors Chapter 4.7: Waste Solvent Reclamation #journal#, #volume#(#issue#), #Pages# | U.S. EPA (1980b) |
| U.S, E. P. A. (1978). Control of volatile organic emissions from perchloroethylene dry cleaning systems #journal#, #volume#(#issue#), #Pages# | 1978) |
| U.S, E. P. A. (1991). Dry cleaning facilities - Draft background information for proposed standards #journal#, #volume#(#issue#), #Pages# | U.S. EPA (1991) |
| U.S, E. P. A. (1998). Cleaner technologies substitutes assessment for professional fabricare processes: Summary #journal#, #volume#(#issue#), #Pages# | U.S. EPA (1998a) |
| ToxNet Hazardous Substances Data, Bank (2017). HSDB: Tetrachloroethylene #journal#, #volume#(#issue#), #Pages# | ToxNet Hazardous Substances Data Bank (2017) |
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| The Massachusetts Toxics Use Reduction Institute, University of Massachusetts Lowell (2006). Five chemicals alternatives assessment study #journal#, #volume#(#issue#), #Pages# | The Massachusetts Toxics Use Reduction Institute (2006) |
| Empe, Inc Consulting Engineers (1986). Hazardous waste management study: Dry cleaners #journal#, #volume#(#issue#), #Pages# | EMPE (1986) |
| Nc, Denr (2001). Alternatives to the predominant dry cleaning processes #journal#, #volume#(#issue#), #Pages# | NC DENR (2001) |

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| European Chlorinated Solvents, Association (2016). Guidance on storage and handling of chlorinated solvents #journal#, #volume#(#issue#), #Pages# | European Chlorinated Solvents Association (ECSA) (2016) |
| Hsia, (2008). Chlorinated solvents - The key to surface cleaning performance #journal#, #volume#(#issue#), #Pages# | HSIA (2008) |
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| Atsdr, (2014). Toxicological profile for tetrachloroethylene #journal#, #volume#(#issue#), #Pages# | ATSDR (2014) |
| Chemistry Industry Association of, Canada (2017). All substances emissions for 2012 and projections for 2015 #journal#, #volume#(#issue#), #Pages# | Chemistry Industry Association of Canada (2017b) |
| Chemistry Industry Association of, Canada (2017). All substances emissions for 2011 and projections for 2014 #journal#, #volume#(#issue#), #Pages# | Chemistry Industry Association of Canada (2017a) |
| Japanese Ministry of, Environment (2004). Manual for PRTR release estimation models: Part II materials #journal#, #volume#(#issue#), 246-291 | Japanese Ministry of Environment (2004b) |
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**Table_Apx B-5. Potentially Relevant Data Sources for Personal Exposure Monitoring and Area Monitoring Data for Perchloroethylene[5]**

| Bibliography | url |
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[5] The data sources identified are based on preliminary results to date of the full-text screening step of the Systematic Review process. Further screening and quality control are on-going.

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# Appendix C SUPPORTING TABLE FOR INDUSTRIAL AND COMMERCIAL ACTIVITIES AND USES CONCEPTUAL MODEL

**Table_Apx C-1. Industrial and Commercial Activities and Uses Conceptual Model Supporting Table**

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Manufacture | Domestic Manufacture | Domestic Manufacture | Manufacture of perchloroethylene via chlorination of ethylene dichloride, chlorination of C1-C3 hydrocarbons, oxychlorination of C2 chlorinated hydrocarbons, and as a byproduct | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <10 min due to volatilization. Number of exposed workers may be high per CDR (2 submissions reported 100-500 workers each). |
| | | | | Vapor | Inhalation | Workers | Yes | perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during manufacturing. |
| Manufacture | Import | Import | Repackaging of import containers | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <10 min due to volatilization. Exposure will only occur in the event the imported material is repackaged. |
| | | | | Vapor | Inhalation | Workers | Yes | Exposure expected only in the event the imported material is repackaged into different sized containers. Exposure frequency may be low. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| | | | | Vapor | Inhalation | ONU | Yes | Exposure expected only in the event the imported material is repackaged into different sized containers. Exposure frequency may be low. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during import. |
| Processing | Processing as a reactant | Intermediate in industrial gas manufacturing; all other basic inorganic chemical manufacturing; all other basic organic chemical manufacturing; and petroleum refining | Manufacture of HCFCs, HFCs, CFCs, trichloroacetyl chloride, HCl, muriatic acid, and refinery reformer and isomerization catalyst regeneration | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <10 min due to volatilization. However, the number of workers may be high per CDR (1 submission reporting 10-25 workers, 2 submissions reporting 100-500 workers, and 5 submissions reporting NKRA). |
| | | | | Vapor | Inhalation | Workers | Yes | perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. However, potential for exposure may be low in scenarios where perchloroethylene is consumed as a chemical intermediate. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. However, potential for exposure may be low in scenarios where perchloroethylene is consumed as a chemical intermediate. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during processing as an intermediate. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Processing | Incorporated into formulation, mixture or reaction product | Solvent for cleaning or degreasing; adhesive and sealant chemicals; paint and coating products; and other chemical products and preparations | Formulation of aerosol and non-aerosol products | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <10 min due to volatilization. However, the number of workers may be high per CDR (1 submission reporting <10 workers, 1 submission reporting 10-25 workers, 1 submission reporting 25-50 workers, 2 submissions reporting 50-100 workers, 2 submissions reporting 100-500 workers, and 3 submissions reporting NKRA). |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected at processing sites that formulate products containing perchloroethylene. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected at processing sites that formulate products containing perchloroethylene. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during processing/formulation operations. |
| Processing | Incorporated into articles | Plastics and rubber products manufacturing; and textile processing | Plastics converting; and textile finishing | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <10 min due to volatilization. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected at processing sites that incorporate perchloroethylene into articles. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected at processing sites that incorporate perchloroethylene into articles. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during processing operations. |
| Processing | Repackaging | Solvent for cleaning or degreasing; and intermediate | Repackaging into large and small containers | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <10 min due to volatilization. Exposure frequency may be low. |
| | | | | Vapor | Inhalation | Workers | Yes | Exposure frequency may be low. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Exposure frequency may be low. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during repackaging. |
| Processing | Recycling | Recycling | Recycling of process solvents containing perchloroethylene | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <10 min due to volatilization. EPA expects significant volume of perchloroethylene to be sent to off-site recycling (~67% of reported releases/transfers in TRI were reported as transfers to off-site recycling). |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected at recycling sites. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. EPA expects significant volume of perchloroethylene to be sent to off-site recycling (~67% of reported releases/transfers in TRI were reported as transfers to off-site recycling). |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected at recycling sites. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. EPA expects significant volume of perchloroethylene to be sent to off-site recycling (~67% of reported releases/transfers in TRI were reported as transfers to off-site recycling). |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during recycling. |
| Distribution in commerce | Distribution | Distribution | Distribution of bulk shipment of perchloroethylene; and distribution of formulated products | Liquid Contact, Vapor | Dermal/ Inhalation | Workers, ONU | No | Exposure will only occur in the event of spills. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Industrial use | Solvents (for cleaning or degreasing) | Batch vapor degreaser (e.g., open-top, closed-loop); and In-line vapor degreaser (e.g., conveyorized, web cleaner) | Open top vapor degreasing (OTVD); OTVD with enclosures; Conveyorized vapor degreasing; Cross-rod and ferris wheel vapor degreasing; Web vapor degreasing; Airtight closed-loop degreasing system; Airless vacuum-to-vacuum degreasing system; Airless vacuum drying degreasing system | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <10 min due to volatilization. However, repeat contact or dermal immersion may occur, especially while cleaning and maintaining degreasing equipment. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected for vapor degreasing activities. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected for vapor degreasing activities. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during degreasing operations. |
| Industrial use | Solvents (for cleaning or degreasing) | Cold cleaner | Cold cleaning - maintenance (manual spray; spray sink; dip tank) | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <10 min due to volatilization. However, repeat contact or dermal immersion may occur. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected for cold cleaning activities. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected for cold cleaning activities. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | EPA will further evaluate to determine if mist generation is applicable. |
| Industrial use | Processing aids | Pesticide, fertilizer and other agricultural chemical manufacturing; and petrochemical manufacturing | Industrial processing aid | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <10 min due to volatilization. Additionally, EPA will need additional information to fully understand the use of perchloroethylene in this scenario to determine potential for dermal exposure. |
| | | | | Vapor | Inhalation | Workers | Yes | perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. However, EPA will need additional information to fully understand the use of perchloroethylene in this scenario to determine potential for inhalation exposure. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. However, EPA will need additional information to fully understand the use of perchloroethylene in this scenario to determine potential for inhalation exposure. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during use of industrial processing aid. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Industrial use | Other uses | Textile processing; wood furniture manufacturing; laboratory chemicals; and foundry applications | See Table XX for specific scenario corresponding to the condition of use. | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <10 min due to volatilization. However, repeat contact may occur for some miscellaneous conditions of use. |
| | | | | Vapor | Inhalation | Workers | Yes | perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | EPA will further analyze to determine if mist generation is applicable to specific conditions of use in this scenario. |
| Industrial / commercial / consumer use | Solvents (for cleaning or degreasing) | Aerosol spray degreaser/ cleaner | Aerosol use in degreasing/ cleaning | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <10 min due to volatilization. However, repeat contact may occur. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected for aerosol degreasing activities. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected for aerosol degreasing activities. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analylzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | Mist generation expected for aerosol applications. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Industrial / commercial / consumer use | Solvents (for cleaning or degreasing); and cleaning and furniture care products | Dry cleaning solvent; and spot cleaner | Industrial and commercial dry cleaning | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <10 min due to volatilization. However, repeat contact may occur. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected for dry cleaning activities. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected for dry cleaning activities. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | Mist generation expected for spot cleaning. |
| | | | | Indoor vapor | Dermal | Co-located population | No | Exposure via dermal and oral routes may be unlikely. |
| | | | | Indoor vapor | Oral | Co-located population | No | Exposure via dermal and oral routes may be unlikely. |
| | | | | Indoor vapor | Inhalation | Co-located population | No | EPA expects persons living in residences co-located with dry cleaners to be exposed to vapor. Exposure will occur primarily via the inhalation route. However, the NESHAP for the use of perchloroethylene in Dry Cleaners required the phase-out of perchloroethylene in co-located buildings by 2020. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Industrial / commercial / consumer use | Lubricants and greases | Lubricants and greases (e.g., penetrating lubricants, cutting tool coolants, aerosol lubricants) | Aerosol application of lubricants to substrates | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <10 min due to volatilization. However, repeat contact may occur. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected for application of aerosol lubricants. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected for application of aerosol lubricants. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | Mist generation expected for aerosol applications. |
| Industrial / commercial / consumer use | Lubricants and greases | Metalworking lubricants (cutting fluids) | Use of metalworking fluids (cutting fluids) | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <10 min due to volatilization. However, repeat contact may occur. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected for use of metalworking fluids. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected for use of metalworking fluids. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | Mist generation expected from use of metalworking fluids. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Industrial / commercial / consumer use | Adhesives and sealants | Solvent-based adhesives and sealants; and light repair adhesives | Spray adhesive application; and other adhesive and sealant applications (e.g. roll) | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <10 min due to volatilization. However, repeat contact may occur. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected from adhesive applications. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected from adhesive applications. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | Mist generation expected for spray and roll applications. EPA will further analyze to determine if mist generation is applicable for each adhesive/sealant product. |
| Industrial / commercial / consumer use | Paints and coatings including paint and coating removers | Solvent-based paints and coatings | Spray coating application; and other paint and coating applications (e.g. roll) | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <10 min due to volatilization. However, repeat contact may occur. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected from coating applications. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected from coating applications. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | Mist generation expected for spray and roll applications. EPA will further analyze to determine if mist generation is applicable for each paint/coating product. |
| Commercial / consumer use | Cleaning and furniture care products | Automotive care products (e.g., engine degreaser and brake cleaner) | Commercial auto repair/ servicing | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <10 min due to volatilization. However, repeat contact may occur. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected for aerosol degreasing activities. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected for aerosol degreasing activities. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | Mist generation expected for aerosol applications. |
| Commercial / consumer use | Cleaning and furniture care products | Non-aerosol cleaner | Wipe cleaning | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <10 min due to volatilization. However, repeat contact may occur. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected from wipe cleaning. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected from wipe cleaning. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further anallyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during wipe cleaning. |
| Commercial / consumer use | Cleaning and furniture care products | Carpet cleaner | Commercial carpet spotting and stain removers | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <10 min due to volatilization. However, repeat contact may occur. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected from carpet cleaning. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected from carpet cleaning. perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be furtheranalyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | EPA will further analyze to determine if mist generation is applicable. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Commercial / consumer use | Other uses | Laboratory chemicals; metal and stone polishes; inks and ink removal products; welding; photographic film; and mold cleaning, release and protectant products | See Table XX for specific scenario corresponding to the condition of use. | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <10 min due to volatilization. However, repeat contact may occur may occur for some miscellaneous conditions of use. |
| | | | | Vapor | Inhalation | Workers | Yes | perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | EPA will further analyze to determine if mist generation is applicable to specific conditions of use in this scenario. |
| Disposal | Waste Handling, Treatment and Disposal | Disposal of perchloroethylene wastes | Worker handling of wastes | Liquid Contact | Dermal | Workers | Yes | Contact time with skin is expected to be <10 min due to volatilization. Frequency of exposure and the potential for dermal immersion needs to be further analyzed. |
| | | | | Vapor | Inhalation | Workers | Yes | perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical. |
| | | | | Vapor | Inhalation | ONU | Yes | perchloroethylene is semi-volatile (VP = 18.5 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected from waste handling. |

# Appendix D SUPPORTING TABLE FOR CONSUMER ACTIVITIES AND USES CONCEPTUAL MODEL

**Table_Apx D-1. Consumer Activities and Uses Conceptual Model Supporting Table**

| Categories of Conditions of Use for Consumer Activities | Exposure Pathway | Exposure Pathway | Receptor | Rationale for Inclusion |
|---|---|---|---|---|
| Cleaning and Furniture Care Products; Lubricants and Greases; Adhesives and Sealants; Paints and Coatings; Dry Cleaned Clothing and Textiles; Other Uses | Liquid Contact | Dermal | Consumer | Perchloroethylene is found in consumer products, dermal contact to perchloroethylene containing liquids will be further analyzed for consumer exposure |
| | Vapor/Mist (Includes Liquid Contact) | Inhalation (includes Oral) | Consumer, Bystanders | Perchloroethylene is found in consumer products and may volatilize, depending on product formulation and percent composition. Inhalation exposure to perchloroethylene containing liquids will be further analyzed for consumers and bystanders |

ONU = Occupational Non-User

# Appendix E SUPPORTING TABLE FOR ENVIRONMENTAL RELEASES AND WASTES CONCEPTUAL MODEL

**Table_Apx E-1. Environmental Releases and Wastes Conceptual Model Supporting Table**

| Life Cycle Stage | Release Category | Release/ Exposure Scenario | Exposure Pathway/ Media | Exposure Routes | Receptor/ Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation/ no Further |
|---|---|---|---|---|---|---|---|
| Manufacture and Import; Processing as Reactant/ Intermediate; Incorporation into Formulation; Mixture or Reaction Product; Incorporation into Article; Use of Product of Article; Repackaging; Recycling | Wastewater or Liquid Wastes | Industrial Pre-Treatment and Industrial WWT and/or Municipal WWT | Water, Sediment | Water | Aquatic Species | Yes | Perchloroethylene toxicity to aquatic and sediment dwelling aquatic species is expected to be low-moderate; perchloroethylene has low bioaccumulation potential, and conservative estimates for surface water and sediment concentrations due to current TSCA uses were below identified COCs |

# Appendix F INCLUSION AND EXCLUSION CRITERIA FOR FULL TEXT SCREENING

Appendix F contains the eligibility criteria for various data streams informing the TSCA risk evaluation: environmental fate; engineering and occupational exposure; exposure to consumers; and human health hazard. The criteria are applied to the *on-topic* references that were identified following title and abstract screening of the comprehensive search results published on June 22, 2017.

Systematic reviews typically describe the study eligibility criteria in the form of PECO statements or a modified framework. PECO stands for Population, Exposure, Comparator and Outcome and the approach is used to formulate explicit and detailed criteria about those characteristics in the publication that should be present in order to be eligible for inclusion in the review. EPA/OPPT adopted the PECO approach to guide the inclusion/exclusion decisions during full text screening.

Inclusion and exclusion criteria were also used during the title and abstract screening, and documentation about the criteria can be found in the *Strategy for Conducting Literature Searches* document published in June 2017 along with each of the TSCA Scope documents. The list of *on-topic* references resulting from the title and abstract screening is undergoing full text screening using the criteria in the PECO statements. The overall objective of the screening process is to select the most relevant evidence for the TSCA risk evaluation. As a general rule, EPA is excluding non-English data/information sources and will translate on a case by case basis.

The inclusion and exclusion criteria for ecotoxicological data have been documented in the ECOTOX SOPs. The criteria can be found at https://cfpub.epa.gov/ecotox/help.cfm?helptabs=tab4) and in the *Strategy for Conducting Literature Searches* document published along with each of the TSCA Scope documents.

Since full text screening commenced right after the publication of the TSCA Scope document, the criteria were set to be broad to capture relevant information that would support the initial risk evaluation. Thus, the inclusion and exclusion criteria for full text screening do not reflect the refinements to the conceptual model and analysis plan resulting from problem formulation. As part of the iterative process, EPA is in the process of refining the results of the full text screening to incorporate the changes in information/data needs to support the revised risk evaluation.

These refinements will include changes to the inclusion and exclusion criteria discussed in this appendix to better support the revised risk evaluation and will likely reduce the number of data/information sources that will undergo evaluation.

## F.1 Inclusion Criteria for Data Sources Reporting Environmental Fate Data

EPA/OPPT developed a generic PESO statement to guide the full text screening of environmental fate data sources. PESO stands for Pathways and Processes, Exposure, Setting or Scenario, and Outcomes. Subsequent versions of the PESO statement may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the inclusion criteria in the PESO statement are eligible for inclusion, considered for evaluation, and possibly included in the environmental fate assessment. On the other hand, data sources are excluded if they do not meet the criteria in the PESO statement.

EPA describes the expected exposure pathways to human receptors from consumer uses of perchloroethylene that EPA plans to include in the risk evaluation in Section 2.5.2. EPA expects that the primary route of exposure for consumers will be via inhalation. There may also be dermal exposure. Environmental fate data will not be used to further assess these exposure pathways as they are expected to occur in the indoor environment.

During problem formulation, exposure pathways to human and ecological receptors from environmental releases and waste stream associated with industrial and commercial activities will not be further analyzed in risk evaluation. For a description of the rationale behind this conclusion, see Section 2.5.3.2. In the absence of exposure pathways for further analysis, environmental fate data will not be further evaluated. Therefore, PESO statements describing fate endpoints, associated processes, media and exposure pathways that were considered in the development of the environmental fate assessment for perchloroethylene will not be presented.

## F.2 Inclusion Criteria for Data Sources Reporting Engineering and Occupational Exposure Data

EPA/OPPT developed a generic RESO statement to guide the full text screening of engineering and occupational exposure literature(Table Apx F-3). RESO stands for Receptors, Exposure, Setting or Scenario, and Outcomes. Subsequent versions of the RESO statement may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the inclusion criteria specified in the RESO statement will be eligible for inclusion, considered for evaluation, and possibly included in the environmental release and occupational exposure assessments, while those that do not meet these criteria will be excluded.

The RESO statement should be used along with the engineering and occupational exposure data needs table (Table_Apx F-3) when screening the literature.

Since full text screening commenced right after the publication of the TSCA Scope document, the criteria for engineering and occupational exposure data were set to be broad to capture relevant information that would support the risk evaluation. Thus, the inclusion and exclusion criteria for full text screening do not reflect the refinements to the conceptual model and analysis plan resulting from problem formulation. As part of the iterative process, EPA is in the process of refining the results of the full text screening to incorporate the changes in information/data needs to support the revised risk evaluation.

**Table_Apx F-1. Inclusion Criteria for Data Sources Reporting Engineering and Occupational Exposure Data**

| RESO Element | Evidence |
|---|---|
| Receptors | • **Humans:**<br>Workers, including occupational non-users<br><br>• **Environment:**<br>Aquatic ecological receptors (release estimates input to Exposure)<br><br>Please refer to the conceptual models for more information about the ecological and human receptors included in the TSCA risk evaluation. |
| Exposure | • Worker exposure to and occupational environmental releases of the chemical substance of interest<br>o Dermal and inhalation exposure routes (as indicated in the conceptual model)<br>o Surface water (as indicated in the conceptual model)<br><br>Please refer to the conceptual models for more information about the routes and media/pathways included in the TSCA risk evaluation. |
| Setting or Scenario | • Any occupational setting or scenario resulting in worker exposure and environmental releases (includes all manufacturing, processing, use, disposal indicated in Table A-3. |
| Outcomes | • Quantitative estimates* of worker exposures and of environmental releases from occupational settings<br>• General information and data related and relevant to the occupational estimates* |

* Metrics (e.g., mg/kg/day or mg/m$^3$ for worker exposures, kg/site/day for releases) are determined by toxicologists for worker exposures and by exposure assessors for releases; also, the Engineering, Release, and Occupational Exposure Data Needs (Table 2) provides a list of related and relevant general information.

TSCA=Toxic Substances Control Act

**Table_Apx F-2. Engineering, Environmental Release and Occupational Data Necessary to Develop the Environmental Release and Occupational Exposure Assessments**

| Objective Determined during Scoping | Type of Data |
|---|---|
| General Engineering Assessment (may apply for either or both Occupational Exposures and / or Environmental Releases) | 1. Description of the life cycle of the chemical(s) of interest, from manufacture to end-of-life (e.g., each manufacturing, processing, or use step), and material flow between the industrial and commercial life cycle stages. [Tags: Life cycle description, Life cycle diagram][a]<br>2. The total annual U.S. volume (lb/yr or kg/yr) of the chemical(s) of interest manufactured, imported, processed, and used; and the share of total annual manufacturing and import volume that is processed or used in each life cycle step. [Tags: Production volume, Import volume, Use volume, Percent PV] [a]<br>3. Description of processes, equipment, unit operations, and material flows and frequencies (lb/site-day or kg/site-day and days/yr; lb/site-batch and batches/yr) of the chemical(s) of interest during each industrial/ commercial life cycle step. Note: if available, include weight fractions of the chemicals (s) of interest and material flows of all associated primary chemicals (especially water). [Tags: Process description, Process material flow rate, Annual operating days, Annual batches, Weight fractions (for each of above, manufacture, import, processing, use)] [a]<br>4. Basic chemical properties relevant for assessing exposures and releases, e.g., molecular weight, normal boiling point, melting point, physical forms, and room temperature vapor pressure. [Tags: Molecular weight, Boiling point, Melting point, Physical form, Vapor pressure, Water solubility] [a]<br>5. Number of sites that manufacture, process, or use the chemical(s) of interest for each industrial/ commercial life cycle step and site locations. [Tags: Numbers of sites (manufacture, import, processing, use), Site locations] [a] |
| Occupational Exposures | 6. Description of worker activities with exposure potential during the manufacture, processing, or use of the chemical(s) of interest in each industrial/commercial life cycle stage. [Tags: Worker activities (manufacture, import, processing, use)] [a]<br>7. Potential routes of exposure (e.g., inhalation, dermal). [Tags: Routes of exposure (manufacture, import, processing, use)] [a]<br>8. Physical form of the chemical(s) of interest for each exposure route (e.g., liquid, vapor, mist) and activity. [Tags: Physical form during worker activities (manufacture, import, processing, use)] [a]<br>9. Breathing zone (personal sample) measurements of occupational exposures to the chemical(s) of interest, measured as time-weighted averages (TWAs), short-term exposures, or peak exposures in each occupational life cycle stage (or in a workplace scenario similar to an occupational life cycle stage). [Tags: PBZ measurements (manufacture, import, processing, use)] [a]<br>10. Area or stationary measurements of airborne concentrations of the chemical(s) of interest in each occupational setting and life cycle stage (or in a workplace scenario similar to the life cycle stage of interest). [Tags: Area measurements (manufacture, import, processing, use)] [a]<br>11. For solids, bulk and dust particle size characterization data. [Tags: PSD measurements (manufacture, import, processing, use)] [a]<br>12. Dermal exposure data. [Tags: Dermal measurements (manufacture, import, processing, use)]<br>13. Data needs associated with mathematical modeling (will be determined on a case-by-case basis). [Tags: Worker exposure modeling data needs (manufacture, import, processing, use)] [a]<br>14. Exposure duration (hr/day). [Tags: Worker exposure durations (manufacture, import, processing, use)] [a]<br>15. Exposure frequency (days/yr). [Tags: Worker exposure frequencies (manufacture, import, processing, use)] [a]<br>16. Number of workers who potentially handle or have exposure to the chemical(s) of interest in each occupational life cycle stage. [Tags: Numbers of workers exposed (manufacture, import, processing, use)] [a]<br>17. Personal protective equipment (PPE) types employed by the industries within scope. [Tags: Worker PPE (manufacture, import, processing, use)] [a]<br>18. Engineering controls employed to reduce occupational exposures in each occupational life cycle stage (or in a workplace scenario similar to the life cycle stage of interest), and associated data or estimates of |

| Objective Determined during Scoping | Type of Data |
|---|---|
| | exposure reductions. [Tags: Engineering controls (manufacture, import, processing, use), Engineering control effectiveness data] [a] |
| Environmental Releases | 19. Description of relvant sources of potential environmental releases, including cleaning of residues from process equipment and transport containers, involved during the manufacture, processing, or use of the chemical(s) of interest in each life cycle stage. [Tags: Release sources (manufacture, import, processing, use)] [a]<br>20. Estimated mass (lb or kg) of the chemical(s) of interest released from industrial and commercial sites to each relevant environmental media (air, water, land) and treatment and disposal methods (POTW, incineration, landfill), including releases per site and aggregated over all sites (annual release rates, daily release rates) [Tags: Release rates (manufacture, import, processing, use)] [a]<br>21. Release or emission factors. [Tags: Emission factors (manufacture, import, processing, use)] [a]<br>22. Number of release days per year. [Tags: Release frequencies (manufacture, import, processing, use)] [a]<br>23. Data needs associated with mathematical modeling (will be determined on a case-by-case basis). [Tags: Release modeling data needs (manufacture, import, processing, use)] [a]<br>24. Waste treatment methods and pollution control devices employed by the industries within scope and associated data on release/emission reductions. [Tags: Treatment/ emission controls (manufacture, import, processing, use), Treatment/ emission controls removal/ effectiveness data] [a] |

**Notes:**

[a] These are the tags included in the full text screening form. The screener makes a selection from these specific tags, which describe more specific types of data or information.

**Abbreviations:**

hr=Hour
kg=Kilogram(s)
lb=Pound(s)
yr=Year
PV=Particle volume
PBZ=
POTW=Publicly owned treatment works
PPE=Personal projection equipment
PSD=Particle size distribution
TWA=Time-weighted average

## F.3 Inclusion Criteria for Data Sources Reporting Exposure Data on Consumers and Ecological Receptors

EPA/OPPT developed PECO statements to guide the full text screening of exposure data/information for human (i.e., consumers, potentially exposed or susceptible subpopulations) and ecological receptors. Subsequent versions of the PECO statements may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the inclusion criteria in the PECO statement are eligible for inclusion, considered for evaluation, and possibly included in the exposure assessment. On the other hand, data sources are excluded if they do not meet the criteria in the PECO statement. The perchloroethylene-specific PECO is provided in Table_Apx F-5.

Since full text screening commenced right after the publication of the TSCA Scope document, the criteria for exposure data were set to be broad to capture relevant information that would support the risk evaluation. Thus, the inclusion and exclusion criteria for full text screening do not reflect the refinements to the conceptual model and analysis plan resulting from problem formulation. As part of the iterative process, EPA is in the process of refining the results of the full text screening to incorporate the changes in information/data needs to support the risk evaluation.

**Table_Apx F-3. Inclusion Criteria for the Data Sources Reporting Perchloroethylene Exposure Data on Consumers and Ecological Receptors**

| PECO Element | Evidence |
|---|---|
| **P**opulation | **Human:** Consumers; bystanders in the home; children; infants; pregnant women; lactating women. |
| | **Ecological:** Aquatic species. |
| **E**xposure | **Expected Primary Exposure Sources, Pathways, Routes:**<br>• Sources: Industrial and commercial activities involving non-closed systems producing releases to surface water; consumer uses in the home producing releases to air and dermal contact<br>• Pathways: indoor air, direct contact and surface water.<br>• Routes of Exposure: Inhalation via indoor air (consumer and bystander populations) and incidental ingestion of aerosols and mists; dermal exposure via direct contact with consumer products containing perchloroethylene |
| **C**omparator (Scenario) | **Human:** Consider media-specific background exposure scenarios and use/source specific exposure scenarios as well as which receptors are and are not reasonably exposed across the projected exposure scenarios. |
| | **Ecological:** Consider media-specific background exposure scenarios and use/source specific exposure scenarios as well as which receptors are and are not reasonably exposed across the projected exposure scenarios. |
| **O**utcomes for Exposure Concentration or Dose | **Human:** Acute, subchronic, and/or chronic external dose estimates (mg/kg/day); acute, subchronic, and/or chronic air and water concentration estimates ($mg/m^3$ or mg/L). Both external potential dose and internal dose based on biomonitoring and reverse dosimetry mg/kg/day will be considered. |
| | **Ecological:** A wide range of ecological receptors will be considered (range depending on available ecotoxicity data). |

**Abbreviations:**
Kg=Kilogram(s)
Mg=Milligram(s)
$M^3$=Cubic meter
L=Liter(s)

## F.4 Inclusion Criteria for Data Sources Reporting Ecological Hazards

**Table_Apx F-4. Ecological Hazard PECO (Populations, Exposures, Comparators, Outcomes) Statement for Perchloroethylene**

| PECO Element | Evidence |
|---|---|
| **Population** | Tests of the single chemical (*i.e.*, PERC) on live, whole, taxonomically verifiable organisms, (including gametes, embryos, or plant or fungal sections capable of forming whole, new organisms) and *in vitro* systems. |
| **Exposure** | **Chemical:** Tests using single, verifiable chemical, administered through an acceptable route. Must also be used in relevant environmental exposure studies, as determined by usual toxicology standards. |
| | **Concentration:** Study must specify the amount of chemical the organisms were exposed to, either as a concentration in the environment when administered via environmental media (e.g. air, soil, water, or sediment), or as a dosage when introduced directly into or on the organism via oral (e.g. diet or gavage), topical or injection routes. |
| | **Duration:** Study must specify the duration from the time of initial exposure to the time of measurement. May be imprecise, as in "less than 6 months," "one growing season," or "from 3 to 5 weeks." |
| **Comparator** | Study must have controls or reference locations. |
| **Outcome** | Measurable/observable biological effect(s) (e.g. mortality, behavioral, population, biochemical, cellular, physiological, growth, reproduction, etc.) of an acceptable organism to a chemical. |

## F.5 Inclusion Criteria for Data Sources Reporting Human Health Hazards

EPA/OPPT developed a perchloroethylene-specific PECO statement (Table _Apx F-7) to guide the full text screening of the human health hazard literature. Subsequent versions of the PECOs may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the criteria specified in the PECO statement will be eligible for inclusion, considered for evaluation, and possibly included in the human health hazard assessment, while those that do not meet these criteria will be excluded according to the exclusion criteria.

In general, the PECO statements were based on (1) information accompanying the TSCA Scope document, and (2) preliminary review of the health effects literature from authoritative sources cited in the TSCA Scope documents. When applicable, these authoritative sources (e.g., IRIS assessments, EPA/OPPT's Work Plan Problem Formulations or risk assessments) will serve as starting points to identify PECO-relevant studies.

## Table_Apx F-5. Inclusion and Exclusion Criteria for Data Sources Reporting Human Health Hazards Related to Perchloroethylene (PERC)[a]

| PECO Element | Evidence Stream | Papers/Features Included | Papers/Features Excluded |
|---|---|---|---|
| **Population** [b] | *Human* | • Any population<br>• All lifestages<br>• All study designs, includes:<br>  ○ Controlled exposure, cohort, case-control, cross-sectional, case-crossover, ecological, case studies and case series | |
| | *Animal* | • All non-human whole-organism mammalian species<br>• All lifestages | • Non-mammalian species |
| ***Exposure*** | *Human* | • Exposure based on administered dose or concentration of perchloroethylene, biomonitoring data (e.g., urine, blood or other specimens), environmental or occupational-setting monitoring data (e.g., air, water levels), job title or residence<br>• Any metabolites of interest as identified in biomonitoring studies<br>• Exposure identified as ***or presumed to be*** from oral, dermal, inhalation routes<br>• Any number of exposure groups<br>• Quantitative, semi-quantitative or qualitative estimates of exposure<br>• Exposures to multiple chemicals/mixtures only if perchloroethylene or related metabolites were independently measured and analyzed | • Route of exposure ***not*** by inhalation, oral or dermal type (e.g., intraperitoneal, injection)<br>• Multiple chemical/mixture exposures with no independent measurement of or exposure to perchloroethylene (or related metabolite) |
| | *Animal* | • A minimum of 2 quantitative dose or concentration levels of perchloroethylene plus a negative control group [a]<br>• Acute, subchronic, chronic exposure from oral, dermal, inhalation routes<br>• Exposure to perchloroethylene only (no chemical mixtures) | • Only 1 quantitative dose or concentration level in addition to the control [a]<br>• Route of exposure ***not*** by inhalation, oral or dermal type (e.g., intraperitoneal, injection)<br>• No duration of exposure stated<br>• Exposure to perchloroethylene in a chemical mixture |
| **Comparator** | *Human* | • Any or no comparison | |
| | *Animal* | • Negative controls that are vehicle-only treatment and/or no treatment | • Negative controls ***other than*** vehicle-only treatment or no treatment |
| **Outcome** | *Human and Animal* | • Endpoints described in the perchloroethylene scope document [c]:<br>  ○ Acute toxicity<br>  ○ Neurotoxicity<br>  ○ Liver toxicity<br>  ○ Reproductive/developmental toxicity<br>  ○ Irritation<br>  ○ Cancer<br>• Other endpoints [d] | |
| **General Considerations** | | **Papers/Features Included** | **Papers/Features Excluded** |
| | | • Written in English [e] | • Not written in English [e] |

| PECO Element | Evidence Stream | Papers/Features Included | Papers/Features Excluded |
|---|---|---|---|
| | | • Reports a primary source or meta-analysis [a]<br>• Full-text available<br>• Reports both perchloroethylene exposure ***and*** a health outcome | • Reports secondary source (e.g., review papers) [a]<br>• No full-text available (e.g., only a study description/abstract, out-of-print text)<br>• Reports a perchloroethylene-related exposure ***or*** a health outcome, but not both (e.g. incidence, prevalence report) |

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May 2018
Office of Chemical Safety and
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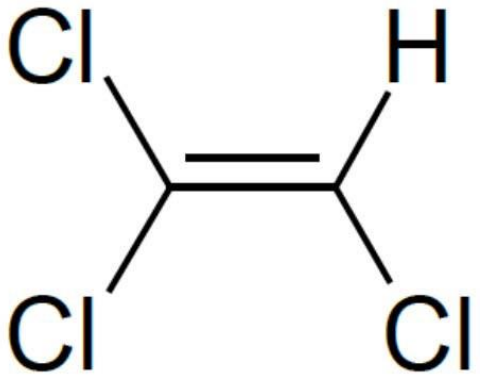
United States
Environmental Protection Agency

# Problem Formulation of the Risk Evaluation for Trichloroethylene

## CASRN: 79-01-6




*May 2018*

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**Docket**

Supporting information can be found in public docket (Docket: EPA-HQ-OPPT-2016-0737).

**Disclaimer**

Reference herein to any specific commercial products, process or service by trade name, trademark, manufacturer or otherwise does not constitute or imply its endorsement, recommendation or favoring by the United States Government.

# ABBREVIATIONS

| | |
|---|---|
| °C | Degrees Celsius |
| $\varepsilon_0$ | Vacuum Permittivity |
| ACGIH | American Conference of Industrial Hygienists |
| AEGL | Acute Exposure Guideline Level |
| AF | Assessment Factor |
| AQS | Air Quality System |
| ATCM | Airborne Toxic Control Measure |
| atm | Atmosphere(s) |
| ATSDR | Agency for Toxic Substances and Disease Registries |
| BAF | Bioaccumulation Factor |
| BCF | Bioconcentration Factor |
| BIOWIN | The EPI Suite™ module that predicts biodegradation rates |
| $BW^{3/4}$ | body weight$^{3/4}$ |
| CAA | Clean Air Act |
| CARB | California Air Resources Board |
| CASRN | Chemical Abstracts Service Registry Number |
| CBI | Confidential Business Information |
| CCR | California Code of Regulations |
| CDC | Centers for Disease Control and Prevention |
| CDR | Chemical Data Reporting |
| CEHD | Chemical Exposure Health Data |
| CEM | Consumer Exposure Model |
| CEPA | Canadian Environmental Protection Act |
| CERCLA | Comprehensive Environmental Response, Compensation, and Liability Act |
| CFC | Chlorofluorocarbon |
| CFR | Code of Federal Regulations |
| ChemSTEER | Chemical Screening Tool for Exposure and Environmental Releases |
| CHIRP | Chemical Risk Information Platform |
| ChV | Chronic Value |
| $cm^3$ | Cubic Centimeter(s) |
| CNS | Central Nervous System |
| COC | Concentration of Concern |
| COU | Conditions of Use |
| CPCat | Chemical and Product Categories |
| CSCL | Chemical Substances Control Law |
| CWA | Clean Water Act |
| CYP2E1 | Cytochrome P450 2E1 |
| DMR | Discharge Monitoring Report |
| $EC_{50}$ | Effect concentration at which 50% of test organisms exhibit an effect |
| ECCC | Environment and Climate Change Canada |
| ECHA | European Chemicals Agency |
| EDC | Ethylene Dichloride |
| E-FAST | Exposure and Fate Assessment Screening Tool |
| EG | Effluent Guidelines |
| EPA | Environmental Protection Agency |
| EPCRA | Emergency Planning and Community Right-to-Know Act |
| EPI Suite™ | Estimation Program Interface Suite™ |
| ESD | Emission Scenario Document |

| | |
|---|---|
| EU | European Union |
| FDA | Food and Drug Administration |
| FFDCA | Federal Food, Drug, and Cosmetic Act |
| FIFRA | Federal Insecticide, Fungicide, and Rodenticide Act |
| FR | Federal Register |
| g | Gram(s) |
| GACT | Generally Available Control Technology |
| GST | Glutathione-S-transferase |
| HAP | Hazardous Air Pollutant |
| HCFC | Hydrochlorofluorocarbon |
| HCl | Hydrochloric Acid |
| HEC | Human Equivalent Concentration |
| HFC | Hydrofluorocarbon |
| HHE | Health Hazard Evaluation |
| HPV | High Production Volume |
| Hr | Hour |
| IARC | International Agency for Research on Cancer |
| ICIS | Integrated Compliance Information System |
| IDLH | Immediately Dangerous to Life and Health |
| IMIS | Integrated Management Information System |
| IRIS | Integrated Risk Information System |
| ISHA | Industrial Safety and Health Act |
| ISOR | Initial Statement of Reasons |
| $K_{oc}$ | Soil Organic Carbon-Water Partitioning Coefficient |
| $K_{ow}$ | Octanol/Water Partition Coefficient |
| kg | Kilogram(s) |
| L | Liter(s) |
| lb | Pound(s) |
| $LC_{50}$ | Lethal Concentration at which 50% of test organisms die |
| LOAEL | Lowest-observed-adverse-effect-level |
| LOEC | Lowest-observable-effect Concentration |
| $m^3$ | Cubic Meter(s) |
| MACT | Maximum Achievable Control Technology |
| MATC | Maximum Acceptable Toxicant Concentration |
| MCCEM | Multi-Chamber Concentration and Exposure Model |
| MCL | Maximum Contaminant Level |
| MCLG | Maximum Contaminant Level Goal |
| mg | Milligram(s) |
| mmHg | Millimeter(s) of Mercury |
| MOA | Mode of Action |
| mPa·s | Millipascal(s)-Second |
| MSDS | Material Safety Data Sheet |
| MSW | Municipal Solid Waste |
| NAICS | North American Industry Classification System |
| NATA | National Scale Air-Toxics Assessment |
| NCEA | National Center for Environmental Assessment |
| NICNAS | Australia National Industrial Chemicals Notification and Assessment Scheme |
| NCP | National Contingency Plan |
| NEI | National Emissions Inventory |

| | |
|---|---|
| NESHAP | National Emission Standards for Hazardous Air Pollutants |
| NHANES | National Health and Nutrition Examination Survey |
| NICNAS | National Industrial Chemicals Notification and Assessment Scheme |
| NIH | National Institute of Health |
| NICNAS | National Industrial Chemicals Notification and Assessment Scheme |
| NIOSH | National Institute for Occupational Safety and Health |
| NITE | National Institute of Technology and Evaluation |
| NOAEL | No-Observed-Adverse-Effect-Level |
| NOEC | No-observable-effect Concentration |
| NPDES | National Pollutant Discharge Elimination System |
| NPDWR | National Primary Drinking Water Regulation |
| NRC | National Research Council |
| NTP | National Toxicology Program |
| NWIS | National Water Information System |
| OCSPP | Office of Chemical Safety and Pollution Prevention |
| OECD | Organization for Economic Co-operation and Development |
| OEHHA | Office of Environmental Health Hazard Assessment |
| OEL | Occupational Exposure Limits |
| ONU | Occupational Non-User |
| OPPT | Office of Pollution Prevention and Toxics |
| OSHA | Occupational Safety and Health Administration |
| OST | Office of Science and Technology |
| OTVD | Open-Top Vapor Degreaser |
| OW | Office of Water |
| PBPK | Physiologically-Based Pharmacokinetic |
| PBZ | Personal Breathing Zone |
| PCE | Tetrachloroethylene |
| PECO | Population, Exposure, Comparator, and Outcome |
| PEL | Permissible Exposure Limit |
| PESS | Potentially Exposed or Susceptible Subpopulations |
| POD | Point of Departure |
| POTW | Publicly Owned Treatment Works |
| ppb | Part(s) per Billion |
| PPE | Personal Protective Equipment |
| ppm | Part(s) per Million |
| PSD | Particle Size Distribution |
| PV | Production Volume |
| QC | Quality Control |
| QSAR | Quantitative Structure Activity Relationship |
| RCRA | Resource Conservation and Recovery Act |
| REACH | Registration, Evaluation, Authorisation and Restriction of Chemicals |
| REL | Relative Exposure Limit |
| RTR | Risk and Technology Review |
| SDS | Safety Data Sheet |
| SDWA | Safe Drinking Water Act |
| SIDS | Screening Information Dataset |
| SNUN | Significant New Use Notice |
| SNUR | Significant New Use Rule |
| SOCMI | Synthetic Organic Chemical Manufacturing Industry |

| | |
|---|---|
| SPARC | SPARC Performs Automated Reasoning in Chemistry |
| SpERC | Specific Environmental Release Categories |
| STEL | Short-Term Exposure Limit |
| STP model | Sewage Treatment Plant model |
| STORET | STOrage and RETrieval |
| TCCR | Transparent, clear, consistent, and reasonable |
| TCE | Trichloroethylene |
| TLV | Threshold Limit Value |
| TRI | Toxics Release Inventory |
| TSCA | Toxic Substances Control Act |
| TWA | Time Weighted Average |
| UIC | Underground Injection Control |
| U.S. | United States |
| UV | Ultraviolet |
| USGS | United States Geological Survey |
| VOC | Volatile Organic Compound |
| VP | Vapor Pressure |
| Yr | Year(s) |

# EXECUTIVE SUMMARY

TSCA § 6(b)(4) requires the U.S. Environmental Protection Agency (EPA) to establish a risk evaluation process. In performing risk evaluations for existing chemicals, EPA is directed to "determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of costs or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator under the conditions of use." In December of 2016, EPA published a list of 10 chemical substances that are the subject of the Agency's initial chemical risk evaluations (81 FR 91927), as required by TSCA § 6(b)(2)(A). Trichloroethylene was one of these chemicals.

TSCA § 6(b)(4)(D) requires that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use and potentially exposed or susceptible subpopulations that the Administrator expects to consider. In June 2017, EPA published the Scope of the Risk Evaluation for trichloroethylene (EPA-HQ-OPPT-2016-0737-0057; U.S. EPA, 2017d). As explained in the Scope Document, because there was insufficient time for EPA to provide an opportunity for comment on a draft of the scope, as EPA intends to do for future scope documents, EPA is publishing and taking public comment on a problem formulation document to refine the current scope, as an additional interim step prior to publication of the draft risk evaluation for trichloroethylene. Comments received on this problem formulation document will inform development of the draft risk evaluation.

This problem formulation document refines the conditions of use, exposures and hazards presented in the scope of the risk evaluation for trichloroethylene and presents refined conceptual models and analysis plans that describe how EPA expects to evaluate the risk for trichloroethylene.

Trichloroethylene, also known as TCE, is a volatile organic liquid that is classified as a human carcinogen. TCE is subject to numerous federal and state regulations and reporting requirements. In the 2014 TCE risk assessment (U.S. EPA, 2014c), EPA assessed inhalation risks from TCE in vapor and aerosol degreasing, spot cleaning at dry cleaning facilities and arts and craft uses and also completed four supplemental analyses. Based on these analyses, EPA published two proposed rules to address the risks presented by TCE use in vapor degreasing and in commercial and consumer aerosol degreasing and for spot cleaning at dry cleaning facilities. TCE is designated as a Hazardous Air Pollutant (HAP) under the Clean Air Act (CAA), a regulated drinking water contaminant under the Safe Drinking Water Act (SDWA), and a toxic pollutant under the Clean Water Act (CWA). TCE is widely used in industrial and commercial processes.

Information on domestic manufacture, processing, use, and disposal of TCE is available to EPA through its Chemical Data Reporting (CDR) Rule, issued under the TSCA, as well as through the Toxics Release Inventory (TRI). In 2015, approximately 172 million pounds of TCE was manufactured or imported in the US. An estimated 83.6% of TCE's annual production volume is used as an intermediate in the manufacture of hydrofluorocarbon (HFC-134a – an alternative to the refrigerant CFC-12). Another 14.7% of TCE production volume is used as a degreasing solvent, leaving approximately 1.7% for other uses, including consumer uses. Based on 2015 TRI data, most reported environmental releases of TCE are to air, with much lower volumes disposed to land or released to water. It is expected to be moderately persistent in the environment and has a low bioaccumulation potential.

This document presents the potential exposures that may result from the conditions of use of TCE. Exposure may occur through inhalation, oral and dermal pathways, due to trichloroethylene's widespread presence in a variety of environmental media. Exposures to the general population may

occur from industrial and/or commercial uses; industrial releases to air, water or land; and other conditions of use. Workers and occupational non-users may be exposed to trichloroethylene during a variety of conditions of use, such as manufacturing, processing and industrial and commercial uses, including uses in paint and coatings, adhesives and degreasing. EPA expects that the highest exposures to trichloroethylene generally involve workers in industrial and commercial settings. Trichloroethylene can be found in numerous products and can, therefore, result in exposures to commercial and consumer users in indoor or outdoor environments. For trichloroethylene, EPA considers workers, occupational non-users, consumers, bystanders, and certain other groups of individuals who may experience greater exposures than the general population due to proximity to conditions of use to be potentially exposed or susceptible subpopulations. EPA will evaluate whether groups of individuals within the general population may be exposed via pathways that are distinct from the general population due to unique characteristics (e.g., life stage, behaviors, activities, duration) that increase exposure, and whether groups of individuals have heightened susceptibility, and should therefore be considered potentially exposed or susceptible subpopulations for purposes of the risk evaluation. For environmental release pathways, EPA plans to further analyze surface water exposure to aquatic species (i.e. aquatic plants) in the risk evaluation.

TCE has been the subject of numerous health hazard and risk assessments. TCE toxicity was assessed in 2011 under the *EPA Integrated Risk Information System (IRIS) Toxicological Review of Trichloroethylene* (U.S. EPA, 2011c), which served as the toxicological basis for the 2014 final TCE risk assessment (U.S. EPA, 2014c). For non-cancer effects, TCE exposure has been associated with acute toxicity, liver toxicity, kidney toxicity, reproductive/developmental toxicity, neurotoxicity, immunotoxicity, and sensitization. TCE is also carcinogenic to humans by all routes of exposures, as documented in the TCE IRIS assessment, through both genotoxic and non-genotoxic mechanisms. These hazards will be evaluated based on the specific exposure scenarios identified.

The revised conceptual models presented in this problem formulation identify conditions of use; exposure pathways (e.g., media); exposure routes (e.g., inhalation, dermal, oral); potentially exposed or susceptible subpopulations; and hazards EPA expects to analyze further in the risk evaluation. The initial conceptual models provided in the scope document were revised during problem formulation based on evaluation of reasonably available information for physical and chemical properties, fate, exposures, hazards, and conditions of use and based upon consideration of other statutory and regulatory authorities. In each problem formulation document for the first 10 chemical substances, EPA also refined the activities, hazards, and exposure pathways that will be included in and excluded from the risk evaluation.

EPA's overall objectives in the risk evaluation process are to conduct timely, relevant, high-quality, and scientifically credible risk evaluations within the statutory deadlines, and to evaluate the conditions of use that raise greatest potential for risk 82 FR 33726, 33728 (July 20, 2017).

# 1 INTRODUCTION

This document presents for comment the problem formulation of the risk evaluation to be conducted for TCE under the Frank R. Lautenberg Chemical Safety for the 21st Century Act. The Frank R. Lautenberg Chemical Safety for the 21st Century Act amended the Toxic Substances Control Act (TSCA), the Nation's primary chemicals management law, on June 22, 2016. The new law includes statutory requirements and deadlines for actions related to conducting risk evaluations of existing chemicals.

In December of 2016, EPA published a list of 10 chemical substances that are the subject of the Agency's initial chemical risk evaluations (81 FR 91927), as required by TSCA § 6(b)(2)(A). These 10 chemical substances were drawn from the 2014 update of EPA's TSCA Work Plan for Chemical Assessments, a list of chemicals that EPA identified in 2012 and updated in 2014 (currently totaling 90 chemicals) for further assessment under TSCA. EPA's designation of the first 10 chemical substances constituted the initiation of the risk evaluation process for each of these chemical substances, pursuant to the requirements of TSCA § 6(b)(4).

TSCA § 6(b)(4)(D) requires that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use and potentially exposed or susceptible subpopulations that the Administrator expects to consider, within 6 months after the initiation of a risk evaluation. The scope documents for all first 10 chemical substances were issued on June 22, 2017. The first 10 problem formulation documents are a refinement of what was presented in the first 10 scope documents. TSCA § 6(b)(4)(D) does not distinguish between scoping and problem formulation, and requires EPA to issue scope documents that include information about the chemical substance, such as the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations that the Administrator expects to consider in the risk evaluation. In the future, EPA expects scoping and problem formulation to be completed prior to the issuance of scope documents and intends to issue scope documents that include problem formulation.

As explained in the scope document, because there was insufficient time for EPA to provide an opportunity for comment on a draft of the scope, as EPA intends to do for future scope documents, EPA is publishing and taking public comment on a problem formulation document to refine the current scope, as an additional interim step prior to publication of the draft risk evaluation for TCE. Comments received on this problem formulation document will inform development of the draft risk evaluation.

The Agency defines problem formulation as the analytical phase of the risk assessment in which "the purpose for the assessment is articulated, the problem is defined and a plan for analyzing and characterizing risk is determined" (U.S. EPA, 2014b). The outcome of problem formulation is a conceptual model(s) and an analysis plan. The conceptual model describes the linkages between stressors and adverse human health effects, including the stressor(s), exposure pathway(s), exposed lifestage(s) and population(s), and endpoint(s) that will be addressed in the risk evaluation (U.S. EPA, 2014b). The analysis plan follows the development of the conceptual model(s) and is intended to describe the approach for conducting the risk evaluation, including its design, methods and key inputs and intended outputs as described in the EPA Human Health Risk Assessment Framework (U.S. EPA, 2014b). The problem formulation documents refine the initial conceptual models and analysis plans that were provided in the scope documents.

First, EPA has removed from the risk evaluation any activities and exposure pathways that EPA has concluded do not warrant inclusion in the risk evaluation. For example, for some activities which were listed as "conditions of use" in the scope document, EPA has insufficient information following the further investigations during problem formulation to find they are circumstances under which the

chemical is actually "intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of."

Second, EPA also identified certain exposure pathways that are under the jurisdiction of regulatory programs and associated analytical processes carried out under other EPA-administered environmental statutes – namely, the Clean Air Act (CAA), the Safe Drinking Water Act (SDWA), the Clean Water Act (CWA), and the Resource Conservation and Recovery Act (RCRA) – and which EPA does not expect to include in the risk evaluation.

As a general matter, EPA believes that certain programs under other Federal environmental laws adequately assess and effectively manage the risks for the covered exposure pathways. To use Agency resources efficiently under the TSCA program, to avoid duplicating efforts taken pursuant to other Agency programs, to maximize scientific and analytical efforts, and to meet the three-year statutory deadline, EPA is planning to exercise its discretion under TSCA 6(b)(4)(D) to focus its analytical efforts on exposures that are likely to present the greatest concern and consequently merit a risk evaluation under TSCA, by excluding, on a case-by-case basis, certain exposure pathways that fall under the jurisdiction of other EPA-administered statutes.[1] EPA does not expect to include any such excluded pathways as further explained below in the risk evaluation. The provisions of various EPA-administered environmental statutes and their implementing regulations represent the judgment of Congress and the Administrator, respectively, as to the degree of health and environmental risk reduction that is sufficient under the various environmental statutes.

Third, EPA identified any conditions of use, hazards, or exposure pathways which were included in the scope document and that EPA expects to include in the risk evaluation but which EPA does not plan to further analyze in the risk evaluation. EPA expects to be able to reach conclusions about particular conditions of use, hazards or exposure pathways without further analysis and therefore plans to conduct no further analysis on those conditions of use, hazards or exposure pathways in order to focus the Agency's resources on more extensive or quantitative analyses. Each risk evaluation will be "fit-for-purpose," meaning not all conditions of use will warrant the same level of evaluation and the Agency may be able to reach some conclusions without comprehensive or quantitative risk evaluations. 82 FR 33726, 33734, 33739 (July 20, 2017).

EPA received comments on the published scope document for trichloroethylene and has considered the comments specific to trichloroethylene in this problem formulation document. EPA is soliciting public comment on this problem formulation document and when the draft risk evaluation is issued the Agency intends to respond to comments that are submitted. In its draft risk evaluation, EPA may revise the conclusions and approaches contained in this problem formulations, including the conditions of use and pathways covered and the conceptual models and analysis plans, based on comments received.

## 1.1 Regulatory History

EPA conducted a search of existing domestic and international laws, regulations and assessments pertaining to TCE. EPA compiled this summary from data available from federal, state, international and other government sources, as cited in Appendix A. EPA evaluated and considered the impact of

[1] As explained in the final rule for chemical risk evaluation procedures, "EPA may, on a case-by-case basis, exclude certain activities that EPA has determined to be conditions of use in order to focus its analytical efforts on those exposures that are likely to present the greatest concern, and consequently merit an unreasonable risk determination." [82 FR 33726, 33729 (July 20, 2017)]

existing laws and regulations (e.g., regulations on landfill disposal, design, and operations) in the problem formulation step to determine what, if any, further analysis might be necessary as part of the risk evaluation. Consideration of the nexus between these existing regulations and TSCA uses may additionally be made as detailed/specific conditions of use and exposure scenarios are developed in conducting the analysis phase of the risk evaluation.

***Federal Laws and Regulations***
TCE is subject to federal statutes or regulations, other than TSCA, that are implemented by other offices within EPA and/or other federal agencies/departments. A summary of federal laws, regulations and implementing authorities is provided in Appendix A.1.

***State Laws and Regulations***
TCE is subject to state statutes or regulations implemented by state agencies or departments. A summary of state laws, regulations and implementing authorities is provided in Appendix A.2.

***Laws and Regulations in Other Countries and International Treaties or Agreements***
TCE is subject to statutes or regulations in countries other than the United States and/or international treaties and/or agreements. A summary of these laws, regulations, treaties and/or agreements is provided in Appendix A.3.

## 1.2 Assessment History

EPA has identified assessments conducted by other EPA Programs and other organizations (see Table 1-1). Depending on the source, these assessments may include information on conditions of use, hazards, exposures and potentially exposed or susceptible subpopulations. Table 1-1 shows the assessments that have been conducted. EPA found no additional assessments beyond those listed in the Scope Document.

In addition to using this information, EPA intends to conduct a full review of the data collected [see *Trichloroethylene (CASRN 79-01-6) Bibliography: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0737; U.S. EPA, 2017g) using the literature search strategy (see *Strategy for Conducting Literature Searches for Trichloroethylene (TCE): Supplemental Document to the TSCA Scope Document, CASRN: 79-01-6*, EPA-HQ-OPPT-2016-0737)] to ensure that EPA is considering information that has been made available since these assessments were conducted.

The final Work Plan Chemical Risk Assessment of TCE was used to support two proposed rules under TSCA section 6 (81 FR 91592; December 16, 2016; 82 FR 7432; January 19, 2017) to address risks from commercial and consumer solvent degreasing (aerosol and vapor), consumer use as a spray-applied protective coating for arts and crafts and commercial use as a spot remover at dry-cleaning facilities. It was also considered in development of a Significant New Use Rule (SNUR) for TCE (81 FR 20535; April 8, 2016).

**Table 1-1. Assessment History of TCE**

| Authoring Organization | Assessment |
|---|---|
| **EPA Assessments** | |
| Office of Chemical Safety and Pollution Prevention (OCSPP)/ Office of Pollution Prevention and Toxics (OPPT) | TSCA Work Plan Chemical Risk Assessment Trichloroethylene: Degreasing, Spot Cleaning and Arts & Crafts Use (U.S. EPA, 2014c) |

| Authoring Organization | Assessment |
|---|---|
| OCSPP/OPPT | Supplemental Occupational Exposure and Risk Reduction Technical Report in Support of Risk Management Options for Trichloroethylene (TCE) Use in Aerosol Degreasing (U.S. EPA, 2016d) |
| OCSPP/OPPT | Supplemental Exposure and Risk Reduction Technical Report in Support of Risk Management Options for Trichloroethylene (TCE) Use in Consumer Aerosol Degreasing (U.S. EPA, 2016c) |
| OCSPP/OPPT | Supplemental Occupational Exposure and Risk Reduction Technical Report in Support of Risk Management Options for Trichloroethylene (TCE) Use in Spot Cleaning (U.S. EPA, 2016e) |
| OCSPP/OPPT | Supplemental Occupational Exposure and Risk Reduction Technical Report in Support of Risk Management Options for Trichloroethylene (TCE) Use in Vapor Degreasing [RIN 2070-AK11] (U.S. EPA, 2016f) |
| Integrated Risk Information System (IRIS) | Toxicological Review of Trichloroethylene (U.S. EPA, 2011c) |
| National Center for Environmental Assessment (NCEA) | Sources, Emission and Exposure for Trichloroethylene (TCE) and Related Chemicals (U.S. EPA, 2001) |
| Office of Water (OW)/ Office of Science and Technology (OST) | Update of Human Health Ambient Water Quality Criteria: Trichloroethylene (TCE) 79-01-6 (U.S. EPA, 2015) |
| **Other U.S.-Based Organizations** | |
| Agency for Toxic Substances and Disease Registries (ATSDR) | Draft Toxicological Profile for Trichloroethylene (ATSDR, 2014a) |
| National Research Council (NRC) | Assessing the Human Health Risks of Trichloroethylene: Key Scientific Issues (NRC, 2006) |
| Office of Environmental Health Hazard Assessment (OEHHA), Pesticide and Environmental Toxicology Section | Public Heath Goal for Trichloroethylene in Drinking Water (CalEPA, 2009) |
| **International** | |
| Institute for Health and Consumer Protection, European Chemicals Bureau | European Union Risk Assessment Report, Trichloroethylene (EC, 2004) |
| Australia National Industrial Chemicals Notification and Assessment Scheme (NICNAS) | Trichloroethylene: Priority Existing Chemical Assessment Report No. 8 (NICNAS, 2000) |

| Authoring Organization | Assessment |
|---|---|
| Environment and Climate Change Canada (ECCC) | Canadian Environmental Protection Act Priority Substances List Assessment Report: Trichloroethylene (Environment Canada, 1993). |

## 1.3 Data and Information Collection

EPA/OPPT generally applies a systematic review process and workflow that includes: (1) data collection, (2) data evaluation and (3) data integration of the scientific data used in risk evaluations developed under TSCA. Scientific analysis is often iterative in nature as new knowledge is obtained. Hence, EPA/OPPT expects that multiple refinements regarding data collection will occur during the process of risk evaluation. Additional information that may be considered and was not part of the initial comprehensive bibliographies will be documented in the Draft Risk Evaluation for TCE.

***Data Collection: Data Search***

EPA/OPPT conducted chemical-specific searches for data and information on: physical and chemical properties; environmental fate and transport; conditions of use information; environmental exposures, human exposures, including potentially exposed or susceptible subpopulations; ecological hazard, human health hazard, including potentially exposed or susceptible subpopulations.

EPA/OPPT designed its initial data search to be broad enough to capture a comprehensive set of sources containing data and/or information potentially relevant to the risk evaluation. Generally, the search was not limited by date and was conducted on a wide range of data sources, including but not limited to: peer-reviewed literature and gray literature (e.g., publicly-available industry reports, trade association resources, government reports). When available, EPA/OPPT relied on the search strategies from recent assessments, such as EPA Integrated Risk Information System (IRIS) assessments and the NTP *Report on Carcinogens*, to identify relevant references and supplemented these searches to identify relevant information published after the end date of the previous search to capture more recent literature. *Strategy for Conducting Literature Searches for Trichloroethylene (TCE): Supplemental Document to the TSCA Scope Document, CASRN: 79-01-6* (EPA-HQ-OPPT-2016-0737) provides details about the data sources and search terms that were used in the literature search.

***Data Collection: Data Screening***

Following the data search, references were screened and categorized using selection criteria outlined in the *Strategy for Conducting Literature Searches for Trichloroethylene (TCE): Supplemental Document to the TSCA Scope Document, CASRN: 79-01-6* (EPA-HQ-OPPT-2016-0737). Titles and abstracts were screened against the criteria as a first step with the goal of identifying a smaller subset of the relevant data to move into the subsequent data extraction and data evaluation steps. Prior to full-text review, EPA/OPPT anticipates refinements to the search and screening strategies, as informed by an evaluation of the performance of the initial title/abstract screening and categorization process.

The categorization scheme (or tagging structure) used for data screening varies by scientific discipline (i.e., physical and chemical properties; environmental fate and transport; chemical use/conditions of use information; environmental exposures, human exposures, including potentially exposed or susceptible subpopulations identified by virtue of greater exposure; human health hazard, including potentially exposed or susceptible subpopulations identified by virtue of greater susceptibility; and ecological hazard), but within each data set, there are two broad categories or data tags: (1) o*n-topic* references or (2) *off-topic* references. *On-topic* references are those that may contain data and/or information relevant to the risk evaluation. O*ff-topic* references are those that do not appear to contain data or information

relevant to the risk evaluation. The *Strategy for Conducting Literature Searches for Trichloroethylene (TCE): Supplemental Document to the TSCA Scope Document, CASRN: 79-01-6* (EPA-HQ-OPPT-2016-0737) discusses the inclusion and exclusion criteria that EPA/OPPT used to categorize references as *on-topic* or *off-topic*.

Additional data screening using sub-categories (or sub-tags) was also performed to facilitate further sorting of data/information. For example, identifying references by source type (e.g., published peer-reviewed journal article, government report); data type (e.g., primary data, review article); human health hazard (e.g., liver toxicity, cancer, reproductive toxicity); or chemical-specific and use-specific data or information. These sub-categories are described in the supplemental document, *Strategy for Conducting Literature Searches for Trichloroethylene (TCE): Supplemental Document to the TSCA Scope Document, CASRN: 79-01-6* (EPA-HQ-OPPT-2016-0737) and will be used to organize the different streams of data during the stages of data evaluation and data integration steps of systematic review.

Results of the initial search and categorization results can be found in the *Tricholoroethylene (79-01-6) Bibliography: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0737; U.S. EPA, 2017g). This document provides a comprehensive list (bibliography) of the sources of data identified by the initial search and the initial categorization for *on-topic* and *off-topic* references. Because systematic review is an iterative process, EPA/OPPT expects that some references may move from the *on-topic* to the *off-topic* categories, and vice versa. Moreover, targeted supplemental searches may also be conducted to address specific needs for the analysis phase (e.g., to locate specific data needed for modeling); hence, additional *on-topic* references not initially identified in the initial search may be identified as the systematic review process proceeds.

## 1.4 Data Screening During Problem Formulation

EPA/OPPT is in the process of completing the full text screening of the *on-topic* references identified in the *Trichloroethylene (CASRN 79-01-6) Bibliography: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0737; U.S. EPA, 2017g). The screening process at the full-text level is described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018). Appendix F provides the inclusion and exclusion criteria applied at the full text screening. The eligibility criteria are guided by the analytical considerations in the revised conceptual models and analysis plan, as discussed in the problem formulation document. Thus, it is expected that the number of data/information sources entering evaluation is reduced to those that are relevant to address the technical approach and issues described in the analysis plan of this document.

Following the screening process, the quality of the included data/information sources will be assessed using the evaluation strategies that are described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018).

# 2 PROBLEM FORMULATION

As required by TSCA, the scope of the risk evaluation identifies the conditions of use, hazards, exposures and potentially exposed or susceptible subpopulations that the Administrator expects to consider. To communicate and visually convey the relationships between these components, EPA included in the scope document a life cycle diagram and conceptual models that describe the actual or potential relationships between TCE and human and ecological receptors. During the problem formulation, EPA revised the conceptual models based on further data gathering and analysis as presented in this Problem Formulation document. An updated analysis plan is also included which

identifies, to the extent feasible, the approaches and methods that EPA may use to assess exposures, effects (hazards) and risks under the conditions of use of TCE.

## 2.1 Physical and Chemical Properties

Physical-chemical properties influence the environmental behavior and the toxic properties of a chemical, thereby informing the potential conditions of use, exposure pathways and routes and hazards that EPA intends to consider. For scope development, EPA considered the measured or estimated physical-chemical properties set forth in Table 2-1 and EPA found no additional information during problem formulation that would change these values.

TCE is a colorless liquid with a pleasant, sweet odor resembling that of chloroform. It is considered a volatile organic compound (VOC) because of its moderate boiling point, 87.2°C, and high vapor pressure, 73.46 mm Hg at 25°C. TCE is moderately water soluble (1.280 g/L at 25°C), and has a log octanol/water partition coefficient ($K_{ow}$) of 2.42. The density of TCE, 1.46 g/$m^3$ at 20°C, is greater than that of water.

**Table 2-1. Physical and Chemical Properties of TCE**

| Property | Value [a] | References |
|---|---|---|
| Molecular Formula | $C_2HCl_3$ | |
| Molecular Weight | 131.39 g/mole | |
| Physical Form | Colorless, liquid, sweet, pleasant odor, resembles chloroform | O'Neil et al. (2006) |
| Melting Point | -84.7°C | Lide (2007) |
| Boiling Point | 87.2°C | Lide (2007) |
| Density | 1.46 g/$cm^3$ at 20°C | EC (2000) |
| Vapor Pressure | 73.46 mmHg at 25°C | Daubert and Danner (1989) |
| Vapor Density | 4.53 | O'Neil et al. (2006) |
| Water Solubility | 1,280 mg/L at 25°C | Horvath et al. (1999) |
| Octanol/Water Partition Coefficient (Log $K_{ow}$) | 2.42 (Estimated) | U.S. EPA (2012a) |
| Henry's Law Constant | 9.85E-03 atm·$m^3$/mole | Leighton and Calo (1981) |
| Flash Point | 90°C (closed cup) | EC (2000) |
| Auto Flammability | 410°C (Estimated) | U.S. EPA (2012a) |
| Viscosity | 0.53 mPa·s at 25°C | Weast and Selby (1966) |
| Refractive Index | 1.4775 at 20°C | O'Neil et al. (2001) |
| Dielectric Constant | 3.4 $\varepsilon_0$ at 16°C | Weast and Selby (1966) |

[a] Measured unless otherwise noted

## 2.2 Conditions of Use

TSCA § 3(4) defines the conditions of use as ‘‘the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of.’’

### 2.2.1 Data and Information Sources

In the scope documents, EPA identified, based on reasonably available information, the conditions of use for the subject chemicals. EPA searched a number of available data sources. Based on this search, EPA published a preliminary list of information and sources related to chemical conditions of use (e.g., *Use and Market Profile for TCE and Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: TCE**Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: TCE:* EPA-HQ-OPPT-2016-0737-0056) prior to a February 2017 public meeting on scoping efforts for risk evaluation convened to solicit comment and input from the public. EPA also convened meetings with companies, industry groups, chemical users and other stakeholders to aid in identifying conditions of use and verifying conditions of use identified by EPA. The information and input received from the public and stakeholder meetings has been incorporated into this problem formulation document to the extent appropriate Thus, EPA believes the identified manufacture, processing, distribution, use and disposal activities identified in these documents constitute the intended, known, and reasonably foreseeable activities associated with the subject chemical, based on reasonably available information.

### 2.2.2 Identification of Conditions of Use

To determine the current conditions of use of TCE, and, inversely, activities that do not qualify as conditions of use, EPA conducted extensive research and outreach. This included EPA’s review of published literature and online databases including the most recent data available from EPA’s Chemical Data Reporting program (CDR) and Safety Data Sheets (SDSs). EPA also conducted online research by reviewing company websites of potential manufacturers, importers, distributors, retailers, or other users of TCE and queried government and commercial trade databases. EPA also received comments on the Scope of the Risk Evaluation for TCE (EPA-HQ-OPPT-2016-0737-0057; U.S. EPA, 2017d) that were used to determine the current conditions of use. Scope of the Risk Evaluation for TCE Scope of the Risk Evaluation for TCE (EPA-HQ-OPPT-2016-0737) that were used to determine the current conditions of use. In addition, EPA convened meetings with companies, industry groups, chemical users, states, environmental groups, and other stakeholders to aid in identifying conditions of use and verifying conditions of use identified by EPA.

EPA has removed from the risk evaluation certain activities that EPA has concluded to not constitute conditions of use – for example, EPA has insufficient information to find certain activities are circumstances under which the chemical is actually “intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used or disposed of”. EPA has also identified any conditions of use that EPA does not plan to include in the risk evaluation. As explained in the final rule for Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act, TSCA section 6(b)(4)(D) requires EPA to identify "the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations that the Agency expects to consider in a risk evaluation," suggesting that EPA may exclude certain activities that EPA has determined to be conditions of use on a case-by-case basis. (82 FR 33736, 33729; July 20, 2017). For example, EPA may exclude conditions of use that the Agency has sufficient basis to conclude would present only de

minimis exposures or otherwise insignificant risks (such as some uses in a closed system that effectively preclude exposure or use as an intermediate).

The activities that EPA no longer believes are conditions of use or that were otherwise excluded during problem formulation are described in Section 2.2.2.1. The conditions of use included in the scope of the risk evaluation are summarized in Section 2.2.2.2.

#### 2.2.2.1 Categories and Subcategories Determined Not to Be Conditions of Use During Problem Formulation

EPA has conducted public outreach and literature searches to collect information about TCE's conditions of use and has reviewed reasonably available information obtained or possessed by EPA concerning activities associated with TCE. As a result of that analysis during problem formulation, EPA determined there is insufficient information to support a finding that certain activities which were listed as conditions of use in the Scope Document (EPA-HQ-OPPT-2016-0737-0057; U.S. EPA, 2017d) for TCE actually constitute "circumstances…under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of." Consequently, EPA intends to exclude these activities not considered conditions of use from the scope of the evaluation.

As shown in Table 2-22, these activities consist of paints and coatings for consumer use. EPA no longer believes that paints and coatings for consumer use contain TCE, as evidenced by SNUR on TCE for Certain Consumer Products (81 FR 20535). Consequently, EPA intends to exclude consumer uses of paints and coatings from the scope of the evaluation.

**Table 2-2. Categories and Subcategories Determined Not to Be Conditions of Use During Problem Formulation**

| Life Cycle Stage | Category [a] | Subcategory | References |
|---|---|---|---|
| Consumer use | Paints and Coatings | Diluent in solvent-based paints and coatings | TCE SNUR on consumer products (81 FR 20535) |

[a] These categories are no longer shown in the Life Cycle Diagram.

#### 2.2.2.2 Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation

EPA has conducted public outreach and literature searches to collect information about trichloroethylene's conditions of use and has reviewed reasonably available information obtained or possessed by EPA concerning activities associated with trichloroethylene. Based on this research and outreach, other than the category and subcategory described above in Section 2.2.2.1, EPA does not have reason to believe that any conditions of use identified in the trichloroethylene scope should be excluded from risk evaluation. Therefore, all the conditions of use for TCE will be included in the risk evaluation.

Table 2-33 summarizes each life cycle stage and the corresponding categories and subcategories of conditions of use for TCE that EPA plans to evaluate in the risk evaluation. Using the 2016 CDR (U.S. EPA, 2016b), EPA identified industrial processing or use activities, industrial function categories and commercial and consumer use product categories. EPA identified the subcategories by supplementing CDR data with other published literature and information obtained through stakeholder consultations. For risk evaluations, EPA intends to consider each life cycle stage (and corresponding use categories

and subcategories) and assess certain potential sources of release and human exposure associated with that life cycle stage. In addition, activities related to distribution (e.g., loading, unloading) will be considered throughout the life cycle, rather than using a single distribution scenario.

Beyond the uses identified in the Scope of the Risk Evaluation for TCE, EPA has received no additional information identifying additional current conditions of use for TCE from public comment and stakeholder meetings.

**Table 2-3. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation**

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| Manufacture | Domestic manufacture | Domestic manufacture | U.S. EPA (2016b) |
| | Import | Import | U.S. EPA (2016b) |
| Processing | Processing as a reactant/ intermediate | Intermediate in industrial gas manufacturing (e.g., manufacture of fluorinated gases used as refrigerants, foam blowing agents and solvents) | U.S. EPA (2016b); EPA-HQ-OPPT-2016-0737-0013; EPA-HQ-OPPT-2016-0737-0013; EPA-HQ-OPPT-2016-0737-0026; EPA-HQ-OPPT-2016-0737-0027 |
| | Processing - Incorporation into formulation, mixture or reaction product | Solvents (for cleaning or degreasing) | U.S. EPA (2016b) |
| | Processing - Incorporation into formulation, mixture or reaction product | Adhesives and sealant chemicals | U.S. EPA (2016b) |
| | | Solvents (which become part of product formulation or mixture) (e.g., lubricants and greases, paints and coatings, other uses) | U.S. EPA (2016b); EPA-HQ-OPPT-2016-0737-0003; EPA-HQ-OPPT-2016-0737-0056 |
| | Processing – incorporated into articles | Solvents (becomes an integral components of articles) | U.S. EPA (2016b) |
| | Repackaging | Solvents (for cleaning or degreasing) | U.S. EPA (2016b) |
| | Recycling | Recycling | U.S. EPA (2017e) |
| Distribution in commerce | Distribution | Distribution | EPA-HQ-OPPT-2016-0737-0003 |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| Industrial/commercial/ consumer use | Solvents (for cleaning or degreasing) | Batch vapor degreaser (e.g., open-top, closed-loop) [c] | EPA-HQ-OPPT-2016-0737-0003, U.S. EPA (2014c), U.S. EPA (2016f), EPA-HQ-OPPT-2016-0737-0056 |
| | | In-line vapor degreaser (e.g., conveyorized, web cleaner) [c] | EPA-HQ-OPPT-2016-0737-0003, U.S. EPA (2014c), U.S. EPA (2016f), EPA-HQ-OPPT-2016-0737-0056 |
| | | Cold cleaner | EPA-HQ-OPPT-2016-0737-0003; U.S. EPA (2017f); EPA-HQ-OPPT-2016-0737-0056 |
| | Solvents (for cleaning or degreasing) | Aerosol spray degreaser/cleaner [c] | EPA-HQ-OPPT-2016-0737-0003, U.S. EPA (2014c), U.S. EPA (2016d), U.S. EPA (2016c), EPA-HQ-OPPT-2016-0737-0056 |
| | | Mold release | EPA-HQ-OPPT-2016-0737-0003; EPA-HQ-OPPT-2016-0737-0056 |
| | Lubricants and greases/lubricants and lubricant additives | Tap and die fluid | U.S. EPA (2016b); EPA-HQ-OPPT-2016-0737-0003; EPA-HQ-OPPT-2016-0737-0028, EPA-HQ-OPPT-2016-0737-0056 |
| | | Penetrating lubricant | U.S. EPA (2016b), EPA-HQ-OPPT-2016-0737-0056; EPA-HQ-OPPT-2016-0737-0003; EPA-HQ-OPPT-2016-0737-0028 |
| | Adhesives and sealants | Solvent-based adhesives and sealants | U.S. EPA (2016b), EPA-HQ-OPPT-2016-0737-0056; EPA-HQ-OPPT-2016-0737-0003 |
| | | Tire repair cement/sealer | U.S. EPA (2016b), EPA-HQ-OPPT-2016-0737-0056; EPA-HQ-OPPT-2016-0737-0003 |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| | Adhesives and sealants | Mirror edge sealant | EPA-HQ-OPPT-2016-0737-0003; U.S. EPA (2014c), EPA-HQ-OPPT-2016-0737-0056 |
| | Functional fluids (closed systems) | Heat exchange fluid | U.S. EPA (2017f) |
| | Paints and coatings [d] | Diluent in solvent-based paints and coatings | U.S. EPA (2016b), EPA-HQ-OPPT-2016-0737-0056; EPA-HQ-OPPT-2016-0737-0003; EPA-HQ-OPPT-2016-0737-0010; EPA-HQ-OPPT-2016-0737-0015; EPA-HQ-OPPT-2016-0737-0027 |
| | Cleaning and furniture care products | Carpet cleaner | EPA-HQ-OPPT-2016-0737-0056; EPA-HQ-OPPT-2016-0737-0003 |
| | | Cleaning wipes | EPA-HQ-OPPT-2016-0737-0056; EPA-HQ-OPPT-2016-0737-0003 |
| | Laundry and dishwashing products | Spot remover [c] | EPA-HQ-OPPT-2016-0737-0003, U.S. EPA (2014c), U.S. EPA (2016e), EPA-HQ-OPPT-2016-0737-0056 |
| | Arts, crafts and hobby materials | Fixatives and finishing spray coatings [c] | U.S. EPA (2014c) |
| | Corrosion inhibitors and anti-scaling agents | Corrosion inhibitors and anti-scaling agents | U.S. EPA (2016b) |
| | Processing aids | Process solvent used in battery manufacture | U.S. EPA (2017f) |
| | | Process solvent used in polymer fiber spinning, fluoroelastomer manufacture and Alcantara manufacture | U.S. EPA (2017f) |
| | | Extraction solvent used in caprolactam manufacture | U.S. EPA (2017f) |
| | | Precipitant used in beta-cyclodextrin manufacture | U.S. EPA (2017f) |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| | Ink, toner and colorant products | Toner aid | EPA-HQ-OPPT-2016-0737-0056; EPA-HQ-OPPT-2016-0737-0003 |
| | Automotive care products | Brake and parts cleaner | EPA-HQ-OPPT-2016-0737-0056; EPA-HQ-OPPT-2016-0737-0003 |
| | Apparel and footwear care products | Shoe polish | U.S. EPA (2017f) |
| | Other uses | Hoof polishes | EPA-HQ-OPPT-2016-0737-0056; EPA-HQ-OPPT-2016-0737-0003 |
| | | Pepper spray | EPA-HQ-OPPT-2016-0737-0056; EPA-HQ-OPPT-2016-0737-0003 |
| | | Lace wig and hair extension glues | EPA-HQ-OPPT-2016-0737-0056; EPA-HQ-OPPT-2016-0737-0003 |
| | | Gun scrubber | EPA-HQ-OPPT-2016-0737-0056; EPA-HQ-OPPT-2016-0737-0003 |
| | | Other miscellaneous industrial, commercial and consumer uses | U.S. EPA (2017f) |
| Disposal | Disposal | Industrial pre-treatment | U.S. EPA (2017e) |
| | | Industrial wastewater treatment | |
| | | Publicly owned treatment works (POTW) | |

[a] These categories of conditions of use appear in the Life Cycle Diagram, reflect CDR codes, and broadly represent conditions of use of TCE in industrial and/or commercial settings.
[b] These subcategories reflect more specific uses of TCE.
[c] This includes uses assessed in the U.S. EPA, 2014c risk assessment.
[d] Paints and coatings only applies to industrial and commercial uses and not consumer uses.

Although EPA indicated in the TCE scope document that EPA did not expect to evaluate the uses assessed in the 2014 risk assessment in the TCE risk evaluation, EPA has decided to evaluate these conditions of use in the risk evaluation as described in this problem formulation. EPA is including these conditions of use so that they are part of EPA's determination of whether TCE presents an unreasonable risk "under the conditions of use," TSCA 6(b)(4)(A). EPA has concluded that the Agency's assessment of the potential risks from this widely used chemical will be more robust if the potential risks from these conditions of use are evaluated by applying standards and guidance under amended TSCA. In particular, this includes ensuring the evaluation is consistent with the scientific standards in Section 26 of TSCA,

the *Procedures for Chemical Risk Evaluation under the Amended Toxic Substances Control Act* (40 CFR Part 702) and EPA's supplemental document, *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018) EPA also expects to consider other available hazard and exposure data to ensure that all reasonably available information is taken into consideration. It is important to note that conducting these evaluations does not preclude EPA from finalizing the proposed TCE regulation (82 FR 7432; January 19, 2017; 81 FR 91592; December 16, 2016).

#### 2.2.2.3 Overview of Conditions of Use and Lifecycle Diagram

The life cycle diagram provided in Figure 2-1 depicts the conditions of use for TCE that are considered within the scope of the risk evaluation during various life cycle stages including manufacturing, processing, distribution, use (industrial, commercial, consumer; when distinguishable), and disposal. The activities that EPA determined are out of scope during problem formulation are not included in the life cycle diagram. The information is grouped according to Chemical Data Reporting (CDR) processing codes and use categories (including functional use codes for industrial uses and product categories for industrial, commercial and consumer uses), in combination with other data sources (e.g., published literature and consultation with stakeholders), to provide an overview of conditions of use. EPA notes that some subcategories of use may be grouped under multiple CDR categories.

Use categories include the following: "industrial use" means use at a site at which one or more chemicals or mixtures are manufactured (including imported) or processed. "Commercial use" means the use of a chemical or a mixture containing a chemical (including as part of an article) in a commercial enterprise providing saleable goods or services. "Consumer use" means the use of a chemical or a mixture containing a chemical (including as part of an article, such as furniture or clothing) when sold to or made available to consumers for their use (U.S. EPA, 2016b).

Descriptions of the industrial, commercial and consumer use categories identified from the 2016 CDR and included in the life cycle diagram are summarized below (U.S. EPA, 2016b). The descriptions provide a brief overview of the use category; Appendix B contains more detailed descriptions (e.g. process descriptions, worker activities, process flow diagrams, equipment illustrations) for each manufacture, processing, distribution, use and disposal category. The descriptions provided below are primarily based on the corresponding industrial function category and/or commercial and consumer product category descriptions from the 2016 CDR and can be found in EPA's Instructions for Reporting 2016 TSCA Chemical Data Reporting (U.S. EPA, 2016b).

The **"Solvents for Cleaning and Degreasing"** category encompasses chemical substances used to dissolve oils, greases and similar materials from a variety of substrates including metal surfaces, glassware and textiles. This category includes the use of TCE in vapor degreasing, cold cleaning and in industrial and commercial aerosol degreasing products.

The **"Lubricants and Greases"** category encompasses chemical substances contained in products used to reduce friction, heat generation and wear between solid surfaces. This category includes the use of TCE in penetrating lubricants, and tap and die fluids for industrial, commercial and consumer uses.

The **"Adhesives and Sealants"** category encompasses chemical substances contained in adhesive and sealant products used to fasten other materials together. This category includes the use of TCE in mirror-edge sealants, lace wig and hair extension glues and other adhesive products.

The "**Functional Fluids (closed system)"** category encompasses liquid or gaseous chemical substances used for one or more operational properties in a closed system. Examples are heat transfer agents (e.g., coolants and refrigerants).

The **"Paints and Coatings"** category encompasses chemical substances contained in paints, lacquers, varnishes and other coating products that are applied as a thin continuous layer to a surface. Coating may provide protection to surfaces from a variety of effects such as corrosion and ultraviolet (UV) degradation; may be purely decorative; or may provide other functions. EPA anticipates that the primary subcategory to be the use of TCE in solvent-based coatings. EPA no longer believes that paints and coatings for consumer use contain TCE, as evidenced by the SNUR on TCE in Certain Consumer Products SNUR (81 FR 20535). Therefore, EPA is only including paints and coatings from industrial and commercial uses as a condition of use for TCE.

The **"Cleaning and Furniture Care Products"** category encompasses chemical substances contained in products that are used to remove dirt, grease, stains and foreign matter from furniture and furnishings, or to cleanse, sanitize, bleach, scour, polish, protect or improve the appearance of surfaces. This category includes the use of TCE for spot cleaning and carpet cleaning.

The **"Laundry and Dishwashing Products"** category encompasses chemical substances contained in laundry and dishwashing products and aids formulated as a liquid, granular, powder, gel, cakes, and flakes that are intended for consumer or commercial use.

The **"Arts, Crafts and Hobby Materials"** category encompasses chemical substances contained in arts, crafts, and hobby materials that are intended for consumer or commercial use.

To understand conditions of use relative to one another and associated potential exposures under those conditions of use, the life cycle diagram includes the production volume associated with each stage of the life cycle, as reported in the 2016 CDR reporting (U.S. EPA, 2016b) when the volume was not claimed confidential business information (CBI).

The 2016 CDR reporting data for TCE are provided in Table 2-4 for TCE from EPA's CDR database (U.S. EPA, 2016b). For the 2016 CDR period, non-confidential data indicate a total of 13 manufacturers and importers of TCE in the United States. This information has not changed during problem formulation from that provided in the scope document.

**Table 2-4. Production Volume of TCE in CDR Reporting Period (2012 to 2015) [a]**

| Reporting Year | 2012 | 2013 | 2014 | 2015 |
|---|---|---|---|---|
| Total Aggregate Production Volume (lbs) | 220,536,812 | 198,987,532 | 191,996,578 | 171,929,400 |

[a] The CDR data for the 2016 reporting period is available via ChemView (https://java.epa.gov/chemview). Because of an ongoing CBI substantiation process required by amended TSCA, the CDR data available in the scope document (Scope Document) is more specific than currently in ChemView.

As seen in Figure 2-1, most information on the production volume associated with the various uses is shown as "Volume CBI" in the life cycle diagram, based on CBI claims in the 2016 CDR (U.S. EPA, 2016b). The production volumes shown are for reporting year 2015 from the 2016 CDR reporting period. As reported in the Use Document [EPA-HQ-OPPT-2016-0737-0003 (U.S. EPA, 2017c)], as well as in the 2014 TCE risk assessment (U.S. EPA, 2014c), an estimated 83.6% of TCE's annual production

volume is used as an intermediate in the manufacture of the hydrofluorocarbon, HFC-134a, an alternative to the refrigerant chlorofluorocarbon, CFC-12. Another 14.7% of TCE production volume is used as a degreasing solvent, leaving approximately 1.7% for other uses. Also reflected in the life cycle diagram is the fact that TCE, as a widely used solvent, has numerous applications across industrial, commercial and consumer settings.

Figure 2-1 depicts the life cycle diagram of trichloroethylene from manufacture to the point of disposal. Activities related to the distribution (e.g., loading, unloading) will be considered throughout the TCE life cycle rather, than using a single distribution scenario.

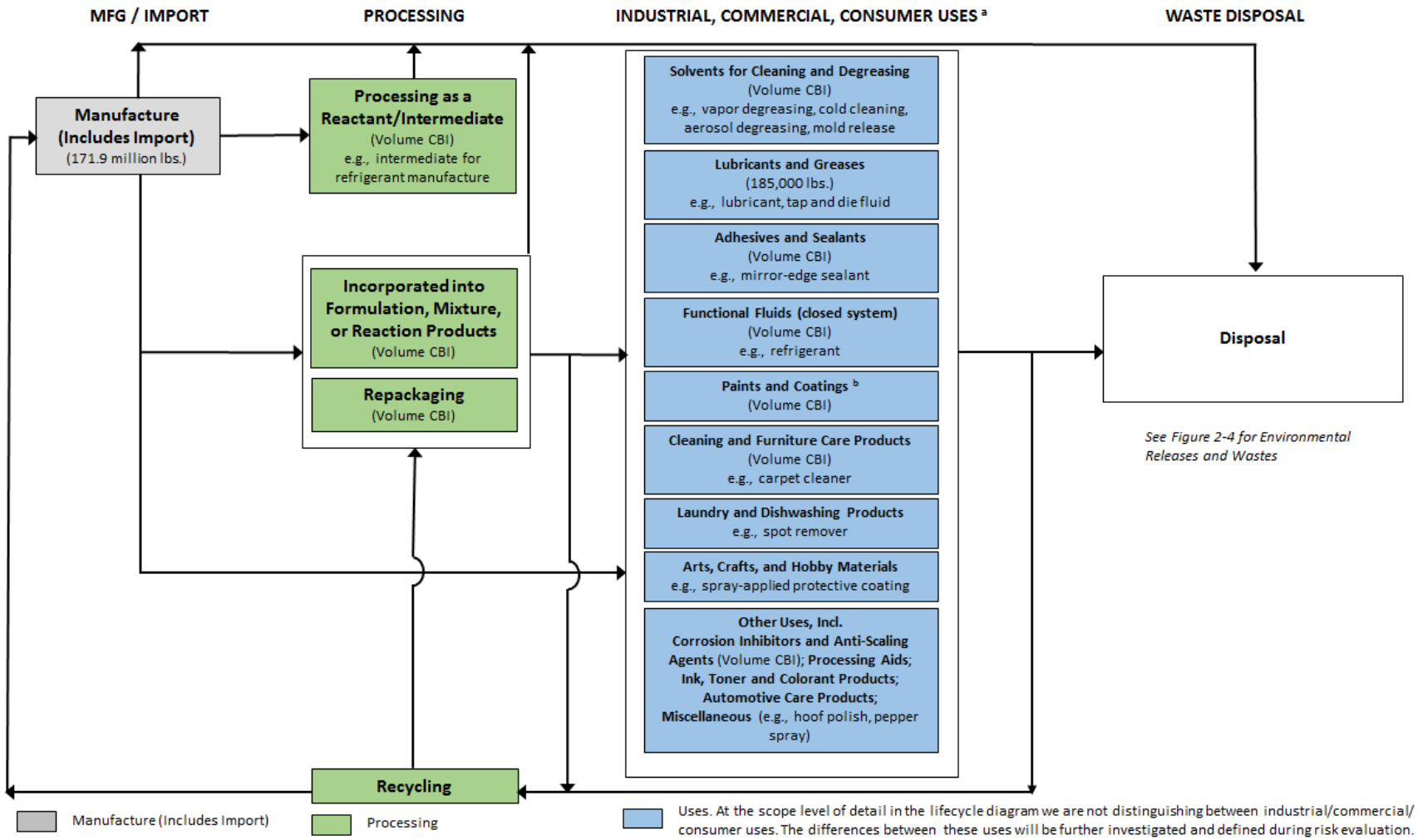


**Figure 2-1. TCE Life Cycle Diagram**

The life cycle diagram depicts the conditions of use that are within the scope of the risk evaluation during various life cycle stages including manufacturing, processing, use (industrial, commercial, consumer), distribution and disposal. The production volumes shown are for reporting year 2015 from the 2016 CDR reporting period (U.S. EPA, 2016b). Activities related to distribution (e.g., loading and unloading) will be considered throughout the TCE life cycle, rather than using a single distribution scenario.

[a] See Table 2-3 for additional uses not mentioned specifically in this diagram.

[b] Paints and coatings only applies to industrial and commercial uses and not consumer uses.

## 2.3 Exposures

For TSCA exposure assessments, EPA expects to evaluate exposures and releases to the environment resulting from the conditions of use applicable to TCE. Post-release pathways and routes will be described to characterize the relationship or connection between the conditions of use for TCE and the exposure to human receptors, including potentially exposed or susceptible subpopulations and ecological receptors. EPA will take into account, where relevant, the duration, intensity (concentration), frequency and number of exposures in characterizing exposures to TCE.

### 2.3.1 Fate and Transport

Environmental fate includes both transport and transformation processes. Environmental transport is the movement of the chemical within and between environmental media. Transformation occurs through the degradation or reaction of the chemical with other species in the environment. Hence, knowledge of the environmental fate of the chemical informs the determination of the specific exposure pathways and potential human and environmental receptors EPA expects to consider in the risk evaluation. Table 2-5 provides environmental fate data that EPA identified and considered in developing the scope for TCE. This information has not changed from that provided in the scope document.

Fate data, including volatilization during wastewater treatment, volatilization from lakes and rivers, biodegradation rates, and organic carbon:water partition coefficient (log $K_{OC}$) and bioaccumulation potential were used when considering changes to the conceptual models. Model results and basic principles were used to support the fate data in problem formulation while literature review is currently underway through the systematic review process.

The Estimation Program Interface Suite™ (EPI Suite™) (U.S. EPA, 2012a) modules were used to predict volatilization of TCE from wastewater treatment plants, lakes, and rivers and to confirm the data showing slow biodegradation. The EPI Suite™ module that estimates chemical removal in sewage treatment plants ("STP" module) was run using default settings (set biodegradation half-life to 10,000 hours) to evaluate the potential for TCE to volatilize to air or adsorb to sludge during wastewater treatment. The STP module estimates that 74% of TCE in wastewater will be removed by volatilization while 1% of TCE will be removed by adsorption.

The EPI Suite™ module that estimates volatilization from lakes and rivers ("Volatilization" module) was run using default settings to evaluate the volatilization half-life of TCE in surface water. The volatilization module estimates that the half-life of TCE in a model river will be 1.2 hours and the half-life in a model lake will be 110 hours.

The EPI Suite™ module that predicts biodegradation rates ("BIOWIN" module) was run using default settings to estimate biodegradation rates of TCE in soil and sediment. Three of the models built into the BIOWIN module (BIOWIN 1, 2, and 5) estimate that TCE will not rapidly biodegrade in aerobic environments, while a fourth (BIOWIN 6) estimates that TCE will rapidly biodegrade in aerobic environments. These results support the biodegradation data presented in the TCE scope document, which demonstrate slow biodegradation under aerobic conditions. The model that estimates anaerobic biodegradation (BIOWIN 7) predicts that TCE will biodegrade under anaerobic conditions. Further, previous assessments of TCE found that biodegradation was slow or negligible.

The log $K_{OC}$ reported in the TCE scoping document was predicted using EPI Suite™ as 1.8 and extracted from measured values which ranged from 1.86 to 2.17 with different soils. That range of values (1.8-2.17) is supported by the basic principles of environmental chemistry which states that the

$K_{OC}$ is typically within one order of magnitude (one log unit) of the octanol:water partition coefficient ($K_{OW}$). The log $K_{OC}$ values reported in previous assessments of TCE were in the range of 1.8-2.17, suggesting low sorption to soil and sediment and is mobile in soil and sediment.

**Table 2-5. Environmental Fate Characteristic of TCE**

| Property or Endpoint | Value [a] | References |
|---|---|---|
| Indirect photodegradation | 5.5-8 days (atmospheric degradation based on measured hydroxyl radical degradation)<br>1-11 days (atmospheric degradation based on measured hydroxyl radical degradation) | ECB (2004), U.S. EPA (2014c) |
| Hydrolysis half-life | Does not undergo hydrolysis at pH 7 | EC (2000) |
| Biodegradation | 19% in 28 days (aerobic in water, OECD 301D)<br>2.4% in 14 days (aerobic in water, OECD 301C)<br><br>25% degradation after 10 days, 95% degradation after 30 days (anaerobic biodegradation in subsurface sediment with methanol)<br><br>65% degradation after 10 days, 99% degradation after 30 days (anaerobic biodegradation in subsurface sediment with glucose)<br><br>TCE removed slowly with a reduction of 40% after 8 weeks (TCE (200 µg/L) incubated with batch bacterial cultures under methanogenic conditions) | ECB (2004) |
| Bioconcentration factor (BCF) | 4-17 (carp) | U.S. EPA (2014c) |
| Bioaccumulation factor (BAF) | 23.7 (estimated) | U.S. EPA (2014c) |
| Organic carbon:water partition coefficient (Log $K_{oc}$) | 2.17 (measured in silty clay Nebraska loam);<br>1.94 (measured in silty clay Nevada loam);<br>1.86 (measured in a forest soil)<br>1.8 (estimated) | U.S. EPA (2014c) |
| [a] Measured unless otherwise noted | | |

If released to the air, TCE does not absorb radiation well at wavelengths that are present in the lower atmosphere (>290 nm) so direct photolysis is not a main degradation process. Degradation by reactants in the atmosphere has a half-life of several days meaning that long range transport is possible.

If released to water, sediment or soil, the fate of TCE is influenced by volatilization from the water surface or from moist soil as indicated by its physical chemical properties (e.g. Henry's law constant)

and by microbial biodegradation under some conditions. The biodegradation of TCE in the environment is dependent on a variety of factors and thus, a wide range of degradation rates have been reported (ranging from days to years). TCE is not expected to accumulate in aquatic organisms due to low measured BCFs and estimated BAF.

### 2.3.2 Releases to the Environment

Releases to the environment from conditions of use (e.g., industrial and commercial processes, commercial or consumer uses resulting in down-the-drain releases) are one component of potential exposure and may be derived from reported data that are obtained through direct measurement, calculations based on empirical data and/or assumptions and models.

A source of information that EPA expects to consider in evaluating exposure are data reported under the Toxics Release Inventory (TRI) program. Under the Emergency Planning and Community Right-to-Know Act (EPCRA) Section 313 rule, TCE is a TRI-reportable substance effective January 1, 1987. During problem formulation EPA further analyzed the TRI data and examined the definitions of elements in the TRI data to determine the level of confidence that a release would result from certain types of disposal to land (e.g. Resource Conservation and Recovery Act (RCRA) Subtitle C hazardous landfill and Class I underground Injection wells) and incineration. EPA also examined how trichloroethylene is treated at industrial facilities.

Table 2-66 provides production-related waste managed data (also referred to as waste managed) for TCE reported by industrial facilities to the TRI program for 2015. Table 2-7 provides more detailed information on the quantities released to air or water or disposed of on land. Release quantities in Table 2-7 are more representative of actual releases during the year. Production-related waste managed shown in Table 2-6 excludes any quantities reported as catastrophic or one-time releases (TRI section 8 data), while release quantities shown in Table 2-7 include both production-related and non-routine quantities (TRI section 5 and 6 data).

**Table 2-6. Summary of TCE TRI Production-Related Waste Managed in 2015 (lbs)**

| Number of Facilities | Recycling | Energy Recovery | Treatment | Releases [a, b, c] | Total Production Related Waste |
|---|---|---|---|---|---|
| 172 | 76,090,421 | 2,585,262 | 10,540,042 | 1,967,576 | 91,183,301 |

Data source: 2015 TRI Data (updated March 2017).
[a] Terminology used in these columns may not match the more detailed data element names used in the TRI public data and analysis access points.
[b] Does not include releases due to one-time event not associated with production such as remedial actions or earthquakes.
[c] Counts all releases including release quantities transferred and release quantities disposed of by a receiving facility reporting to TRI.

**Table 2-7. Summary of TCE TRI Releases to the Environment in 2015 (lbs)**

| | | Air Releases | | | Land Disposal | | | | Total On- and Off-site Disposal or Other Releases [b, c] |
|---|---|---|---|---|---|---|---|---|---|
| | Number of Facilities | Stack Air Releases | Fugitive Air Releases | Water Releases | Class I Under-ground Injection | RCRA Subtitle C Landfills | All other Land Disposal [a] | Other Releases [a] | |
| Subtotal | 172 | 689,627 | 1,190,942 | 52 | 122 | 49,500 | 405 | 36,890 | 1,967,538 |

| | Number of Facilities | Air Releases | | Water Releases | Land Disposal | | | Other Releases [a] | Total On- and Off-site Disposal or Other Releases [b, c] |
|---|---|---|---|---|---|---|---|---|---|
| | | Stack Air Releases | Fugitive Air Releases | | Class I Under-ground Injection | RCRA Subtitle C Landfills | All other Land Disposal [a] | | |
| Totals | | 1,880,569 | | | 50,027 | | | | |

Data source: 2015 TRI Data (updated March 2017).
[a] Terminology used in these columns may not match the more detailed data element names used in the TRI public data and analysis access points.
[b] These release quantities do include releases due to one-time events not associated with production such as remedial actions or earthquakes.
[c] Counts release quantities once at final disposition, accounting for transfers to other TRI reporting facilities that ultimately dispose of the chemical waste.

Facilities are required to report if they manufacture (including import) or process more than 25,000 pounds of TCE, or if they otherwise use more than 10,000 pounds of TCE. In 2015, 172 facilities reported a total of 91 million pounds of TCE waste managed. Of this total, 76 million pounds were recycled, 2.5 million pounds were recovered for energy, 10.5 million pounds were treated, and nearly 2 million pounds were released into the environment (Table 2-6).

Of the nearly 2 million pounds of total disposal or other releases, there were stack and fugitive air releases, water releases, Class I underground injection, releases to Resource Conservation and Recovery Act (RCRA) Subtitle C landfills and other land disposal, and other releases. Of these releases, 96% were released to air. For stack releases, multiple types of facilities report on incineration destruction, including hazardous waste facilities and facilities that perform other industrial activities and may be privately or publicly (i.e., federal, state, or municipality) owned or operated. Approximately 690,000 pounds of TCE releases were reported to TRI as on-site stack releases, and account for any incineration destruction. Stack releases reported to TRI represent the total amount of TCE being released to the air at the facility from stacks, confined vents, ducts, pipes, or other confined air streams.

In 2015, 1,928,867 pounds of TCE were disposed of or otherwise released on-site, and 38,671 pounds were disposed of or otherwise released off-site. Of the on-site releases, 97.496% (1,880,569 pounds) were released to air, including both stack and fugitive releases, 2.501% (48,245 pounds) went to land disposal, and 0.003% (52 pounds) were released to water. Of the on-site land disposal, nearly all went to RCRA Subtitle C landfills. Just 3 pounds went to on-site landfills other than RCRA Subtitle C, and none was disposed of in on-site underground injection wells, on-site land treatment, or on-site surface impoundments. Of the off-site releases, 46.1% (17,815 pounds) was transferred for other off-site management, 31.3% (12,105 pounds) was transferred to a waste broker for disposal, 16.1% (6,246 pounds) was transferred for storage only, 3.3% (1,263 pounds) was transferred to a RCRA Subtitle C landfill, 1% (397 pounds) was transferred to a non-RCRA Subtitle C landfill, 1.9% (722 pounds) was transferred for unknown disposal, and 0.3% (122 pounds) was transferred to an off-site underground injection Class I well.

While most TCE going to land disposal went to Subtitle C Hazardous Waste Landfills in 2015, in past years, the TRI data show TCE going to other types of land disposal as well. In 2014, 12,600 pounds was transferred for off-site land treatment, and in both 2013 and 2014 over 11,000 pounds were transferred to off-site landfills other than RCRA subtitle C landfills. From 2012 through 2014, 24,000 pounds to over 100,000 pounds of TCE were released on-site to other land disposal. That volume decreased to only 5 pounds in 2015.

While the volume of production-related waste managed shown in Table 2-6 excludes any quantities reported as catastrophic or one-time releases (TRI section 8 data), release quantities shown in Table 2-7 includes both production-related and non-routine quantities (TRI section 5 and 6 data). As a result, release quantities may differ slightly and may reflect differences in TRI calculation methods for reported release range estimates (U.S. EPA, 2017e). In addition, Table 2-6 counts all release quantities reported to TRI, while Table 2-7 counts releases once at final disposition, accounting for transfers of chemical waste from one TRI reporting facility and received by another TRI reporting facility for final disposition. As a result, release quantities may differ slightly and may further reflect differences in TRI calculation methods for reported release range estimates (U.S. EPA, 2017e).

Other sources of information provide evidence of releases of TCE, including EPA effluent guidelines (EGs) promulgated under the Clean Water Act (CWA), National Emission Standards for Hazardous Air Pollutants (NESHAPs) promulgated under the Clean Air Act (CAA), or other EPA standards and regulations that set legal limits on the amount of TCE that can be emitted to a particular media. There are additional sources of TCE emissions data, including National Emissions Inventory (NEI) (U.S. EPA, 2017h) and the Discharge Monitoring Report (DMR) Pollutant Loading Tool (U.S. EPA, 2010), which provide additional release data specific to air and surface water, respectively. NEI provides comprehensive and detailed estimates of air emissions for criteria pollutants, criteria precursors, Hazardous Air Pollutants (HAPs) on a 3-year cycle. Another source is EPA's AP-42, *Compilation of Air Pollutant Emission Factors*. AP-42 sections provide general process and emission information for a variety of industry sectors. AP-42 sections relevant to the conditions of use of TCE include: 4.2 on surface coating, 4.6 on solvent degreasing, 4.7 on waste solvent reclamation, 4.8 on tanks and drum cleaning, 4.10 on commercial/consumer solvent use, and 6.7 on printing inks. The DMR loading tool calculates pollutant loadings from permit and DMR data from EPA's Integrated Compliance Information System for the National Pollutant Discharge Elimination System (ICIS-NPDES). EPA expects to consider these data in conducting the exposure assessment component of the risk evaluation for TCE.

### 2.3.3 Presence in the Environment and Biota

Monitoring studies or a collection of relevant and reliable monitoring studies provide(s) information that can be used in an exposure assessment. Monitoring studies that measure environmental concentrations or concentrations of chemical substances in biota provide evidence of exposure. Monitoring and biomonitoring data were identified in EPA's data search for TCE.

***Environment***

TCE is widely detected in a number of environmental media. While the primary fate of TCE released to surface waters or surface soils is volatilization, TCE is more persistent in air and ground water, where it is commonly detected through national and state-level monitoring efforts. TCE is frequently found at Superfund sites as a contaminant in soil and ground water.

TCE has been detected in ambient air across the United States, though ambient levels vary by location and proximity to industrial activities. EPA's Air Quality System (AQS) is EPA's repository of Criteria Pollutant and Hazardous Air Pollutant (HAP) monitoring data. A summary of the ambient air monitoring data for TCE (i.e., measured data) in the United States from 1999 to 2006 suggests that TCE levels in ambient air have remained fairly constant in ambient air for the United States since 1999, with an approximate mean value of 0.23 $\mu g/m^3$ (U.S. EPA, 2011c, 2007). EPA also compiles modeled air concentrations in its National-scale Air Toxics Assessments (NATA) using NEI data for the Criteria Pollutants and HAPs, like TCE. Recent ambient air concentration data from both sources, as well as those identified in open literature, will be reviewed and considered for risk evaluation.

The presence of TCE in indoor air may result from ambient air releases from industrial and commercial activities, volatilization from tap water and household uses of TCE-containing consumer products. Additionally, TCE in ground water may volatilize through soil and into indoor environments of overlying buildings in a process called vapor intrusion. There are a number of studies that have reported indoor air levels of TCE in residences, schools and stores, and recent indoor air data from open literature, agency databases (e.g., EPA's Vapor Intrusion Database) and other authoritative documents addressing vapor intrusion.

TCE is one of the most frequently detected organic solvents in U.S. ground water. The U.S. Geological Survey (USGS) conducted a national assessment of VOCs in ground water, including TCE. Between 1985 and 2001, the detection frequency of TCE was 2.6%, with a median concentration of 0.15 $\mu g/m^3$ (U.S. EPA, 2011c; Zogorski et al., 2006). Recent sources of national and state-level (U.S. EPA, 2011c) groundwater monitoring data will be reviewed and considered for risk evaluation.

TCE has been detected in drinking water systems through national and state-wide monitoring efforts. EPA's second and third Six-Year Review (Six-Year Review 2 and 3) contains a compilation of state drinking water monitoring data from 1998-2005 and 2006-2011, which are available through EPA's Six-Year Review 2 Contaminant Occurrence Data site and EPA's Six-Year Review 3 Contaminant Occurrence Data site. These sources, as well as additional drinking water monitoring data from states and/or the open literature, will be used to inform the magnitude and extent of TCE's presence in drinking water.

EPA's STOrage and RETrieval (STORET) is an electronic data system for water quality monitoring data. Based on a recent search of STORET surface water monitoring data covering the past ten years, there are detections with a maximum of 50 ppb and average of 4.5 ppb. Data from other sources will also be reviewed for a better understanding of current levels of TCE in surface water. EPA's STORET database will also be examined for recent data on TCE levels in sediment.

Compared with other environmental media, there is a relative lack of nationally representative monitoring data on levels of TCE in ambient soil.

***Biota***

Biological studies have detected TCE in human blood and urine in the United States and several other countries, with those exposed through occupational degreasing activities reporting the highest frequency of positive detections (U.S. EPA, 2011c; IARC, 1995). The Third National Health and Nutrition Examination Survey (NHANES III) analyzed blood concentrations of TCE in non-occupationally exposed individuals in the United States and found that 10% of those sampled had TCE levels in whole blood at or above the detection limit of 0.01 ppb (U.S. EPA, 2011c).

### 2.3.4 Environmental Exposures

The manufacturing, processing, use and disposal of TCE can result in releases to the environment. In this section, EPA presents exposures to aquatic and terrestrial organisms.

**Aquatic Environmental Exposures**

TCE is released to surface water from ongoing industrial and/or commercial activities, as reported in recent TRI and DMR release and loading data. TRI reporting from 2015 indicates direct releases to surface water of 52 pounds/ year. In 2016, the top ten DMR dischargers reported site-specific loadings to surface water of 17.5 to 1,564 lbs/yr. Within the past ten years of surface water monitoring data from

STORET, there are detections (e.g., maximum of 50 ppb and average of 4.5 ppb), that do not exceed the preliminary acute concentration of concern (COC) for TCE (acute COC = 340 ppb), but do exceed the preliminary chronic COC (chronic COC = 3 ppb).

**Terrestrial Environmental Exposures**
Exposure to terrestrial organisms is expected to be low since physical chemical properties do not support an exposure pathway through water and soil pathways to these organisms. The partition of TCE into sediments is very low. Furthermore, the primary fate of TCE released to surface waters or surface soils is volatilization.

### 2.3.5 Human Exposures

In this section, EPA presents occupational exposures, consumer exposures and general population exposures. Subpopulations, including potentially exposed and susceptible subpopulations within these exposure categories are also presented.

#### 2.3.5.1 Occupational Exposures

Exposure pathways and exposure routes are listed below for worker activities under the various conditions of use described in Section 2.2. In addition, exposures to occupational non-users (ONU), who do not directly handle the chemical but perform work in an area where the chemical is present are listed. Engineering controls and/or personal protective equipment may affect the occupational exposure levels.

In the previous 2014 risk assessment (U.S. EPA, 2014c), EPA assessed inhalation exposures to TCE for occupational use in vapor degreasing, aerosol degreasing, and spot cleaning in dry cleaning facilities, which will be considered in the TCE risk evaluation. Based on information identified during scoping, as described in Section 2.3, additional conditions of use resulting in occupational exposure will be considered during the risk evaluation.

***Worker Activities***
Workers and occupational non-users may be exposed to TCE when performing activities associated with the conditions of use described in Section 2.2, including but not limited to:

- Unloading and transferring TCE to and from storage containers to process vessels;
- Cleaning and maintaining equipment;
- Sampling chemicals, formulations or products containing TCE for quality control;
- Repackaging chemicals, formulations or products containing TCE;
- Using TCE in process equipment (e.g., vapor degreasing machine);
- Applying formulations and products containing TCE onto substrates (e.g., spray applying coatings or adhesives containing TCE);
- Handling, transporting and disposing waste containing TCE; and
- Performing other work activities in or near areas where TCE is used.

***Inhalation***
Based on these occupational exposure scenarios, inhalation exposure to vapor is expected. EPA anticipates this is the most important TCE exposure pathway for workers and occupational non-users based on high volatility. Based on the potential for spray application of some products containing TCE exposures to mists are also expected for workers and ONU and will be incorporated into the worker inhalation exposure.

The United States has several regulatory and non-regulatory exposure limits for trichloroethylene: an Occupational Safety and Health Administration (OSHA) permissible exposure limit (PEL) of 100 ppm

8-hour time-weighted average (TWA), an acceptable ceiling concentration of 200 ppm provided the 8-hour PEL is not exceeded, and an acceptable maximum peak of 300 ppm for a maximum duration of 5 minutes in any 2 hours (OSHA, 1997), and an American Conference of Government Industrial Hygienists (ACGIH) Threshold Limit Value (TLV) of 10ppm 8-hour TWA and a short-term exposure level (STEL) of 25ppm (ACGIH, 2010). (ACGIH, 2010)The National Institute for Occupational Safety and Health (NIOSH) has classified trichloroethylene as a potential occupational carcinogen and established an immediately dangerous to life or health (IDLH) value of 1,000 ppm. NIOSH has a recommended exposure limit of 2 ppm (as a 60-minute ceiling) during the usage of TCE as an anesthetic agent and 25 ppm (as a 10-hour TWA) during all other exposures (NIOSH, 2016).

***Dermal***

Based on the conditions of use EPA expects dermal exposures for workers, who are expected to have skin contact with liquids and vapors. Occupational non-users are not directly handling TCE; therefore, skin contact with liquid TCE is not expected for occupational non-users but skin contact with vapors is expected for occupational non-users.

***Oral***

Worker exposure via the oral route is not expected. Exposure may occur through mists that deposit in the upper respiratory tract however, based on physical chemical properties, mists of TCE will likely be rapidly absorbed in the respiratory tract and will be considered as an inhalation exposure.

***Key Data***

Key data that inform occupational exposure assessment include: OSHA Integrated Management Information System (IMIS) and NIOSH Health Hazard Evaluation (HHE) program data. OSHA data are workplace monitoring data from OSHA inspections. The inspections can be random or targeted, or can be the result of a worker complaint. OSHA data can be obtained through the OSHA Chemical Exposure Health Data (CEHD) at https://www.osha.gov/oshstats/ index.html. Table_Apx B-1 provides a mapping of scenarios to industry sectors with trichloroethylene personal monitoring air samples obtained from OSHA inspections conducted between 2003 and 2017.

NIOSH HHEs are conducted at the request of employees, union officials, or employers and help inform potential hazards at the workplace. HHEs can be downloaded at https://www.cdc.gov/niosh/hhe/. Table_Apx B-2 provides a summary of personal and area monitoring air samples obtained from NIOSH HHEs occurring after 1990.

#### 2.3.5.2 Consumer Exposures

TCE can be found in consumer products and commercial products that are readily available for public purchase at common retailers [EPA-HQ-OPPT-2016-0737-003, Sections 3 and 4, (U.S. EPA, 2017c)] and can therefore result in exposures to consumers/product users (i.e., receptors who use a product directly) and bystanders (i.e., receptors who are a non-product users that are incidentally exposed to the product or article) (U.S. EPA, 2017b).

***Inhalation***

EPA expects that exposure via inhalation will be the most significant route of exposure for consumer exposure scenarios, including those involving users and bystanders. This assumption is in line with EPA/OPPT's 2014 inhalation risk assessment of TCE, which evaluated inhalation exposure to consumers and bystanders from degreasing and arts & crafts uses.

***Dermal***
There is potential for dermal exposures to TCE from consumer uses. Exposures to skin that are instantaneous would be expected to evaporate before significant dermal absorption could occur based on the physical chemical properties including the vapor pressure, water solubility and log $K_{OW}$ (the estimate from IHSkinPerm, a mathematical tool for estimating dermal absorption, is 0.8% absorption and 99.2% volatilization). Exposure that occurs as a deposition over time or a repeated exposure that maintains a thin layer of liquid TCE would have greater absorption (the estimate from IHSkinPerm for an 8-hr exposure is 1.6% absorption and 98.4% volatilization). Furthermore, dermal exposures to liquid TCE are expected to be concurrent with inhalation exposures, which reflect the preponderance of overall exposure from a particular use or activity for most consumer exposure scenarios. This is in agreement with the NIOSH skin notation profile for TCE, which estimates a low hazard potential by dermal absorption for systemic effects when inhalation and dermal exposures are concurrent (NIOSH, 2017). There may also be certain scenarios with a higher dermal exposure potential, for example, an occluded scenario where liquid TCE is not able to evaporate readily such as a user holding a rag soaked with liquid TCE against their palm during a cleaning activity.

Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, dermal exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. There is potential for bystanders or users to have indirect dermal contact via contact with a surface upon which TCE has been applied (e.g., counter, floor). Based on the expectation that TCE would evaporate from the surface rapidly, with <1% dermal absorption predicted from instantaneous contact, this route is unlikely to contribute significantly to overall exposure.

***Oral***
Oral exposure to TCE may occur through incidental ingestion of TCE mists that deposit in the upper respiratory tract. EPA initially assumed that mists may be swallowed. However, based on physical chemical properties, mists of TCE are expected to be rapidly absorbed in the respiratory tract or evaporate upon being introduced into the respiratory tract, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. Furthermore, based on available toxicological data, EPA does not expect inhalation and oral routes of exposure to differ significantly in the toxicity of trichloroethylene. Oral exposures may also occur through hand-to-mouth patterns following dermal contact with TCE. As described, dermal contact would not be expected for bystanders, and any TCE present on surfaces of the home or skin surfaces is expected to volatilize rapidly – making it available for inhalation as a vapor before oral ingestion may occur through such patterns.

***Disposal***
EPA does not expect exposure to consumers from disposal of consumer products. It is anticipated that most products will be disposed of in original containers, particularly those products that are purchased as aerosol cans. Liquid products may be recaptured in an alternate container following use (refrigerant flush or coin cleaning).

#### 2.3.5.3 General Population Exposures
Wastewater/liquid wastes, solid wastes or air emissions of TCE could result in potential pathways for oral, dermal or inhalation exposure to the general population.

***Inhalation***
Based on TRI data and TCE physical-chemistry and fate properties, it is expected that inhalation represents the primary route of exposure for the general population from ongoing industrial and/or commercial activities. As noted in Section 2.3.3, Presence in the Environment and Biota, levels of TCE in ambient air vary based on proximity to industrial and commercial activities and urban environments

and there are a number of possible sources that may contribute to TCE levels in indoor air. Like other VOCs, TCE in drinking water can also contribute to general population inhalation exposures from volatilization from water during activities such as showering, bathing or washing (McKone and Knezovich, 1991)

***Oral***

The general population may ingest TCE via contaminated drinking water and other ingested media. It is anticipated that ingestion of drinking water containing TCE, for on-going TSCA uses, represents the primary route of oral exposure for this chemical. TCE has been detected in national-scale drinking water monitoring datasets (i.e., EPA's Six-Year Review 3) and is released to surface water from ongoing TSCA uses and activities. The primary oral exposure route for TCE is expected to be via drinking water. TCE's presence in drinking water may also contribute, to a lesser degree, to oral ingestion through showering or other non-drinking activities.

***Dermal***

General population dermal exposures are expected to primarily result from dermal contact with TCE-containing tap water during showering, bathing and/or washing. TCE has been detected in national-scale drinking water monitoring datasets (i.e., EPA's Six-Year Review 3) and is released to surface water from ongoing TSCA uses and activities. While instantaneous contact with TCE is expected to result primarily in inhalation exposures (see Section 2.3.5.2), activities such as bathing or showering involve longer durations, large surface area for exposure, and a different exposure medium (i.e., a more dilute solution).

#### 2.3.5.4 Potentially Exposed or Susceptible Subpopulations

TSCA requires that the determination of whether a chemical substance presents an unreasonable risk to "a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation" by EPA. TSCA § 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." General population is "the total of individuals inhabiting an area or making up a whole group" and refers here to the U.S. general population (U.S. EPA, 2011a).

As part of the Problem Formulation, EPA identified potentially exposed and susceptible subpopulations during the development and refinement of the life cycle, conceptual models, the development of the exposure scenarios and the development of the analysis plan. In this section, EPA addresses the potentially exposed or subpopulations identified as relevant based on greater exposure. EPA will address the subpopulation identified as relevant based on greater susceptibility in the hazard section.

EPA identifies the following as potentially exposed or susceptible subpopulations due to their *greater exposure:*

- Workers and occupational non-users.
- Populations in buildings co-located with facilities using TCE.
- Consumers and bystanders associated with consumer use. TCE has been identified as being used in products available to consumers; however, only some individuals within the general population may use these products. Therefore, those who do use these products are a potentially exposed or susceptible subpopulation due to greater exposure.
- Other groups of individuals within the general population who may experience greater exposures due to their proximity to conditions of use that result in releases to the environment and

subsequent exposures (e.g., individuals who live or work near manufacturing, processing, use or disposal sites).

In developing exposure scenarios, EPA will analyze available data to ascertain whether some human receptor groups may be exposed via exposure pathways that may be distinct to a particular subpopulation or lifestage (e.g., children's crawling, mouthing or hand-to-mouth behaviors) and whether some human receptor groups may have higher exposure via identified pathways of exposure due to unique characteristics (e.g., activities, duration or location of exposure) when compared with the general population (U.S. EPA, 2006).

In summary, in the risk evaluation for TCE, EPA plans to analyze the following potentially exposed groups of human receptors: workers, occupational non-users, consumers, bystanders associated with consumer use and other groups within the general population who may experience greater exposure. EPA may also identify additional potentially exposed or susceptible subpopulations that will be considered based on greater exposure.

## 2.4 Hazards (Effects)

For scoping, EPA conducted comprehensive searches for data on hazards of TCE, as described in *Strategy for Conducting Literature Searches for Trichloroethylene (TCE): Supplemental Document to the TSCA Scope Document, CASRN: 79-01-6* (EPA-HQ-OPPT-2016-0737). Based on initial screening, EPA plans to analyze the hazards of TCE identified in the scope document. However, when conducting the risk evaluation, the relevance of each hazard within the context of a specific exposure scenario will be judged for appropriateness. For example, hazards that occur only as a result of chronic exposures may not be applicable for acute exposure scenarios. This means that it is unlikely that every hazard identified in the scope document will be considered for every exposure scenario.

### 2.4.1 Environmental Hazards

EPA identified the following sources of environmental hazard data for TCE: European Chemicals Agency (ECHA) Database (ECHA, 2017a), EPA Chemical Test Rule Data (U.S. EPA, 2017a), and Ecological Hazard Literature Search Results in *Trichloroethylene (CASRN 79-01-6) Bibliography: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0737; U.S. EPA, 2017g). Only the *on-topic* references listed in the Ecological Hazard Literature Search Results were considered as potentially relevant data/ information sources for the risk evaluation. Inclusion criteria were used to screen the results of the ECOTOX literature search (as explained in the *Strategy for Conducting Literature Searches for Trichloroethylene (TCE): Supplemental Document to the TSCA Scope Document, CASRN: 79-01-6*) (EPA-HQ-OPPT-2016-0737). Data from the screened literature are summarized below (Table 2-8) as ranges (min-max). EPA plans to review these data/information sources during risk evaluation using the data quality review evaluation metrics and the rating criteria described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018).

EPA also evaluated studies previously reviewed in the 2004 European Union (EU) environmental risk assessment on TCE (ECHA, 2004) and in the ECHA Database on TCE that supplements the 2004 EU environmental risk assessment.

The EPA TSCA 2014 TCE Risk Assessment (U.S. EPA, 2014c) did not analyze aquatic risk from TCE exposures due to low hazard for aquatic toxicity. The low hazard was based on moderate persistence, low bioaccumulation, and physical-chemical properties of TCE. The assessment concluded that the potential environmental impacts, i.e., risk, is expected to be low from environmental releases.

Additionally, TCE meets the criteria under Section 64 of the Canadian Environmental Protection Act (CEPA), 1999 and is therefore on the List of Toxic Substances (Schedule 1). Under Section 64 of CEPA, TCE is a substance that is determined to be toxic since it is entering or may enter the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity. A risk assessment was completed by the Environment and Climate Change Canada (ECCC) under Schedule 1 concluded that TCE has the potential to cause harm to the environment (Environment Canada, 1993). Specifically, ECCC concluded that TCE is not expected to cause adverse effects to aquatic biota or terrestrial wildlife but may cause adverse effects to terrestrial plants from atmospheric concentrations of TCE.

***Toxicity to Aquatic Organisms***

Aquatic toxicity data were identified for fish, aquatic invertebrates, algae, and amphibians. Acute and chronic aquatic toxicity studies considered in this assessment are summarized in Table 2-8 (below). Fish acute 96-hour lethal concentration at which 50% of test organisms die ($LC_{50}$) values ranged from 1.9 mg/L to 66.8 mg/L. For aquatic invertebrates, the acute effect concentration at which 50% of test organisms exhibit an effect ($EC_{50}$) values ranged from 7.8 mg/L (a 48-hour $EC_{50}$ in *Daphnia magna*) to 22 mg/L (a 24-hour $EC_{50}$ in *Daphnia magna*). For aquatic plants, acute $EC_{50}$ values range from 26.24 mg/L to 820 mg/L. For amphibians, acute 96-hour $LC_{50}$ values range from 412.0 mg/L to 490.0 mg/L, and acute 96-hr $EC_{50}$ values range from 22 mg/L to more than 85 mg/L. For planarian (*Dugesia japonica*), an $LC_{50}$ of 1.7 mg/L was reported over 7 days.

For chronic fish toxicity, a no-observable-effect concentration (NOEC) of 10.568 mg/L and a lowest-observable-effect concentration (LOEC) of 20.915 mg/L were reported for mortality, resulting in a chronic value (ChV) for fish of 14.850 mg/L. For aquatic invertebrates, a NOEC of 7.1 mg/L and a LOEC of 12 mg/L was reported for reproduction, resulting in a ChV of 9.2 mg/L. For aquatic plants, a NOEC of 0.02 mg/L and a LOEC of 0.05 mg/L were reported for growth, resulting in a ChV of 0.03 mg/L.

As stated in Section 2.3.1, TCE is not expected to accumulate in aquatic organisms. The COCs calculated later in this section show an acute COC of 340 ppb and a chronic COC of 3 ppb. As stated in Section 2.3.4, surface water monitoring data show detection concentrations for TCE below the acute COC but above the chronic COC.

***Toxicity to Terrestrial Organisms***

Terrestrial toxicity data were identified for terrestrial invertebrates, plants, avian, fungi, and mammals (Table 2-8) (U.S. EPA, 2017g). For terrestrial invertebrates, an acute value was reported in earthworms (*Eisenia fetida*) with a 48-hour $LC_{50}$ of 105 µg/cm$^2$. Acute toxicity was observed in terrestrial plants exposed through hydroponic root exposure at 118 mg/L for two weeks, and in terrestrial plants exposed through the air at 10.8 µg/m$^3$ for five hours. Another study reported an $EC_{50}$ of greater than 1,000 mg/L for oat and turnip plants exposed to TCE through the soil for two weeks. Limited relevant data was available for avian and fungi. Acute toxicity values for mammals exposed to TCE ranged from 457 mg/kg bd wt to 2,190 mg/kg bd wt (LOEC).

For chronic values in terrestrial invertebrates, a NOEC of 1 mg/L and a LOEC of 30 mg/L were reported in nematodes over 28 days, resulting in a ChV of 5 mg/L. Chronic toxicity values were reported for terrestrial plants exposed to TCE through soil with a NOEC of 50 mg/L, a LOEC of 150 mg/L, and a ChV of 87 mg/L over two months. Chronic toxicity was also observed in terrestrial plants exposed through the air with concentrations of TCE as low as 2.7-10.8 µg/m$^3$ over a 6-month time-period.

As stated in Section 2.3.1, TCE is not expected to partition to soil but is expected to volatilize to air, based on its physical chemical properties. Review of hazard data for terrestrial organisms shows potential hazard; however, physical chemical properties do not support an exposure pathway through water and soil pathways to these organisms.

***Toxicity to Sediment Organisms***

No data on the toxicity to sediment organisms (e.g. *Lumbriculus variegatus*, *Hyalella azteca*, *Chironomus riparius*) were found; however, as stated in Section 2.3.1, TCE is not expected to partition to sediment, based on physical chemical properties.

***Toxicity to Microorganisms***

Toxicity values for microorganisms, including microorganisms in activated sludge and ciliates, were found during EPA's review. Values range from a 3-hour $EC_{50}$ of 260 mg/L for inhibition of respiration in activated sludge to a 24-hour $EC_{50}$ of 410 mg/L for growth inhibition in the ciliate *Tetrahymena pyriformis*.

**Table 2-8. Ecological Hazard Characterization of TCE**

| Duration | Test organism | Endpoint | Hazard value* | Units | Effect Endpoint | Citation |
|---|---|---|---|---|---|---|
| **Aquatic Organisms** | | | | | | |
| Acute | Fish | $LC_{50}$ | 1.9 – 66.8 | mg/L | Mortality | Yoshioka (1986); Alexander (1978) |
| | Aquatic invertebrates | $EC_{50}$ | 7.8 – 22 | mg/L | Mortality | Abernethy (1986); Leblanc (1980) |
| | Algae | $EC_{50}$ | 26.24 – 820 | mg/L | Growth | Tsai (2007); Lukavsky et al. (2011) |
| | Amphibian | $LC_{50}$ | 412.0 – 490.0 | mg/L | Mortality | Fort (2001) |
| | | $EC_{50}$ | 22 – >85 | mg/L | Deformities | McDaniel et al. (2004) |
| | Planarian | $LC_{50}$ | 1.7 | mg/L | Mortality | Yoshioka (1986) |
| | Acute COC | 0.34 | | mg/L | | |
| Chronic | Fish | NOEC<br>LOEC<br>ChV | 10.568<br>20.915<br>14.850 | mg/L | Mortality | Smith (1991) |
| | Aquatic invertebrates | NOEC<br>LOEC<br>ChV | 7.1<br>12<br>9.2 | mg/L | Reproduction | Niederlehner et al. (1998) |
| | Algae | NOEC<br>LOEC<br>ChV | 0.02<br>0.05<br>0.03 | mg/L | Growth | Labra et al. (2010) |
| | Chronic COC | 0.003 | | mg/L | | |
| **Terrestrial Organisms** | | | | | | |
| Acute | Earthworm | $LC_{50}$ | 105 | $\mu g/cm^2$ | Mortality | Neuhauser (1985); Neuhauser (1986) |
| | Terrestrial plant (Hydroponic or soil exposure) | $LOEC/EC_{50}$ | 118 - >1,000 | mg/L | Zero growth; growth | Dietz and Schnoor (2001); Ballhorn (1984) |
| | Terrestrial plant (air exposure) | LOEC | 10.8 | $\mu g/m^3$ | Reduction in Photosynthetic Pigment | Environment Canada (1993) |

| | | | | | | |
|---|---|---|---|---|---|---|
| | Mammalian | LOEC | 457 – 2,190 | mg/kg bdwt | Ratio of polychromatic cells to micronucleated in bone marrow; survival | Hrelia et al. (1994); Hoffmann (1987) |
| Chronic | Nematode | NOEC<br>LOEC<br>ChV | 1<br>30<br>5 | mg/L | Abundance | Fuller et al. (1997) |
| | Terrestrial plant (soil exposure) | NOEC<br>LOEC<br>ChV | 50<br>150<br>87 | mg/L | Growth | Strycharz and Newman (2009) |
| | Terrestrial plant (air exposure) | LOEC | 2.7 – 10.8 | µg/m$^3$ | Reduction in Photosynthetic Pigment | Environment Canada (1993) |
| **Microorganisms** | | | | | | |
| Acute | Microorganisms | $EC_{50}$ | 260 – 410 | mg/L | Respiration inhibition; population growth rate | ECHA (2017a); Yoshioka (1985) |

* Values in the table are presented in the number of significant figures reported by the study authors.

***Concentrations of Concern***

The concentrations of concern (COCs) for aquatic ecological endpoints were derived based on the ecological hazard data for TCE. The information below describes how the acute and chronic COCs were calculated for aquatic toxicity.

The acute COC is derived by dividing the planarian 7-day $LC_{50}$ of 1.7 mg/L (the lowest acute value in the dataset for aquatic organisms) by an assessment factor (AF) of 5 as described in (U.S. EPA, 2013):

- Lowest value for the 7-day planarian $LC_{50}$ (1.7 mg/L) / AF of 5 = 0.34 mg/L; 0.34 x 1,000 = 340 µg/L.

The acute COC of 340 ppb, derived from the acute planarian endpoint, will be used for TCE.

The chronic COC is derived by dividing the algae ChV of 0.03 mg/L (the lowest chronic value in the dataset for aquatic organisms) by an assessment factor of 10 as described in (U.S. EPA, 2013):

- Lowest value for algae ChV (0.03 mg/L) / AF of 10 = 0.003 mg/L; 0.003 x 1,000 = 3 µg/L.

The chronic COC of 3 ppb, derived from the chronic algal endpoint, will be used for TCE.

The application of assessment factors is based on established EPA/OPPT methods (U.S. EPA, 2012b), (U.S. EPA, 2013) and were used in this hazard assessment to calculate lower bound effect levels (referred to as the concentration of concern or COC) that would likely encompass more sensitive species not specifically represented by the available experimental data. Also, assessment factors are included in the COC calculation to account for differences in inter- and intra-species variability, as well as laboratory-to-field variability. It should be noted that these assessment factors are dependent upon the availability of datasets that can be used to characterize relative sensitivities across multiple species within a given taxa or species group, but are often standardized in risk assessments conducted under TSCA, since the data available for most industrial chemicals are limited.

In conclusion, the hazard of TCE to aquatic organisms from acute exposures is moderate, and the hazard from chronic exposures is high based on available data. The hazard of TCE is expected to be low for sediment-dwelling organisms and terrestrial organisms based on physical and chemical properties of TCE.

### 2.4.2 Human Health Hazards

TCE has an existing EPA IRIS Assessment (U.S. EPA, 2011c) and an ATSDR Toxicological Profile (ATSDR, 2014a); hence, many of the hazards of TCE have been previously compiled and systematically reviewed. Furthermore, EPA previously reviewed data/information on health effects endpoints, identified hazards and conducted dose-response analysis in the TSCA Work Plan Chemical Risk Assessment of TCE (U.S. EPA, 2014c). EPA has relied heavily on these comprehensive reviews in preparing this problem formulation. EPA expects to use these previous analyses as a starting point for identifying key and supporting studies to inform the human health hazard assessment, including dose-response analysis. The relevant studies will be evaluated using the data quality criteria in the *Application of Systematic Review in TSCA Risk Evaluations document* (U.S. EPA, 2018). EPA also expects to consider other studies (e.g., more recently published, alternative test data) that have been published since these reviews, as identified in the literature search conducted by the Agency for TCE [*Trichloroethylene (CASRN 79-01-6) Bibliography: Supplemental File for the TSCA Scope Document*) (EPA-HQ-OPPT-2016-0737; U.S. EPA, 2017g)]. Based on reasonably available information, the following sections describe the potential hazards associated with TCE.

#### 2.4.2.1 Non-Cancer Hazards

***Acute Toxicity***

Human volunteers reported mild nose and throat irritation in TCE inhalation studies (U.S. EPA, 2014c) and laboratory studies have also demonstrated acute effects of TCE on the respiratory tract in the form of both localized irritation and broad fibrosis as well as labored breathing (U.S. EPA, 2011c). Acute exposures to TCE have additionally shown to cause central nervous system depression and cardiac arrhythmias while there are also reports of deaths following accidental exposure (NAC/AEGL, 2009). An Acute Exposure Guideline Level (AEGL) has been derived for TCE (NAC/AEGL, 2009).

***Liver toxicity***

Several available human studies have reported clinical and functional evidence of TCE-induced liver toxicity. The primary effect of TCE on liver in laboratory rodents is hepatomegaly (which has also been observed in humans), with only mild effects seen in other indicators of toxicity such as necrosis and enzyme changes (U.S. EPA, 2011c).

***Kidney toxicity***

Multiple lines of evidence in human and animal studies support the conclusion that TCE induces toxic nephropathy. Visible effects resulting from TCE exposure include both histopathological and weight changes in the kidney (U.S. EPA, 2011c).

***Reproductive/developmental toxicity***
Human studies have reported TCE exposure to be associated with increased sperm density and decreased sperm quality, altered sexual drive or function, and altered serum endocrine levels. Male reproductive effects have been corroborated by several laboratory animal studies reporting effects on sperm, libido/copulatory behavior and serum hormone levels, while histopathological lesions in testis or epididymis, altered sperm-oocyte binding and reduced fertilization have also been observed. Evidence for female reproductive toxicity is more limited, however delayed parturition (giving birth) was identified as an adverse effect (U.S. EPA, 2011c). Additionally, epidemiological and/or experimental animal studies of TCE have reported increases in total birth defects, central nervous system (CNS) defects, oral cleft defects, eye/ear defects, kidney/urinary tract disorders, musculoskeletal birth anomalies, lung/respiratory tract disorders, skeletal defects, developmental immunotoxicity, and cardiac defects (U.S. EPA, 2011c). Increased incidence of fetal cardiac malformations was identified as the most sensitive health endpoint within the developmental toxicity domain in the TSCA Work Plan Chemical Risk Assessment of TCE (U.S. EPA, 2014c).

***Neurotoxicity***
Both epidemiologic and animal studies have reported abnormalities in trigeminal nerve function and psychomotor effects in association with TCE exposure. Laboratory animal studies have demonstrated additional critical effects from TCE exposure including auditory impairment and decreased wakefulness (U.S. EPA, 2011c).

***Immunotoxicity***
TCE promotes both immunosuppressive and auto-immune effects in humans and animals. Sensitive markers of immunosuppression that have been observed include decreased thymus weight and cellularity as well as reduced immune cell response. Auto-immune effects include hypersensitivity (discussed in sensitization section) and increased anti dsDNA/ssDNA antibodies (U.S. EPA, 2011c).

***Sensitization***
Limited epidemiological data do not support an association between TCE exposure and allergic respiratory sensitization or asthma; however, there is strong human evidence for severe skin sensitization resulting in dermatitis, mucosal lesions and often systemic effects such as hepatitis. Skin sensitization tests on rodents corroborate the contact allergenicity potential of TCE and its metabolites along with the resulting immune-mediated hepatitis (U.S. EPA, 2011c).

#### 2.4.2.2 Genotoxicity and Cancer Hazards

Studies in humans have shown convincing evidence of a causal association between TCE exposure in humans and kidney cancer as well as human evidence of TCE carcinogenicity in the liver and lymphoid tissues. Further support for TCE's carcinogenic characterization comes from positive results in multiple rodent cancer bioassays in rats and mice of both sexes, similar toxicokinetics between rodents and humans, mechanistic data supporting a mutagenic mode of action for kidney tumors, and the lack of mechanistic data supporting the conclusion that any of the mode(s) of action for TCE-induced rodent tumors are irrelevant to humans (U.S. EPA, 2011c). TCE is considered to have both genotoxic and non-genotoxic mechanisms. Following EPA's Guidelines for Carcinogen Risk Assessment (U.S. EPA, 2005), including a weight of evidence judgement, TCE is considered "carcinogenic to humans" by all

routes of exposure and calculated quantitative estimates of risk from oral and inhalation exposures (U.S. EPA, 2011c).

#### 2.4.2.3 Potentially Exposed or Susceptible Subpopulations

TSCA requires that the determination of whether a chemical substance presents an unreasonable risk include consideration of unreasonable risk to "a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation" by EPA. TSCA § 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." In developing the hazard assessment, EPA will evaluate available data to ascertain whether some human receptor groups may have greater susceptibility than the general population to the chemical's hazard(s).

## 2.5 Conceptual Models

EPA risk assessment guidance (U.S. EPA, 2014b, 1998), defines Problem Formulation as the part of the risk assessment framework that identifies the factors to be considered in the assessment. It draws from the regulatory, decision-making and policy context of the assessment and informs the assessment's technical approach.

A conceptual model describes the actual or predicted relationships between the chemical substance and receptors, either human or environmental. These conceptual models are integrated depictions of the conditions of use, exposures (pathways and routes), hazards and receptors. The initial conceptual models describing the scope of the assessment for trichoroethylene, have been refined during problem formulation. The changes to the conceptual models in this problem formulation are described along with the rationales.

In this section, EPA outlines those pathways that will be included and further analyzed in the risk evaluation; will be included but will not be further analyzed in risk evaluation; and will not be included in the TSCA risk evaluation and the underlying rationale for these decisions.

EPA determined as part of problem formulation that it is not necessary to conduct further analysis on certain exposure pathways that were identified in the trichloroethylene scope document and that remain in the risk evaluation. Each risk evaluation will be "fit-for-purpose," meaning not all conditions of use will warrant the same level of evaluation and the Agency may be able to reach some conclusions without extensive or quantitative risk evaluations. 82 FR 33726, 33734, 33739 (July 20, 2017).

As part of this problem formulation, EPA also identified exposure pathways under other environmental statutes, administered by EPA, which adequately assess and effectively manage exposures and for which long-standing regulatory and analytical processes already exist, i.e., the Clean Air Act (CAA), the Safe Drinking Water Act (SDWA), the Clean Water Act (CWA) and the Resource Conservation and Recovery Act (RCRA). EPA worked closely with the offices within EPA that administer and implement the regulatory programs under these statutes. In some cases, EPA has determined that chemicals present in various media pathways (i.e., air, water, land) fall under the jurisdiction of existing regulatory programs and associated analytical processes carried out under other EPA-administered statutes and have been assessed and effectively managed under those programs. EPA believes that the TSCA risk evaluation should focus on those exposure pathways associated with TSCA uses that are not subject to the regulatory regimes discuss above because these pathways are likely to represent the greatest areas of concern to EPA. As a result, EPA does not plan to include in the risk evaluation certain exposure pathways identified in the TCE scope document.

### 2.5.1 Conceptual Model for Industrial and Commercial Activities and Uses: Potential Exposures and Hazards

The revised conceptual model (Figure 2-2) describes the pathways of exposure from industrial and commercial activities and uses of trichloroethylene that EPA plans to include in the risk evaluation. There are exposures to workers and/or occupational non-users via inhalation routes and/or exposures to workers via dermal routes for all conditions of use identified in this problem formulation. In EPA's 2014 risk assessment (U.S. EPA, 2014c), inhalation exposures to vapor were assessed as the most likely exposure route; however, there are potential dermal exposures for some conditions of use, such as maintenance of industrial degreasing tanks and manual handling of metal parts removed from industrial degreasing tanks. In addition to the pathways illustrated in the figure, EPA will evaluate activities resulting in exposures associated with distribution in commerce (e.g. loading, unloading) throughout the various lifecycle stages and conditions of use (e.g. manufacturing, processing, industrial use, commercial use, disposal) rather than a single distribution scenario.

***Inhalation***

There is potential for inhalation exposures to TCE in worker scenarios. EPA's 2014 risk assessment (U.S. EPA, 2014c) of TCE in degreasing, spot cleaning and arts & crafts uses assumed that inhalation as the primary exposure route based on the physical-chemical properties of TCE (e.g., high vapor pressure). Inhalation exposures for workers are regulated by OSHA's occupational safety and health standards for TCE, which include a PEL of 100 ppm TWA, exposure monitoring, control measures and respiratory protection. EPA expects that exposure via inhalation will be the most significant route of exposure for occupational exposure scenarios, including those involving workers and occupational non-users and will be further analyzed.

***Dermal***

There is potential for dermal exposures to TCE in many worker scenarios. Exposures to skin that are instantaneous would be expected to evaporate before significant dermal absorption could occur based on the physical chemical properties including the vapor pressure, water solubility and log $K_{OW}$ (the estimate from IHSkinPerm, a mathematical tool for estimating dermal absorption, is 0.8% absorption and 99.2% volatilization). Exposure that occurs as a deposition over time or a repeated exposure that maintains a thin layer of liquid TCE would have greater absorption (the estimate from IHSkinPerm for an 8-hr exposure is 1.6% absorption and 98.4% volatilization). In both instantaneous or repeated exposure scenarios, the dermal exposures to liquid TCE would be concurrent with inhalation exposures and overall the contribution of dermal exposure to the total exposure is relatively small. This is in agreement with the NIOSH skin notation profile for TCE, which estimates a low hazard potential by dermal absorption for systemic effects when inhalation and dermal exposures are concurrent (NIOSH, 2017). Therefore, it is not anticipated that dermal absorption will be significant for the majority of occupational exposure scenarios; thus, non-occluded dermal exposure scenarios will not be analyzed for workers. Based on the 2017 NIOSH Skin Notation Profile for TCE, TCE is associated with systemic and direct (i.e., irritation) effects, as well as sensitization. An occluded exposure scenario, wherein liquid TCE is not able to evaporate readily, may have dermal exposures that significantly contribute to the total exposure or effects on the skin (e.g., dermal sensitization). An example of such an occluded scenario includes TCE being trapped under a worker's glove during occupational activities, thus preventing the rapid volatilization that generally inhibits dermal absorption. Therefore, occluded dermal exposure scenarios will be analyzed for workers.

Generally, occupational non-users would not be expected to have dermal contact with liquid TCE; therefore, dermal exposure for these receptors will not be analyzed.

***Waste Handling, Treatment and Disposal***

Figure 2-2 shows that waste handling, treatment and disposal is expected to lead to the same pathways as other industrial and commercial activities and uses. The path leading from the "Waste Handling, Treatment and Disposal" box to the "Hazards Potentially Associated with Acute and/or Chronic Exposures See Section 2.4.2" box was re-routed to accurately reflect the expected exposure pathways, routes, and receptors associated with these conditions of use of TCE.

For each condition of use identified in Figure 2-2, a determination was made as to whether or not each unique combination of exposure pathway, route, and receptor will be further analyzed in the risk evaluation. The results of that analysis along with the supporting rationale are presented in Appendix C and Appendix E.

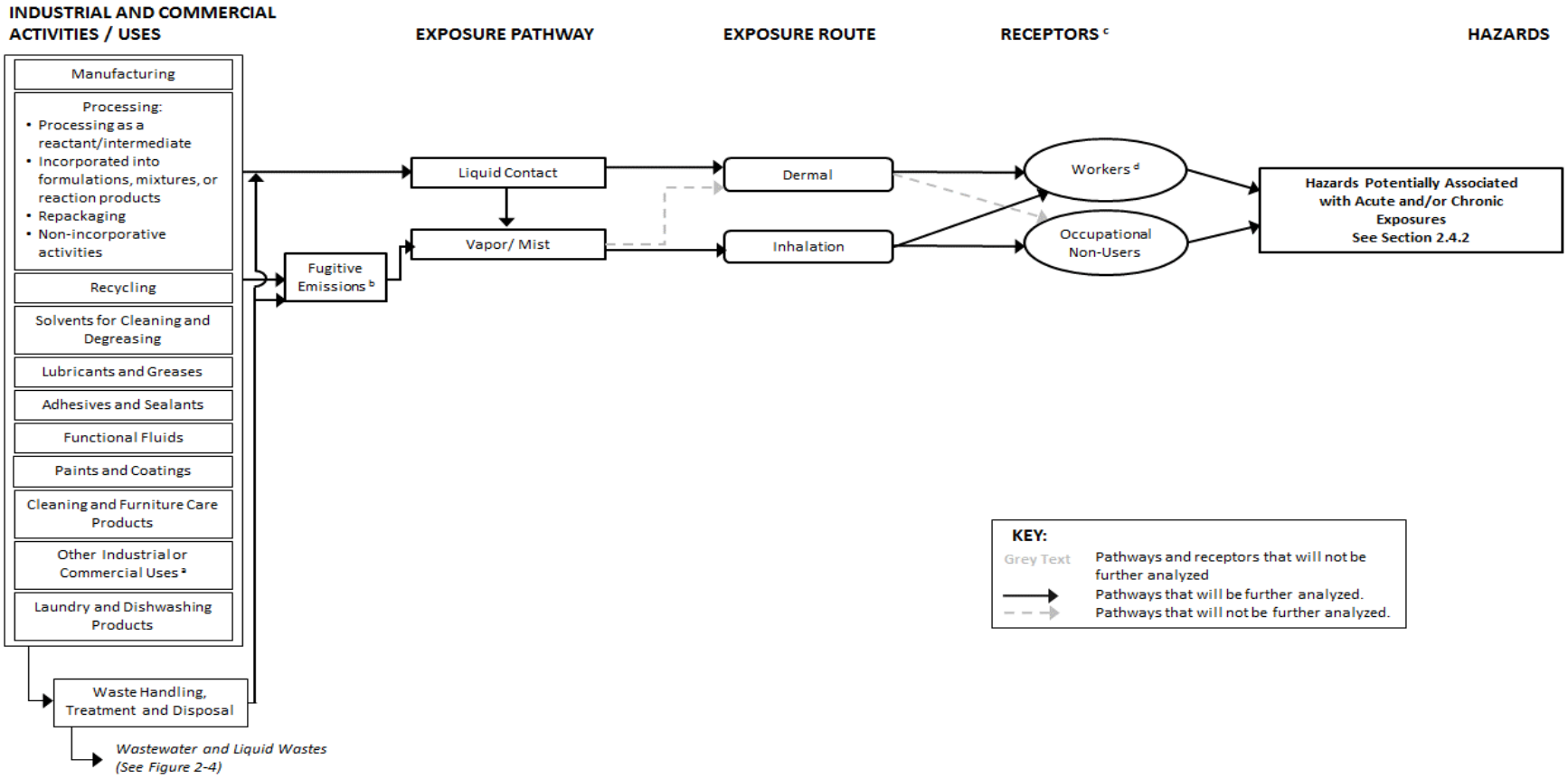


**Figure 2-2. TCE Conceptual Model for Industrial and Commercial Activities and Uses: Potential Exposures and Hazards**

The conceptual model presents the exposure pathways, exposure routes and hazards to human receptors from industrial and commercial activities and uses of TCE.

[a] Some products are used in both commercial and consumer applications. Additional uses of TCE are included in Table 2-3.

[b] Fugitive air emissions are those that are not stack emissions, and include fugitive equipment leaks from valves, pump seals, flanges, compressors, sampling connections and open-ended lines; evaporative losses from surface impoundment and spills; and releases from building ventilation systems.

[c] Receptors include potentially exposed or susceptible subpopulations.

[d] When data and information are available to support the analysis, EPA also considers the effect that engineering controls and/or personal protective equipment have on occupational exposure levels.

### 2.5.2 Conceptual Model for Consumer Activities and Uses: Potential Exposures and Hazards

The revised conceptual model (Figure 2-3) illustrates the pathways of exposure from consumer uses of TCE that EPA plans to include in the risk evaluation. In the (U.S. EPA, 2014c) risk assessment, inhalation exposures to vapor and mist were assessed as the most likely exposure route; however, there are potential dermal exposures for some conditions of use. It should be noted that some consumers may purchase and use products primarily intended for commercial use.

***Inhalation***

There is potential for inhalation exposures to TCE from consumer uses. As mentioned above, EPA/OPPT's 2014 risk assessment (U.S. EPA, 2014c) of TCE in degreasing, spot cleaning and arts & crafts uses assumed that inhalation is the main exposure pathway based on the physical-chemical properties of TCE (e.g., high vapor pressure). EPA expects that exposure via inhalation will be the primary route of exposure for consumer exposures to consumers and bystanders and will be evaluated.

***Dermal***

There is potential for dermal exposures to TCE from consumer uses. As described in section 2.5.1, TCE in direct contact with skin would be expected to evaporate before significant dermal absorption could occur. Based on TCE's physical chemical properties, including the vapor pressure, water solubility and log $K_{OW}$, only 0.8% is expected to be absorbed dermally after instantaneous exposure and only 1.6% of TCE is expected to be absorbed dermally after an 8-hour duration of continual deposition. Furthermore, dermal exposures to liquid TCE are expected to be concurrent with inhalation exposures, which reflect the preponderance of overall exposure from a particular use or activity for most consumer exposure scenarios. Therefore, non-occluded dermal exposure scenarios will not be analyzed for systemic effects for users. However, dermal sensitization will still be considered for these scenarios. There may also be certain scenarios with a higher dermal exposure potential, for example, an occluded scenario where liquid TCE is not able to evaporate readily such as a user holding a rag soaked with liquid TCE against their palm during a cleaning activity. Therefore, occluded dermal exposure scenarios will be evaluated for both systemic effects and sensitization and non-occluded scenarios will only be evaluated for sensitization. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures would also be concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be analyzed in these cases.

Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, dermal exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. There is potential for bystanders or users to have indirect dermal contact via contact with a surface upon which TCE has been applied (e.g., counter, floor). Based on the expectation that TCE would evaporate from the surface rapidly, with <1% dermal absorption predicted from instantaneous contact, this route is unlikely to contribute significantly to overall exposure. Therefore, dermal exposure scenarios will not be analyzed for bystanders.

***Oral***

Oral exposure to TCE may occur through incidental ingestion of TCE mists that deposit in the upper respiratory tract. EPA initially assumed that mists may be swallowed. However, based on physical chemical properties, mists of TCE are expected to be rapidly absorbed in the respiratory tract or evaporate being introduced into the respiratory tract, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. Furthermore, based on available toxicological data, EPA does not expect inhalation and oral routes of exposure to differ significantly in the toxicity of TCE. Therefore,

EPA will not analyze oral exposures to mists and instead will assume mists will be absorbed in the lungs.

Oral exposures could also occur through hand-to-mouth patterns following dermal contact with TCE. As described, dermal contact would not be expected for bystanders, and any TCE present on surfaces of the home or skin surfaces is expected to volatilize rapidly – making it available for inhalation as a vapor before oral ingestion may occur through such patterns. Therefore, EPA will not analyze oral exposures for users or bystanders and instead assume any mists present are absorbed in the lungs and any TCE present on surfaces are inhaled as vapors.

***Disposal***

EPA does not plan to further analyze exposure to consumers from disposal of consumer products. It is anticipated that most products will be disposed of in original containers, particularly those products that are purchased as aerosol cans. There may be some consumer exposure (dermal or inhalation) during clean up following use (e.g., spills, drips) leading to transient dermal exposure or inhalation exposure. Disposal of spent products are expected to be taken to municipal landfill sites and collected and disposed of as part of their waste handling practices.

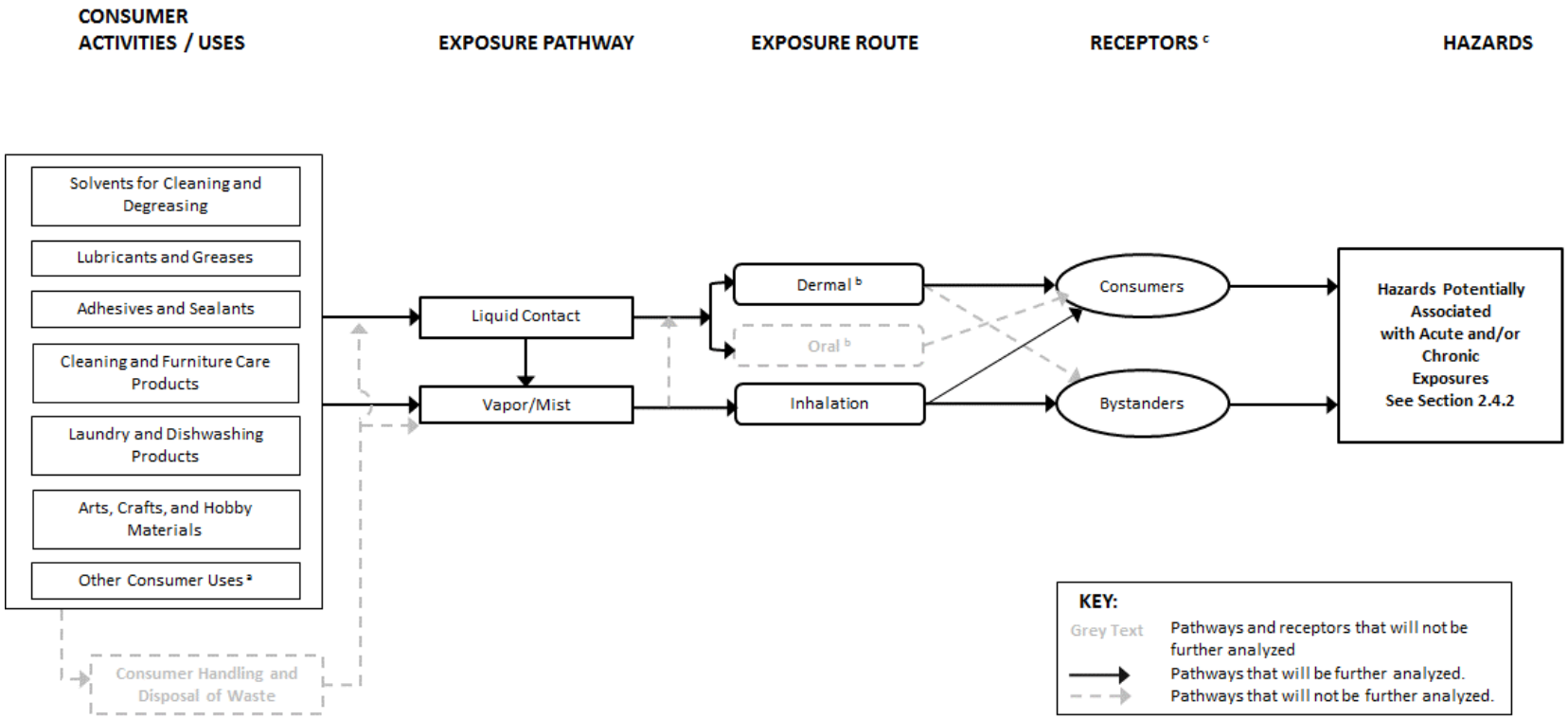


**Figure 2-3. TCE Conceptual Model for Consumer Activities and Uses: Potential Exposures and Hazards**

The conceptual model presents the exposure pathways, exposure routes and hazards to human receptors from consumer activities and uses of TCE.

[a] Some products are used in both commercial and consumer applications. Additional uses of TCE are included in Table 2-3.

[b] Exposure may occur through mists that deposit in the upper respiratory tract however, based on physical chemical properties, mists of TCE will likely be rapidly absorbed in the respiratory tract or evaporate and not result in an oral exposure. Although less likely given the physical-chemical properties, oral exposure may also occur from incidental ingestion of residue on hand/body.

[c] Receptors include potentially exposed or susceptible subpopulations.

### 2.5.3 Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards

The revised conceptual model Figure 2-4 illustrates the expected exposure pathways to human and ecological receptors from environmental releases and waste streams associated with industrial and commercial activities for TCE. The pathways that EPA plans to include and analyze further in risk evaluation are described in Section 2.5.3.1 and shown in the conceptual model. The pathways that EPA plans to include but not further analyze in risk evaluation are described in Section 2.5.3.2 and shown in the conceptual model. The pathways that EPA does not plan to include in risk evaluation are described in Section 2.5.3.3.

#### 2.5.3.1 Pathways That EPA Plans to Include and Further Analyze in Risk Evaluation

EPA expects to analyze aquatic species (i.e. aquatic plants) exposed via contaminated surface water. There are no national recommended water quality criteria for the protection of aquatic life for TCE and as a result EPA does not believe that TCE exposure to aquatic organisms in surface water has been adequately assessed or effectively managed under other EPA statutory authorities. Trichloroethylene is released to surface water from ongoing industrial and/or commercial activities, as reported in recent TRI and DMR release and loading data. TRI reporting from 2015 indicates direct releases to surface water of 52 lbs/yr and indirect releases to surface water (i.e., sent off-site to a publically owned treatment works (POTW)) of 28 lbs/yr. In 2016, the top ten DMR dischargers reported site-specific loadings to surface water of 17.5 to 1,564 lbs/yr. Within the past ten years of surface water monitoring data from STORET, there are detections (e.g., maximum of 50 ppb and average of 4.5 ppb), that do not exceed the preliminary acute COCs (acute COC = 340 ppb, based on an acute planarian endpoint), but did exceed the preliminary chronic COC (chronic COC = 3 ppb, based on a chronic algal endpoint). EPA has not developed CWA section 304(a) recommended water quality criteria for the protection of aquatic life for trichloroethylene, and there are no national recommended criteria for this use available for adoption into state water quality standards and available for use in NPDES permits (see Section 2.5.3.3). Due to the rational above, EPA will further analyze aquatic life risk evaluation.

#### 2.5.3.2 Pathways that EPA Plans to Include But Not Further Analyze

Based on TCE's fate properties, it is not anticipated to partition to biosolids during wastewater treatment. TCE has a predicted 81% wastewater treatment removal efficiency, predominately due to volatilization during aeration. Any TCE present in the water portion of biosolids following wastewater treatment and land application would be expected to rapidly volatilize into air. Furthermore, TCE is not anticipated to remain in soil, as it is expected to either volatilize into air or migrate through soil into groundwater. Therefore, the land application of biosolids will not be analyzed as a pathway for human or ecological exposure.

Based on TCE's fate properties, it is anticipated to primarily volatilize following discharge to surface water; thus, it is not expected that a significant portion of TCE would be available to enter the sediment compartment.

Review of hazard data for terrestrial organisms shows potential hazard; however, physical chemical properties do not support an exposure pathway through water and soil pathways to these organisms. Therefore, exposure to terrestrial organisms will not be analyzed.

#### 2.5.3.3 Pathways that EPA Does Not Plan to Include in the Risk Evaluation

Exposures to receptors (i.e. general population, terrestrial species) may occur from industrial and/or commercial uses, industrial releases to air, water or land, and other conditions of use. As described in Section 2.5, EPA does not expect to include in the risk evaluation pathways under programs of other environmental statutes, administered by EPA, which adequately assess and effectively manage exposures and for which long-standing regulatory and analytical processes already exist. These pathways are described below.

***Ambient Air Pathway***

The Clean Air Act (CAA) contains a list of hazardous air pollutants (HAP) and provides EPA with the authority to add to that list pollutants that present, or may present, a threat of adverse human health effects or adverse environmental effects. For stationary source categories emitting HAP, the CAA requires issuance of technology-based standards and, if necessary, additions or revisions to address developments in practices, processes, and control technologies, and to ensure the standards adequately protect public health and the environment. The CAA thereby provides EPA with comprehensive authority to regulate emissions to ambient air of any hazardous air pollutant.

TCE is a HAP. EPA has issued a number of technology-based standards for source categories that emit TCE to ambient air and, as appropriate, has reviewed, or is in the process of reviewing remaining risks. Because stationary source releases of TCE to ambient air are adequately assessed and any risks effectively managed when under the jurisdiction of the CAA, EPA does not plan to evaluate emission pathways to ambient air from commercial and industrial stationary sources or associated inhalation exposure of the general population or terrestrial species in this TSCA evaluation.

***Drinking Water Pathway***

EPA has regular analytical processes to identify and evaluate drinking water contaminants of potential regulatory concern for public water systems under the Safe Drinking Water Act (SDWA). Under SDWA EPA must also review and revise "as appropriate" existing drinking water regulations every 6 years.

EPA has promulgated National Primary Drinking Water Regulations (NPDWRs) under the Safe Drinking Water Act for trichloroethylene. EPA has set an enforceable Maximum Contaminant Level (MCL) as close as feasible to a health based, non-enforceable Maximum Contaminant Level Goal (MCLG). Feasibility refers to both the ability to treat water to meet the MCL and the ability to monitor water quality at the MCL, SDWA Section 1412(b)(4)(D), and public water systems are required to monitor for the regulated chemical based on a standardized monitoring schedule to ensure compliance with the MCL.

Hence, because the drinking water exposure pathway for trichloroethylene is currently addressed in the SDWA regulatory analytical process for public water systems, EPA does not plan to include this pathway in the risk evaluation for trichloroethylene under TSCA. EPA's Office of Water and Office of Pollution Prevention and Toxics will continue to work together providing understanding and analysis of the SDWA regulatory analytical processes and to exchange information related to toxicity and occurrence data on chemicals undergoing risk evaluation under TSCA.

***Ambient Water Pathway***

EPA develops recommended water quality criteria under section 304(a) of the CWA for pollutants in surface water that are protective of aquatic life or human health designated uses. A criterion is a hazard assessment only; i.e., there is no exposure assessment or risk estimation. When states adopt criteria that EPA approves as part of state's regulatory water quality standards, exposure is considered when state

permit writers determine if permit limits are needed and at what level for a specific discharger of a pollutant to ensure protection of the designated uses of the receiving water. This is the process used under the CWA to address risk to human health and aquatic life from exposure to a pollutant in ambient waters.

EPA has developed CWA section 304(a) recommended human health criteria for 122 chemicals and aquatic life criteria for 47 chemicals. A subset of these chemicals is identified as “priority pollutants” (103 human health and 27 aquatic life), including trichloroethylene. The CWA requires that states adopt numeric criteria for priority pollutants for which EPA has published recommended criteria under section 304(a), the discharge or presence of which in the affected waters could reasonably be expected to interfere with designated uses adopted the state. For other pollutants with recommended human health criteria, EPA regulations require that state criteria contain sufficient parameters and constituents to protect designated uses. Once states adopt criteria as water quality standards, the CWA requires that National Pollutant Discharge Elimination System (NPDES) discharge permits include effluent limits as stringent as necessary to meet standards. CWA section 301(b)(1)(C). This permit issuance process accounts for risk in accordance with the applicable ambient water exposure pathway (human health or aquatic life as applicable) for the designated water use and, therefore, can the risk from the pathway can be considered assessed and managed. If numeric water quality criteria are not available for a pollutant for permit writers to develop permit limits, the risk associated with the ambient water exposure pathway cannot be considered assessed and managed.

EPA has developed recommended water quality criteria for protection of human health for trichloroethylene which are available for possible adoption into state water quality standards and are available for possible use by NPDES permitting authorities in deriving effluent limits to meet state narrative criteria. As such, this pathway will not be included in the risk evaluation under TSCA. EPA’s Office of Water and Office of Pollution Prevention and Toxics will continue to work together providing understanding and analysis of the CWA water quality criteria development process and to exchange information related to toxicity of chemicals undergoing risk evaluation under TSCA. EPA may update its CWA section 304(a) water quality criteria for trichloroethylene in the future under the CWA.

***Disposal, Sediment and Soil Pathways***

TCE is included on the list of hazardous wastes under the Resource Conservation and Recovery Act (RCRA) (40 CFR §§ 261.22, 261.31, 261.32, 261.24; Appendix VII of 40 CFR 261). The general RCRA standard in section 3004(a) for the technical (regulatory) criteria that govern the management (treatment, storage, and disposal) of hazardous waste (i.e., Subtitle C) are those "necessary to protect human health and the environment," RCRA 3004(a). The regulatory criteria for identifying “characteristic” hazardous wastes and for “listing” a waste as hazardous also relate solely to the potential risks to human health or the environment (40 CFR §§ 261.11, 261.21-261.24). RCRA statutory criteria for identifying hazardous wastes require EPA to “tak[e] into account toxicity, persistence, and degradability in nature, potential for accumulation in tissue, and other related factors such as flammability, corrosiveness, and other hazardous characteristics.” Subtitle C controls cover not only hazardous wastes that are landfilled, but also hazardous wastes that are incinerated (subject to joint control under RCRA Subtitle C and the Clean Air Act (CAA) hazardous waste combustion Maximum Achievable Control Technology (MACT)) or injected into Underground Injection Control (UIC) Class I hazardous waste wells (subject to joint control under Subtitle C and the Safe Drinking Water Act (SDWA)).

Emissions to ambient air from municipal and industrial waste incineration and energy recovery units will not be included in the risk evaluation, as they are regulated under section 129 of the Clean Air Act. CAA section 129 also requires EPA to review and, if necessary, add provisions to ensure the standards

adequately protect public health and the environment. Thus, combustion by-products from incineration treatment of TCE wastes ((< 2 million lbs identified in Table 2-6) would be subject to these regulations, as would TCE burned for energy recovery (2.6 million lbs).

EPA does not plan to include on-site releases to land that go to underground injection in the risk evaluation. TRI reporting in 2015 indicated 122 pounds released to underground injection to a Class I well and no releases to underground injection wells of Classes II-VI. Environmental disposal of trichloroethylene injected into Class I well types are presumed to be managed and prevented from further environmental release by RCRA and SDWA regulations. Therefore, disposal of trichloroethylene via underground injection is not likely to result in environmental and general population exposures.

EPA does not plan to include releases to land that go to RCRA Subtitle C hazardous waste landfills in the risk evaluation. Based on 2015 reporting, the majority of TRI land disposal includes Subtitle C landfills (49,501 pounds) with a much smaller amount transferred to "other landfills" both on-site and off-site (400 pounds reported in 2015). TCE is present in commercial and consumer products that may be disposed of in landfills, such as Municipal Solid Waste landfills. Design standards for Subtitle C landfills require double liner, double leachate collection and removal systems, leak detection system, run on, runoff, and wind dispersal controls, and a construction quality assurance program. They are also subject to closure and post-closure care requirements including installing and maintaining a final cover, continuing operation of the leachate collection and removal system until leachate is no longer detected, maintaining and monitoring the leak detection and groundwater monitoring system. Bulk liquids may not be disposed in Subtitle C landfills. Subtitle C landfill operators are required to implement an analysis and testing program to ensure adequate knowledge of waste being managed, and to train personnel on routine and emergency operations at the facility. Hazardous waste being disposed in Subtitle C landfills must also meet RCRA waste treatment standards before disposal. Given these controls, general population exposure in groundwater from Subtitle C landfill leachate is not expected to be a significant pathway.

EPA does not plan to include on-site releases to land from RCRA Subtitle D municipal solid waste landfills or exposures of the general population (including susceptible populations) or terrestrial species from such releases in this TSCA evaluation. While permitted and managed by the individual states, municipal solid waste (MSW) landfills are required by federal regulations to implement some of the same requirements as Subtitle C landfills. MSW landfills generally must have a liner system with leachate collection and conduct groundwater monitoring and corrective action when releases are detected. MSW landfills are also subject to closure and post-closure care requirements, and must have financial assurance for funding of any needed corrective actions. MSW landfills have also been designed to allow for the small amounts of hazardous waste generated by households and very small quantity waste generators (less than 220 lbs per month). Bulk liquids, such as free solvent, may not be disposed of at MSW landfills.

EPA does not expect to include on-site releases to land from industrial non-hazardous and construction/demolition waste landfills. Industrial non-hazardous and construction/demolition waste landfills are primarily regulated under state regulatory programs. States must also implement limited federal regulatory requirements for siting, groundwater monitoring, and corrective action, and a prohibition on open dumping and disposal of bulk liquids. States may also establish additional requirements such as for liners, post-closure and financial assurance, but are not required to do so. Therefore, EPA does not expect to include this pathway in the risk evaluation.

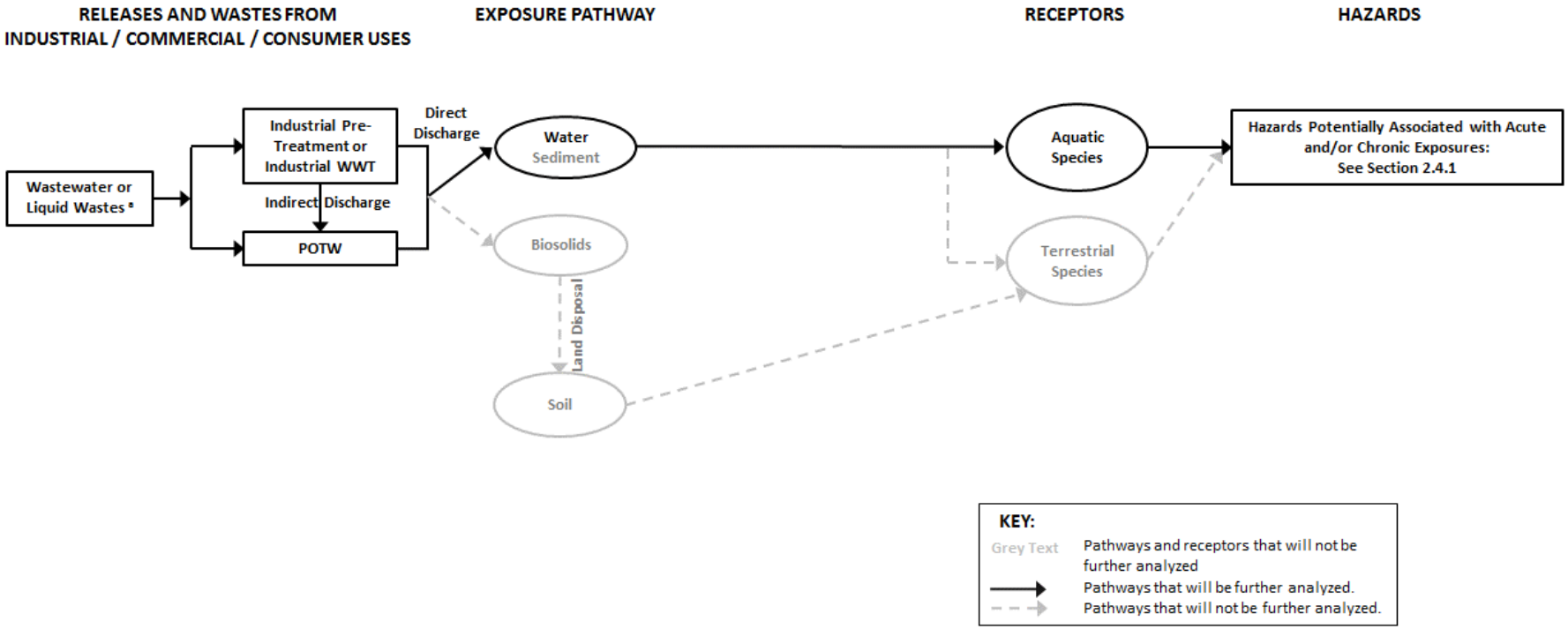


**Figure 2-4. TCE Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards**

The conceptual model presents the exposure pathways, exposure routes and hazards to human and environmental receptors from environmental releases and wastes of TCE.

[a] Industrial wastewater or liquid wastes may be treated on-site and then released to surface water (direct discharge), or pre-treated and released to POTW (indirect discharge).

## 2.6 Analysis Plan

The analysis plan presented here is a refinement of the initial analysis plan that was published in the Scope of the Risk Evaluation for Trichloroethylene (EPA-HQ-OPPT-2016-0737-0057; U.S. EPA, 2017d).

The analysis plan outlined here is based on the conditions of use for trichloroethylene, as described in Section 2.2 of this problem formulation. EPA is implementing systematic review approaches to identify, select, assess, integrate and summarize the findings of studies supporting the TSCA risk evaluation. The analytical approaches and considerations in the analysis plan are used to frame the scope of the systematic review activities for this assessment. The supplemental document, *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018), provides additional information about criteria and methods that have been and will be applied to the first 10 chemical risk evaluations.

While EPA has conducted a comprehensive search for reasonably available data as described in the Scope for TCE (EPA-HQ-OPPT-2016-0737-0057; U.S. EPA, 2017d), EPA encourages submission of additional existing data, such as full study reports or workplace monitoring from industry sources, that may be relevant for refining conditions of use, exposures, hazards and potentially exposed or susceptible subpopulations during the risk evaluation. EPA will continue to consider new information submitted by the public.

During risk evaluation, EPA will rely on the comprehensive literature results *Trichloroethylene (CASRN 79-01-6) Bibliography: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0737; U.S. EPA, 2017g) or supplemental literature searches to address specific questions. Further, EPA may consider any relevant confidential business information (CBI) in the risk evaluation in a manner that protects the confidentiality of the information from public disclosure. The analysis plan is based on EPA's knowledge of trichloroethylene to date, which includes partial, but not complete review of identified literature. If additional data or approaches become available, EPA may refine its analysis plan based on this information.

### 2.6.1 Exposure

Based on their physical-chemical properties, expected sources, and transport and transformation within the outdoor and indoor environment, chemical substances are more likely to be present in some media and less likely to be present in others. Media-specific exposure levels will vary based on the chemical substance of interest. For most high-priority chemical substances, non-zero background level(s) can be characterized through a combination of available monitoring data and modeling approaches.

#### 2.6.1.1 Environmental Releases

EPA plans to further analyze releases to water, based on information described in Section 2.5. For the purposes of developing estimates of occupational exposure, EPA may use release related data in selected data sources such as the Toxics Release Inventory (TRI) and National Emissions Inventory (NEI) programs.

EPA expects to consider and analyze releases to water as follows:

1) **Review reasonably available published literature or information on processes and activities associated with TCE conditions of use to evaluate the types of releases and wastes generated.**

EPA plans to evaluate other sources of information such as the EPA Effluent Guidelines and may use these data in conducting the exposure assessment component of the risk evaluation.

EPA has reviewed some key data sources containing information on processes and activities resulting in releases, and the information found is shown below as well as in Appendix B.3. EPA will continue to review data sources identified in Appendix B.3 during risk evaluation. The evaluation strategy for engineering and occupational data sources discussed in the *Application of Systematic Review in TSCA Risk Evaluations document* (U.S. EPA, 2018) describes how studies will be reviewed.

| |
|---|
| 2014 Draft ATSDR Toxicological Profile for TCE |
| U.S. EPA TRI Data (Reporting Year 2016 only) |
| U.S. EPA Generic Scenarios |
| OECD Emission Scenario Documents |
| U.S. EPA NEI Data |
| EU Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) Specific Environmental Release Categories (SpERC) factsheets |
| Discharge Monitoring Report (DMR) surface water discharge data from NPDES-permitted facilities |
| EPA AP-42 Air Emission Factors |

**2) Review reasonably available chemical-specific release data, including measured or estimated release data (e.g., data collected under the TRI program).**

EPA has reviewed key release data sources including the Toxics Release Inventory (TRI). EPA will continue to review relevant data sources as identified in Table_Apx B-4 during risk evaluation. EPA will match identified data to applicable conditions of use and identify data gaps when no data are found.

Additionally, for conditions of use where no published release data are available, EPA may use a variety of methods including the application of conservative release estimation approaches and assumptions in the Chemical Screening Tool for Exposures and Environmental Releases (ChemSTEER).

**3) Review measured or estimated release data for surrogate chemicals that have similar uses and physical-chemical properties.**

Data for similar solvents that are used in the same applications, such as 1-bromopropane or perchloroethylene, may be used as surrogate for TCE. EPA will review literature sources identified and if surrogate data are found, EPA will match these data to applicable conditions of use for potentially filling data gaps.

**4) Understand and consider regulatory limits that may inform estimation of environmental releases.**

EPA has identified information from various EPA statutes (including, for example, regulatory limits, reporting thresholds, or disposal requirements) that may be relevant to release estimation. Some of the information has informed revision of the conceptual models during problem

formulation. EPA will further consider relevant regulatory requirements and their potential impact on environmental releases during risk evaluation.

For example, TCE is a hazardous air pollutant (HAP) regulated under the Clean Air Act (CAA), and both a priority pollutant and toxic pollutant regulated under the Clean Water Act (CWA). EPA has identified several regulations under the CAA and CWA that regulate the release of TCE into the environment, including the National Emission Standards for Hazardous Air Pollutants (NESHAP) for Halogenated Solvent Cleaning (40 CFR Part 63, Subpart T), the NESHAP for the Synthetic Organic Chemical Manufacturing Industry (SOCMI) (40 CFR Part 63, Subparts F, G, H, and I), and the Industrial Effluent Guidelines for Organic Chemicals, Plastics, and Synthetic Fibers (40 CFR Part 414).

**5) Review and determine applicability of Organisation for Economic Co-operation and Development (OECD) Emission Scenario Documents (ESDs) and EPA Generic Scenarios (GS) to the estimation of environmental releases.**

EPA has identified OECD Emission Scenario Documents (ESDs) and EPA Generic Scenarios that correspond to some conditions of use; for example, the ESD on Industrial Use of Industrial Cleaners and the ESD on Industrial Use of Adhesives for Substrate Bonding may be useful. EPA will need to critically review these generic scenarios and ESDs to determine their applicability to the conditions of use assessed. EPA was not able to identify release scenarios corresponding to several conditions of use, including recycling of TCE, commercial carpet cleaning, and as an industrial process solvent. EPA will perform additional targeted research to understand those conditions of use, which may inform identification of release scenarios. EPA may also need to perform targeted research for applicable models and associated parameters that EPA may use to estimate releases for certain conditions of use.

**6) Map or group condition(s) of use to a release assessment scenario(s).**

EPA has identified release scenarios and mapped (i.e., grouped) them to relevant conditions of use as shown in Appendix C. As presented in the fourth column in Table_Apx C-1, EPA has grouped the scenarios into seventeen representative release/exposure scenarios, of which five scenarios will be further analyzed. For example, some scenario groupings include Industrial Batch Cold Cleaning and Industrial Roll Applications of paints/coatings and adhesives/sealants. EPA was not able to identify release scenarios corresponding to several conditions of use (e.g. recycling, commercial carpet cleaning, and use as an industrial process solvent) due generally to a lack of knowledge of those conditions of use. EPA will perform additional targeted research to understand those uses which may inform identification of release scenarios. EPA will group similar conditions of use (based on factors including process equipment and handling, release sources, and usage rates of TCE and formulations containing TCE) into scenario groupings but may further refine these groupings as additional information becomes available during risk evaluation.

**7) Evaluate the weight of evidence for environmental release scenarios.**

EPA will rely on the weight of the scientific evidence when evaluating and integrating environmental release data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and

integration of the evidence. Refer to the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018) document for more information on the general process for data integration.

#### 2.6.1.2 Environmental Fate

EPA expects to consider and analyze fate and transport in environmental media as follows:

1) **Review reasonably available measured or estimated environmental fate endpoint data collected through the literature search.**

   Data on measured concentrations in water will be collected and used along with chemical and physical properties to evaluate exposures in surface water groundwater wastewater treatment systems, landfill leachate and other aqueous systems. Measured data on the chemical behavior of TCE in aqueous systems will be collected via systematic review. When not available chemical and biological fate parameters will be estimated using Estimation Program Interface Suite™ (EPI Suite™), SPARC and other estimation models.

2) **Using measured data and/or modeling, determine the influence of environmental fate endpoints (e.g., persistence, bioaccumulation, partitioning, transport) on exposure pathways and routes of exposure to human and environmental receptors.**

   Measured fate data including volatilization from water, sorption to organic matter in soil and sediments, aqueous and atmospheric photolysis rates, and aerobic and anaerobic biodegradation rates, along with physical-chemical properties and models such as the EPI Suite™ STP model (which estimates removal in wastewater treatment due to adsorption to sludge and volatilization to air) and volatility model (which estimates half-life from volatilization from a model river and model lake), will be used to characterize the movement and persistence of trichloroethylene in environmental media.

3) **Evaluate the weight of the evidence of environmental fate data.**

   EPA will rely on the weight of the scientific evidence when evaluating and integrating environmental fate data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

#### 2.6.1.3 Environmental Exposures

EPA expects to consider the following in developing its environmental exposure assessment of trichloroethylene:

1) **Refine and finalize exposure scenarios for environmental receptors by considering unique combinations of sources (use descriptors), exposure pathways, exposure settings, populations exposed, and exposure routes.**

   For trichloroethylene, exposure scenarios for environmental receptors include exposures from surface water.

2) **Review reasonably available environmental and biological monitoring data for environmental exposure to surface water.**

   EPA will rely on databases (see examples below) and literature obtained during systematic review to include ranges and trends of chemical in surface water, including any trends seen in concentrations and spatial trends.
   - STORET and NWIS (USGS/EPS)
   - OPPT monitoring database

3) **Review reasonably available information on releases to determine how modeled estimates of concentrations near industrial point sources compare with available monitoring data.**

   Available exposure models that estimate surface water (e.g. E-FAST) will be evaluated and considered alongside available surface water data to characterize environmental exposures. Modeling approaches to estimate surface water concentrations generally consider the following inputs: direct release into surface water and transport (partitioning within media) and characteristics of the environment (river flow, volume of pond, meteorological data).

4) **Determine applicability of existing additional contextualizing information for any monitored data or modeled estimates during risk evaluation.**

   For example, site/location, time period, and conditions under which monitored data were collected will be evaluated to determine relevance and applicability to wider scenario development. Any studies which relate levels of trichloroethylene in the environment or biota with specific sources or groups of sources will be evaluated.

5) **Evaluate the weight of evidence of environmental occurrence data and modeled estimates.**

   EPA will rely on the weight of the scientific evidence when evaluating and integrating environmental exposure data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence. Refer to the supplemental document, Application of Systematic Review in TSCA Risk Evaluations, for more information on the general process for data evaluation.

#### 2.6.1.4 General Population

EPA does not plan to consider and analyze general population exposures in the risk evaluation for TCE. EPA has determined that the existing regulatory programs and associated analytical processes have addressed or are in the process of addressing potential risks of TCE that may be present in various media pathways (e.g., air, water, land) for the general population. For these cases, EPA believes that the TSCA risk evaluation should focus not on those exposure pathways, but rather on exposure pathways associated with TSCA uses that are not subject to those regulatory processes.

#### 2.6.1.5 Occupational Exposures

EPA will analyze exposures to workers and occupational non-users as follows:

1) **Review reasonably available exposure monitoring data for specific condition(s) of use.**

EPA expects to review exposure data including workplace monitoring data collected by government agencies such as the Occupational Safety and Health Administration (OSHA) and the National Institute for Occupational Safety and Health (NIOSH), and monitoring data found in published literature (including both personal exposure monitoring data (direct exposures) and area monitoring data (indirect exposures)). EPA has reviewed available monitoring data collected by OSHA and NIOSH and matched them to applicable conditions of use. EPA has also identified data sources that may contain relevant monitoring data for the various conditions of use. EPA will review these sources (identified in Table_Apx B-5) and other data sources to extract relevant data for consideration and analysis during risk evaluation.

2) **Review reasonably available exposure data for surrogate chemicals that have uses and chemical and physical properties similar to TCE.**

EPA will review literature sources identified and if surrogate data are found, these data will be matched to applicable conditions of use for potentially filling data gaps. For several conditions of use (e.g., cold cleaning, coating applications, adhesive applications), EPA may consider other similar solvents that share the same conditions of use as possible surrogates for TCE.

3) **For conditions of use where data are limited or not available, review existing exposure models that may be applicable in estimating exposure levels.**

EPA has identified Emission Scenario Documents (ESDs) from the Organization for Economic Co-operation and Development (OECD) and EPA Generic Scenarios (GS's) corresponding to some conditions of use. For example, the ESD on Industrial Use of Adhesives for Substrate Bonding, the ESD on Metalworking Fluids, and the GS for textile finishing are some of the ESDs and GS's that EPA may use to estimate occupational exposures. EPA will need to critically review these generic scenarios and ESDs to determine their applicability to the conditions of use assessed. EPA was not able to identify ESDs and GSs corresponding to several conditions of use, including manufacture of TCE, use of TCE as an intermediate, recycling of TCE, and commercial carpet cleaning. EPA may conduct industry outreach efforts or perform supplemental, targeted research to understand those conditions of use, which may inform identification of exposure scenarios. EPA will consider inhalation exposure to vapor and mist models in the Chemical Screening Tool for Exposure and Environmental Releases (ChemSTEER) Tool that are routinely used for assessing new chemicals. EPA may also need to perform targeted research to identify applicable models that EPA could use to estimate exposures for certain conditions of use.

4) **Review reasonably available data that may be used in developing, adapting, or applying exposure models to the particular risk evaluation scenario.**

This step will be performed after Steps #2 and #3 above. Based on information developed from Step #2 and Step #3, EPA will evaluate relevant data to determine whether the data can be used to develop, adapt, or apply models for specific conditions of use (and corresponding exposure scenarios). EPA may utilize existing, peer-reviewed exposure models developed by EPA/OPPT, other government agencies, or available in the scientific literature, or EPA may elect to develop additional models to assess specific condition(s) of use. Inhalation exposure models may be simple box models or two-zone (near-field/far-field) models. In two-zone models, the near-field

exposure represents potential inhalation exposures to workers, and the far-field exposure represents potential inhalation exposures to occupational non-users.

As part of the 2014 RA and subsequent Section 6 rulemaking, EPA developed models to assess inhalation exposures to workers and occupational non-users during the use of TCE in spot cleaning, vapor degreasing, and aerosol degreasing. The results of the RA and Section 6 analyses resulted in proposed rules banning the use of TCE in these scenarios. Scenarios previously examined in the 2014 publication will be considered in this risk evaluation to ensure previous assessments are in alignment with the Procedures for Chemical Risk Evaluation under the Amended Toxic Substances Control Act (40 CFR Part 702). During risk evaluation, EPA will evaluate the applicability of the models to other conditions of use and adapt and refine these models as necessary for evaluating exposure to TCE in scenarios not covered by the proposed rules.

EPA will consider the effect of evaporation when evaluating options for dermal exposure assessment. In addition, EPA will consider the impact of occluded exposure or repeated dermal contacts. EPA anticipates that existing EPA/OPPT dermal exposure models would not be suitable for quantifying dermal exposure to highly volatile chemicals such as TCE.

5) **Consider and incorporate applicable engineering controls and/or personal protective equipment into exposure scenarios.**

EPA will review data sources on engineering controls and personal protective equipment as identified in Table_Apx B-6 and to determine their applicability and incorporation into exposure scenarios during risk evaluation. Studies will be evaluated using the evaluation strategies laid out in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018).

6) **Evaluate the weight of the evidence of occupational exposure data, which may include qualitative and quantitative sources of information.**

EPA will rely on the weight of the scientific evidence when evaluating and integrating occupational data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence. Refer to the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018) document for more information on the general process for data evaluation.

7) **Map or group each condition of use to occupational exposure assessment scenario(s).**

EPA has identified occupational exposure scenarios and mapped them to relevant conditions of use as shown in Appendix C. As presented in the fourth column in Table_Apx C-1, EPA has grouped the scenarios into 17 representative release/exposure scenarios, of which five scenarios will be further analyzed. For example, one scenario grouping is the aerosol application of mold release and lubricant products to substrates, where mold release and lubricant products containing TCE are applied to substrates via aerosol cans. EPA was not able to identify occupational exposure scenarios corresponding to several conditions of use due generally to a lack of understanding of those conditions of use. EPA will perform targeted research to

understand those uses which may inform identification of occupational exposure scenarios and analyze those uses identified. EPA may refine the mapping/grouping of occupational exposures scenarios based on factors (e.g. process equipment and handling, usage rates of TCE and formulations containing TCE, exposure/release sources) corresponding to conditions of use as additional information is identified during risk evaluation.

#### 2.6.1.6 Consumer Exposures

EPA will analyze consumer exposures as follows:

1) **Review reasonably available consumer product-specific exposure data related to consumer uses/exposures**.

   The availability of TCE concentrations in consumer products will be evaluated. These data provide the source term for any subsequent consumer modeling. Additional product-specific data will be reviewed and considered, including formulation type, application method, percentage of TCE in product, and likely use patterns (e.g., frequency of use, duration of activity, room of use).

2) **Evaluate the weight of the evidence for consumer exposures.**

   EPA will rely on the weight of the scientific evidence when evaluating and integrating data related to consumer exposure. The weight of the evidence may include qualitative and quantitative sources of information. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence. Refer to the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018) document for more information on the general process for data integration.

3) **Review existing exposure models that may be applicable in estimating exposure levels for exposure pathways where data are not available.**

   EPA will review existing consumer exposure models that may be applicable in estimating indoor air concentrations (near field and far field) for the user and bystander, and in estimating dermal exposure to the consumer in transient exposures (e.g., typical consumer activities) and longer term (e.g., occluded) exposure scenarios. Determine the applicability of the identified models for use in a quantitative exposure assessment. Review reasonably available data that may be used in developing, adapting or applying exposure models to the particulars of this risk evaluation.

4) **Review reasonably available data that may be used in developing, adapting or applying exposure models to the particular risk evaluation. For example, existing models developed for a chemical assessment may be applicable to another chemical assessment if model parameter data are available.**

   EPA will review reasonably available empirical data that may be used in developing, adapting or applying exposure models to the exposure assessment of TCE. For example, existing models developed for a chemical assessment may be applicable to another chemical evaluation if model parameter data are available.

5) **Review reasonably available consumer product-specific sources to determine how those exposure estimates compare with those reported in monitoring data.**

EPA will evaluate the relative potential and magnitude of exposure routes based on available data. For TCE, inhalation of vapor is expected to result in relatively higher exposure to consumers and bystanders in the home compared with dermal absorption through direct contact and ingestion of mists. The data sources associated with these respective pathways have not been comprehensively evaluated, therefore quantitative comparisons across exposure pathways or in relation to toxicity thresholds are not yet possible.

6) **Review reasonably available population- or subpopulation-specific exposure factors and activity patterns to determine if potentially exposed or susceptible subpopulations need be further refined.**

Based on hazard concerns, certain subpopulations such as pregnant women may be included for any consumer use scenarios, as a user or bystander. Children and/or infants are generally not considered "users," but may be assessed as bystanders of consumer uses in the home. Other subpopulations may be subject to greater exposure, such as DIY users or those in the business of arts and crafts.

Considerations will include:

- Age-specific differences (exposure factors and activity patterns) for populations defined in the exposure scenarios. Exposure factors and activities patterns will be sourced from EPA's 2011 Exposure Factors Handbook.
- Characteristics of the user of the consumer product and the bystander in the room, including for example, women of child bearing age and children.
- Subpopulations that may have greater exposure due to magnitude, frequency or duration of exposure as they apply to specific consumer products.

7) **Map or group each condition of use to consumer exposure assessment scenario(s).**

EPA has identified consumer exposure scenarios that include sources of exposure (i.e., consumer products), exposure pathways, exposure settings, exposure routes, and populations exposed and mapped them to relevant conditions of use, as shown in Appendix C. As presented in the fourth column in Table_Apx D-1, EPA has grouped the scenarios into 141 representative release/exposure scenarios, of which 38 scenarios will be analyzed during risk evaluation. These scenarios are associated with different receptor groups (i.e., consumers and bystanders) and different subcategories of use (e.g., liquid / non-spray applications of penetrating lubricant). EPA may refine the mapping/grouping of consumer exposures scenarios as product use patterns and are further characterized.

EPA will further refine and finalize exposure scenarios for consumers with the following considerations:

- Reasonably available data on consumer products or products available for consumer use including the weight fraction of TCE in products;
- Information characterizing the use patterns of consumer products containing TCE including the following: intended or likely consumer activity, method of application (e.g.,

spray-applied, brush-applied, dip), formulation type, amount of product used, frequency and duration of individual use events, and room or setting of use;
- The associated route of exposure for consumers; and
- Populations who may be exposed to products as users or bystanders in the home, including potentially exposed and susceptible subpopulations such as children or women of child bearing age and subsets of consumers who may use commercially-available products or those who may use products more frequently than typical consumers.

During consumer exposure modeling, these factors determine the resulting exposure route and magnitude. For example, while the product with the highest weight fraction in a given consumer product scenario could be run early on to indicate preliminary levels of exposure, that product may not actually result in the highest potential exposure due to having a lower frequency of use.

### 2.6.2 Hazards (Effects)

#### 2.6.2.5 Environmental Hazards

EPA will conduct an environmental hazard assessment of TCE as follows:

1) **Review reasonably available environmental hazard data, including data from alternative test methods (e.g., computational toxicology and bioinformatics; high-throughput screening methods; data on categories and read-across; *in vitro* studies).**

   Environmental hazard data will be evaluated using the ecological toxicity data quality criteria outlined in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018) document. The study evaluation results will be documented in the risk evaluation phase and data from suitable studies will be extracted and integrated in the risk evaluation process.

   Conduct hazard identification (the qualitative process of identifying acute and chronic endpoints) and concentration-response assessment (the quantitative relationship between hazard and exposure) for all identified environmental hazard endpoints. Suitable environmental hazard data will be reviewed for acute and chronic endpoints for mortality and other effects (e.g. growth, immobility, reproduction, etc.). EPA will evaluate the character of the concentration-response relationship (*i.e.* positive, negative or no response) as part of the review.

   Sufficient environmental hazard studies are available to assess the hazards of environmental concentrations of TCE to aquatic species (i.e. aquatic plants).

2) **Derive aquatic concentrations of concern (COC) for acute and chronic endpoints.**

   The aquatic environmental hazard studies may be used to derive acute and chronic concentrations of concern (COC) for mortality, growth or other endpoints determined to be detrimental to environmental populations. Depending on the robustness of the evaluated data for a particular organism (*e.g.* aquatic plants), environmental hazard values (e.g. ECx/LCx/NOEC/LOEC, etc.) may be derived and used to further understand the hazard characteristics of TCE to aquatic species.

3) **Evaluate the weight of the evidence of environmental hazard data.**

EPA will rely on the weight of the scientific evidence when evaluating and integrating environmental hazard data. The data integration strategy will be designed to be fit-for-purpose. EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence. Refer to the supplemental document, *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018), for more information on the general process for data evaluation.

4) **Consider the route(s) of exposure, available biomonitoring data and available approaches to integrate exposure and hazard assessments.**

EPA believes there is sufficient information to evaluate the potential risks to aquatic species (i.e. aquatic plants) from exposures to TCE in surface water.

#### 2.6.2.6 Human Health Hazards

EPA expects to analyze human health hazards as follows:

1) **Review reasonably available human health hazard data, including data from alternative test methods (e.g., computational toxicology and bioinformatics; high-throughput screening methods; data on categories and read-across; *in vitro* studies; systems biology).**

Human health studies will be evaluated using the evaluation strategies laid out in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018). Human, animal and mechanistic data will be identified and included as described in the Population, Exposure, Comparator, and Outcome (PECO) statement for TCE (see Appendix F.4). The protocol describes how studies will be evaluated using specific data evaluation criteria and a predetermined systematic approach. Study results will be extracted and presented in evidence tables by hazard endpoint. For the TCE risk evaluation, EPA will evaluate information in the IRIS assessment (U.S. EPA, 2011c), the final TSCA Work Plan Chemical Risk Assessment of TCE (U.S. EPA, 2014c) and studies published after 2010 that were captured in the comprehensive literature search conducted by the Agency for TCE [*Tricholoroethylene (79-01-6) Bibliography: Supplemental File for the TSCA Scope Document;* (EPA-HQ-OPPT-2016-0737; U.S. EPA, 2017g)] using OPPT's structured process described in the document, *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018). EPA intends to review studies published after the IRIS assessment to ensure that EPA is considering information that has been made available since these assessments were conducted. Evidence for each health outcome will be integrated by synthesizing the lines of human epidemiology and animal experimental evidence. The final TSCA Work Plan Chemical Risk Assessment of TCE (U.S. EPA, 2014c) included an assessment of fetal cardiac malformations. EPA will use the systematic review approach (U.S. EPA, 2018) to re-evaluate key studies in this assessment as well as more recent information on this endpoint. of mechanistic data as part of EPA's reevaluation of key studies. Mechanistic data related to all other endpoints will be identified as "Supplemental Information."

2) **In evaluating reasonably available data, determine whether particular human receptor groups may have greater susceptibility to the chemical's hazard(s) than the general population.**

Reasonably available human health hazard data will be evaluated to ascertain whether some human receptor groups may have greater susceptibility than the general population to TCE hazard(s). Susceptibility of particular human receptor groups to TCE will be determined by evaluating information on factors that influence susceptibility.

3) **Conduct hazard identification (the qualitative process of identifying non-cancer and cancer endpoints) and dose-response assessment (the quantitative relationship between hazard and exposure) for all identified human health hazard endpoints.**

Human health hazards from acute and chronic exposures will be identified by evaluating the human and animal data that meet the systematic review data quality criteria described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018) document. Data quality evaluation will be performed on key studies identified from the Integrated Risk Information System (IRIS) Toxicological Review of TCE (U.S. EPA, 2011c), the final TSCA Work Plan Chemical Risk Assessment of TCE (U.S. EPA, 2014c) and studies published after 2010 that were captured in the comprehensive literature search conducted by the Agency for TCE [*Tricholoroethylene (79-01-6) Bibliography: Supplemental File for the TSCA Scope Document;* (EPA-HQ-OPPT-2016-0737; U.S. EPA, 2017g)]. Hazards identified by studies meeting data quality criteria will be grouped by routes of exposure relevant to humans (oral, dermal, inhalation) and by cancer and noncancer endpoints.

Dose-response assessment will be performed in accordance with EPA guidance (U.S. EPA, 2011b, 1994). Dose-response analyses performed for the U.S. EPA (2011c) IRIS oral and inhalation reference dose determinations may be used if the data meet data quality criteria and if additional information on the identified hazard endpoints are not available or would not alter the analysis.

The cancer mode of action (MOA) determines how cancer risks can be quantitatively evaluated. EPA will evaluate information on genotoxicity and the mode of action for all cancer endpoints to determine the appropriate approach for quantitative cancer assessment in accordance with the U.S. EPA Guidelines for Carcinogen Risk Assessment (U.S. EPA, 2005).

4) **Derive points of departure (PODs) where appropriate; conduct benchmark dose modeling depending on the available data. Adjust the PODs as appropriate to conform (e.g., adjust for duration of exposure) to the specific exposure scenarios evaluated.**

Hazard data will be evaluated to determine the type of dose-response modeling that is applicable. Where modeling is feasible, a set of dose-response models that are consistent with a variety of potentially underlying biological processes will be applied to empirically model the dose-response relationships in the range of the observed data consistent with the EPA *Benchmark Dose Technical Guidance Document.* Where dose-response modeling is not feasible, no-observed-adverse-effect-levels (NOAELs) or lowest-observed-adverse-effect-levels (LOAELs) will be identified. Non-quantitative data will also be evaluated for contribution to weight of evidence or for evaluation of qualitative endpoints that are not appropriate for dose-response assessment.

EPA will evaluate whether the available physiologically-based pharmacokinetic (PBPK) and empirical kinetic models are adequate for route-to-route and interspecies extrapolation of the POD, or for extrapolation of the POD to standard exposure durations (e.g., lifetime continuous

exposure). If application of the PBPK model is not possible, oral PODs may be adjusted by body weight$^{3/4}$ ($BW^{3/4}$) scaling in accordance with (U.S. EPA, 2011b), and inhalation PODs may be adjusted by exposure duration and chemical properties in accordance with (U.S. EPA, 1994).

5) **Evaluate the weight of the evidence for human health hazards.**

   EPA will rely on the weight of the scientific evidence when evaluating and integrating human health hazard data. The data integration strategy will be designed to be fit-for-purpose in which EPA will use systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and including strengths and limitations, followed by synthesis and integration of the evidence. Refer to the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018) document for more information on the general process for data evaluation.

6) **Consider the route(s) of exposure (oral, inhalation, dermal), available route-to-route extrapolation approaches, available biomonitoring data and available approaches to correlate internal and external exposures to integrate exposure and hazard assessment.**

   EPA believes there will be sufficient data to conduct dose-response analysis and/or benchmark dose modeling for both inhalation and oral routes of exposure.

   If sufficient dermal toxicity studies are not identified in the literature search to assess risks from dermal exposures, then a route-to-route extrapolation from the inhalation and oral toxicity studies would be needed to assess systemic risks from dermal exposures. Without an adequate PBPK model for the dermal route of exposure, the approaches described in the EPA guidance document *Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part E, Supplemental Guidance for Dermal Risk Assessment)* could be applied. These approaches may be able to further inform the relative importance of dermal exposures compared with other routes of exposure.

### 2.6.3 Risk Characterization

Risk characterization is an integral component of the risk assessment process for both ecological and human health risks. EPA will derive the risk characterization in accordance with EPA's *Risk Characterization Handbook* (U.S. EPA, 2000). As defined in EPA's *Risk Characterization Policy*, "the risk characterization integrates information from the preceding components of the risk evaluation and synthesizes an overall conclusion about risk that is complete, informative and useful for decision makers." Risk characterization is considered to be a conscious and deliberate process to bring all important considerations about risk, not only the likelihood of the risk but also the strengths and limitations of the assessment, and a description of how others have assessed the risk into an integrated picture.

Risk characterization at EPA assumes different levels of complexity depending on the nature of the risk assessment being characterized. The level of information contained in each risk characterization varies according to the type of assessment for which the characterization is written. Regardless of the level of complexity or information, the risk characterization for TSCA risk evaluations will be prepared in a manner that is transparent, clear, consistent, and reasonable (TCCR) (U.S. EPA, 2000). EPA will also present information in this section consistent with approaches described in the Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act Risk Evaluation Framework Rule

(82 FR 33726). For instance, in the risk characterization summary, EPA will further carry out the obligations under TSCA section 26; for example, by identifying and assessing uncertainty and variability in each step of the risk evaluation, discussing considerations of data quality such as the reliability, relevance and whether the methods utilized were reasonable and consistent, explaining any assumptions used, and discussing information generated from independent peer review. EPA will also be guided by EPA's Information Quality Guidelines (U.S. EPA, 2002) as it provides guidance for presenting risk information. Consistent with those guidelines, in the risk characterization, EPA will also identify: (1) Each population addressed by an estimate of applicable risk effects; (2) the expected risk or central estimate of risk for the potentially exposed or susceptible subpopulations affected; (3) each appropriate upper-bound or lower bound estimate of risk; (4) each significant uncertainty identified in the process of the assessment of risk effects and the studies that would assist in resolving the uncertainty; and (5) peer reviewed studies known to the Agency that support, are directly relevant to, or fail to support any estimate of risk effects and the methodology used to reconcile inconsistencies in the scientific information.

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# APPENDICES

# Appendix A REGULATORY HISTORY

## A.1 Federal Laws and Regulations

**Table_Apx A-1. Federal Laws and Regulations**

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| **EPA Regulations** | | |
| Toxics Substances Control Act (TSCA) - Section 6(a) | Provides EPA with the authority to prohibit or limit the manufacture (including import), processing, distribution in commerce, use or disposal of a chemical if EPA evaluates the risk and concludes that the chemical presents an unreasonable risk to human health or the environment. | Proposed rule under section 6 of TSCA to address the unreasonable risks presented by TCE use in vapor degreasing (82 FR 7432; January 19, 2017). |
| TSCA - Section 6(a) | Provides EPA with the authority to prohibit or limit the manufacture (including import), processing, distribution in commerce, use or disposal of a chemical if EPA evaluates the risk and concludes that the chemical presents an unreasonable risk to human health or the environment | Proposed rule under section 6 of TSCA to address the unreasonable risks presented by TCE use in commercial and consumer aerosol degreasing and for spot cleaning at dry cleaning facilities (81 FR 91592; December 16, 2016). |
| TSCA - Section 6(b) | Directs EPA to promulgate regulations to establish processes for prioritizing chemicals and conducting risk evaluations on priority chemicals. In the meantime, EPA is directed to identify and begin risk evaluations on 10 chemical substances drawn from the 2014 update of the TSCA Work Plan for Chemical Assessments. | TCE is on the initial list of chemicals to be evaluated for unreasonable risks under TSCA (81 FR 91927, December 19, 2016). |
| TSCA - Section 5(a) | Once EPA determines that a use of a chemical substance is a significant new use under TSCA section 5(a), persons are required to submit a significant new use notice (SNUN) to EPA at least 90 days before they manufacture (including import) or process the chemical substance for that use. | Significant New Use Rule (SNUR) (81 FR 20535; April 8, 2016). TCE is subject to reporting under the SNUR for manufacture (including import) or processing of TCE for use in a consumer product except for use in cleaners and solvent degreasers, film cleaners, hoof polishes, lubricants, mirror edge sealants and pepper spray. This SNUR ensures that EPA will |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | | have the opportunity to review any new consumer uses of TCE and, if appropriate, take action to prohibit or limit those uses. |
| TSCA - Section 8(a) | The TSCA section 8(a) CDR rule requires manufacturers (including importers) to give EPA basic exposure-related information on the types, quantities and uses of chemical substances produced domestically and imported into the United States. | TCE manufacturing (including importing), processing and use information is reported under the CDR rule (76 FR 50816, August 16, 2011). |
| TSCA - Section 8(b) | EPA must compile, keep current and publish a list (the TSCA Inventory) of each chemical substance manufactured, processed or imported in the United States. | TCE was on the initial TSCA Inventory and was therefore not subject to EPA's new chemicals review process (60 FR 16309, March 29, 1995). |
| TSCA - Section 8(e) | Manufacturers (including imports), processors and distributors must immediately notify EPA if they obtain information that supports the conclusion that a chemical substance or mixture presents a substantial risk of injury to health or the environment. | 28 substantial risk notifications received for TCE (U.S. EPA, ChemView. Accessed April 13, 2017). |
| TSCA - Section 4 | Provides EPA with authority to issue rules and orders requiring manufacturers (including importers) and processors to test chemical substances and mixtures. | Seven studies received for TCE (U.S. EPA, ChemView. Accessed April 13, 2017). |
| Emergency Planning and Community Right-to-Know Act (EPCRA) - Section 313 | Requires annual reporting from facilities in specific industry sectors that employ 10 or more full time equivalent employees and that manufacture, process, or otherwise use a TRI-listed chemical in quantities above threshold levels. A facility that meets reporting requirements must submit a reporting form for each chemical for which it triggered reporting, providing data across a variety of categories, including activities and uses of the chemical, releases and other waste management (e.g., quantities recycled, treated, combusted) and pollution prevention activities (under section 6607 of the Pollution Prevention Act). These data include on- and off-site data as well | TCE is a listed substance subject to reporting requirements under 40 CFR 372.65 effective as of January 1, 1987. |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | as multimedia data (i.e., air, land and water). | |
| Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) - Section 6 | FIFRA governs the sale, distribution and use of pesticides. Section 3 of FIFRA generally requires that pesticide products be registered by EPA prior to distribution or sale. Pesticides may only be registered if, among other things, they do not cause "unreasonable adverse effects on the environment." Section 6 of FIFRA provides EPA with the authority to cancel pesticide registrations if either: (1) the pesticide, labeling, or other material does not comply with FIFRA or (2) when used in accordance with widespread and commonly recognized practice, the pesticide generally causes unreasonable adverse effects on the environment. | TCE is no longer used as an inert ingredient in pesticide products. |
| Clean Air Act (CAA) - Section 112(b) | Defines the original list of 189 HAPs. Under 112(c) of the CAA, EPA must identify and list source categories that emit HAPs and then set emission standards for those listed source categories under CAA section 112(d). CAA section 112(b)(3)(A) specifies that any person may petition the Administrator to modify the list of HAPs by adding or deleting a substance. Since 1990, EPA has removed two pollutants from the original list, leaving 187 at present. | Lists TCE as a HAP (42 U.S.C. 7412(b)(1)). |
| CAA - Section 112(d) | Section 112(d) states that the EPA must establish a National Emission Standards for Hazardous Air Pollutants (NESHAP) for each category or subcategory of major sources and area sources of HAPs (listed pursuant to Section 112(c)). The standards must require the maximum degree of emission reduction that EPA determines to be achievable by each particular source category. Different criteria for maximum achievable control technology (MACT) apply for new and existing sources. Less stringent standards, known as generally available control technology (GACT) standards, | EPA has promulgated a number of NESHAP regulating industrial source categories that emit trichloroethylene and other HAP https://www.epa.gov/stationary-sources-air-pollution/halogenated-solvent-cleaning-national-emission-standards-hazardou-0 . These include, for example, the NESHAP for Halogenated Solvent Cleaning (59 FR 61801; December 2, 1994), among others. |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | are allowed at the Administrator's discretion for area sources. | |
| CAA - Sections 112(d) and 112 (f) | Risk and technology review (RTR) of section 112(d) MACT standards. Section 112(f)(2) requires EPA to conduct risk assessments for each source category subject to section 112(d) MACT standards, and to determine if additional standards are needed to reduce remaining risks. Section 112(d)(6) requires EPA to review and revise the MACT standards, as necessary, taking into account developments in practices, processes and control technologies. | EPA has promulgated a number of RTR NESHAP (e.g., the RTR NESHAP for Halogenated Solvent Cleaning (72 FR 25138; May 3, 2007) and will do so, as required, for the remaining source categories with NESHAP. |
| CWA – Sections 301(b), 304(b), 306, and 307(b) | Requires establishment of Effluent Limitations Guidelines and Standards for conventional, toxic, and non-conventional pollutants. For toxic and non-conventional pollutants, EPA identifies the best available technology that is economically achievable for that industry after considering statutorily prescribed factors and sets regulatory requirements based on the performance of that technology. Regulations apply to existing and new sources. | TCE is designated as a toxic pollutant under section 307(a)(1) of the CWA and as such, is subject to effluent limitations. |
| CWA - Section 307(a) | Establishes a list of toxic pollutants or combination of pollutants under the to the CWA. The statute specifies a list of families of toxic pollutants also listed in 40 CFR 401.15. The “priority pollutants” specified by those families are listed in 40 CFR part 423, Appendix A. These are pollutants for which best available technology effluent limitations must be established on either a national basis through rules, or on a case-by-case best professional judgement basis in National Pollutant Discharge Elimination System (NPDES) permits. | |
| Safe Drinking Water Act (SDWA) - Section 1412 | Requires EPA to publish a non-enforceable maximum contaminant level goals (MCLGs) for contaminants which 1. may have an adverse effect on the health of persons; 2. are known to occur | EPA issued drinking water standards for TCE pursuant to section 1412 of the SDWA. EPA promulgated the NPDWR for TCE in 1987 with a MCLG of zero an |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | or there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern; and 3. in the sole judgement of the Administrator, regulation of the contaminant presents a meaningful opportunity for health risk reductions for persons served by public water systems. When EPA publishes an MCLG, EPA must also promulgate a National Primary Drinking Water Regulation (NPDWR) which includes either an enforceable maximum contaminant level (MCL), or a required treatment technique. Public water systems are required to comply with NPDWRs | enforceable MCL of 0.005 mg/L (52 FR 25690, July 8, 1987). |
| RCRA - Section 3001 | Directs EPA to develop and promulgate criteria for identifying the characteristics of hazardous waste, and for listing hazardous waste, taking into account toxicity, persistence, and degradability in nature, potential for accumulation in tissue and other related factors such as flammability, corrosiveness, and other hazardous characteristics. | TCE is included on the list of commercial chemical products, manufacturing chemical intermediates or off-specification commercial chemical products or manufacturing chemical intermediates that, when disposed (or when formulations containing any one of these as a sole active ingredient are disposed) unused, become hazardous wastes pursuant to RCRA 3001. RCRA Hazardous Waste Status: D040 at 0.5 mg/L; F001, F002; U228 |
| Comprehensive Environmental Response, Compensation and Liability Act (CERCLA) - Section 102(a) | Authorizes EPA to promulgate regulations designating as hazardous substances those substances which, when released into the environment, may present substantial danger to the public health or welfare or the environment. EPA must also promulgate regulations establishing the quantity of any hazardous substance the release of which must be reported under Section 103.<br><br>Section 103 requires persons in charge of vessels or facilities to report to the National Response Center if they have knowledge of a release of a hazardous | TCE is a hazardous substance with a reportable quantity pursuant to section 102(a) of CERCLA (40 CFR 302.4) and EPA is actively overseeing cleanup of sites contaminated with TCE pursuant to the National Contingency Plan (NCP) (40 CFR 751). |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | substance above the reportable quantity threshold. | |
| **Other Federal Regulations** | | |
| OSHA | Requires employers to provide their workers with a place of employment free from recognized hazards to safety and health, such as exposure to toxic chemicals, excessive noise levels, mechanical dangers, heat or cold stress or unsanitary conditions. | In 1971, OSHA issued occupational safety and health standards for TCE that included a Permissible Exposure Limit (PEL) of 100 ppm TWA, exposure monitoring, control measures and respiratory protection (29 CFR 1910.1000).<br><br>While OSHA has established a PEL for TCE, OSHA has recognized that many of its permissible exposure limits (PELs) are outdated and inadequate for ensuring protection of worker health. Most of OSHA's PELs were issued shortly after adoption of the Occupational Safety and Health (OSH) Act in 1970, and have not been updated since that time. Section 6(a) of the OSH Act granted the Agency the authority to adopt existing Federal standards or national consensus standards as enforceable OSHA standards. For TCE, OSHA recommends the use of the NIOSH REL of 2 ppm (as a 60-minute ceiling) during the usage of TCE as an anesthetic agent and 25 ppm (as a 10-hour TWA) during all other exposures. |
| Atomic Energy Act | The Atomic Energy Act authorizes the Department of Energy to regulate the health and safety of its contractor employees | 10 CFR 851.23, Worker Safety and Health Program, requires the use of the 2005 ACGIH TLVs if they are more protective than the OSHA PEL. The 2005 TLV for TCE is 50 ppm. |
| Federal Food, Drug, and Cosmetic Act (FFDCA) | Provides the FDA with authority to oversee the safety of food, drugs and cosmetics. | Tolerances are established for residues of TCE resulting from its use as a solvent in the manufacture of decaffeinated coffee and spice oleoresins (21 CFR 173.290). |

## A.2 State Laws and Regulations

**Table_Apx A-2. State Laws and Regulations**

| State Actions | Description of Action |
|---|---|
| California Code of Regulations (CCR), Title 17, Section 94509(a) | Lists standards for VOCs for consumer products sold, supplied, offered for sale or manufactured for use in California. As part of that regulation, use of consumer general purpose degreaser products that contain TCE are banned in California and safer substitutes are in use (17 CCR, Section 94509(a). |
| State Permissible Exposure Limits (PELs) | Most states have set PELs identical to the OSHA 100 ppm 8-hour TWA PEL. Nine states have PELs of 50 ppm. California's PEL of 25 ppm is the most stringent (CCR, Title 8, Table AC-1). |
| VOC regulations for consumer products | Many states regulate TCE as a VOC. These regulations may set VOC limits for consumer products and/or ban the sale of certain consumer products as an ingredient and/or impurity. Regulated products vary from state to state, and could include contact and aerosol adhesives, aerosols, electronic cleaners, footwear or leather care products and general degreasers, among other products. California (Title 17, California Code of Regulations, Division 3, Chapter 1, Subchapter 8.5, Articles 1, 2, 3 and 4), Connecticut (R.C.S.A Sections 22a-174-40, 22a-174-41, and 22a-174-44), Delaware (Adm. Code Title 7, 1141), District of Columbia (Rules 20-720, 20-721, 20-735, 20-736, 20-737), Illinois (35 Adm Code 223), Indiana ( 326 IAC 8-15), Maine (Chapter 152 of the Maine Department of Environmental Protection Regulations), Maryland (COMAR 26.11.32.00 to 26.11.32.26), Michigan (R 336.1660 and R 336. 1661), New Hampshire (Env-A 4100) New Jersey (Title 7, Chapter 27, Subchapter 24), New York (6 CRR-NY III A 235), Rhode Island (Air Pollution Control Regulation No. 31) and Virginia (9VAC5 Chapter 45) all have VOC regulations or limits for consumer products. Some of these states also require emissions reporting. |
| Other | TCE is on California Proposition 65 List of chemicals known to cause cancer in 1988 or birth defects or other reproductive harm in 2014 (CCR Title 27, section 27001). TCE is on California's Safer Consumer Products Regulations Candidate List of chemicals that exhibit a hazard trait and are on an authoritative list (CCR Title 22, Chapter 55). |

## A.3 International Laws and Regulations

**Table_Apx A-3. Regulatory Actions by Other Governments and Tribes**

| Country/ Organization | Requirements and Restrictions |
|---|---|
| **Canada** | TCE is on the Canadian List of Toxic Substances (CEPA 1999 Schedule 1). TCE is also regulated for use and sale for solvent degreasing under *Solvent Degreasing Regulations (SOR/2003-283)* (*Canada Gazette*, Part II on August 13, 2003). The purpose of the regulation is to reduce releases of TCE into the environment from solvent degreasing facilities using more than 1000 kilograms of TCE per year. The regulation includes a market intervention by establishing tradable allowances for the use of TCE in solvent degreasing operations that exceed the 1000 kilograms threshold per year. |
| **European Union** | In 2011, TCE was added to Annex XIV (Authorisation list) of regulation (EC) No 1907/2006 - REACH (Registration, Evaluation, Authorization and Restriction of Chemicals). Entities that would like to use TCE needed to apply for authorization by October 2014, and those entities without an authorization must stop using TCE by April 2016. The European Chemicals Agency (ECHA) received 19 applications for authorization from entities interested in using TCE beyond April 2016.<br>TCE is classified as a carcinogen category 1B, and was added to the EU REACH restriction of substances classified as carcinogen category 1A or 1B under the EU Classification and Labeling regulation (among other characteristics) in 2009. The restriction bans the placing on the market or use of TCE as substance, as constituent of other substances, or, in mixtures for supply to the general public when the individual concentration in the substance or mixture is equal to or greater than 0.1 % w/w (Regulation (EC) No 1907/2006 - REACH (Registration, Evaluation, Authorization and Restriction of Chemicals)). Previous regulations, such as the Solvent Emissions Directive (Directive 1999/13/EC) introduced stringent emission controls of TCE. |
| **Australia** | In 2000, TCE was assessed (National Industrial Chemicals Notification and Assessment Scheme, NICNAS (2000), *Trichloroethylene*. Accessed April, 18 2017). |
| **Japan Chemical Substances Control Law** | TCE is regulated in Japan under the following legislation:<br>• Act on the Evaluation of Chemical Substances and Regulation of Their Manufacture, etc. (Chemical Substances Control Law; CSCL) |

| | |
|---|---|
| | • Act on Confirmation, etc. of Release Amounts of Specific Chemical Substances in the Environment and Promotion of Improvements to the Management Thereof<br>• Industrial Safety and Health Act (ISHA)<br>• Air Pollution Control Law<br>• Water Pollution Control Law<br>• Soil Contamination Countermeasures Act<br>• Law for the Control of Household Products Containing Harmful Substances<br><br>(National Institute of Technology and Evaluation (NITE) Chemical Risk Information Platform (CHIRP), Accessed April 18, 2017). |
| **Australia, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Hungary, Ireland, Israel, Japan, Latvia, New Zealand, People's Republic of China, Poland, Singapore, South Korea, Spain, Sweden, Switzerland, United Kingdom** | Occupational exposure limits for TCE (GESTIS International limit values for chemical agents (Occupational exposure limits, OELs) database. Accessed April 18, 2017). |

# Appendix B PROCESS, RELEASE AND OCCUPATIONAL EXPOSURE INFORMATION

This appendix provides information and data found in preliminary data gathering for TCE.

## B.1 Process Information

Process-related information to the risk evaluation may include process diagrams, descriptions and equipment. Such information may inform potential release sources and worker exposure activities for consideration.

### B.1.1 Manufacture (including Import)

#### B.1.1.1 Import

EPA has also not identified specific activities related to the import of TCE. EPA expects imported chemicals are stored in warehouses prior to distribution for further processing and use. In some cases, the chemicals may be repackaged into differently sized containers, depending on customer demand, and quality control (QC) samples may be taken for analyses.

According to Snedecor et al. (2004b), TCE is typically shipped by truck or rail car or in 55-gallon drums. TCE may be stored in mild steel tanks equipped with vents and vent dryers to prevent water accumulation (Snedecor et al., 2004b) .

#### B.1.1.2 Manufacturing

TCE was previously produced through chlorination of acetylene to 1,1,2,2-tetrachloroethane, then dehydrochlorination to TCE in an aqueous base or by thermal cracking (Snedecor et al., 2004b). Due to rising costs of acetylene, this process has largely been phased-out (ATSDR, 2014a; Snedecor et al., 2004b). Currently, most TCE is manufactured via chlorination or oxychlorination of ethylene, dichloroethane or ethylene dichloride (EDC) (ATSDR, 2014a; Snedecor et al., 2004b).

- Chlorination - The chlorination process involves a catalytic reaction of chlorine and ethylene, dichloroethane or EDC to form TCE and perchloroethylene (PCE) as co-products and hydrochloric acid (HCl) as a byproduct (ATSDR, 2014; Snedecor et al., 2004; (U.S. EPA, 1985). Typical catalysts include potassium chloride, aluminum chloride, Fuller's earth, graphite, activated carbon and activated charcoal (Snedecor et al., 2004b).
- Oxychlorination - The oxychlorination process involves the reaction of either chlorine or HCl and oxygen with ethylene, dichloroethane or EDC in the presence of a catalyst to produce TCE and PCE as co-products (ATSDR, 2014a; Snedecor et al., 2004b) . The process usually occurs in a fluidized-bed reactor (Snedecor et al., 2004b). Common catalysts are mixtures of potassium and cupric chlorides (Snedecor et al., 2004b).

In either process the product ratio of TCE to PCE products are controlled by adjusting the reactant rations (Snedecor et al., 2004b).

### B.1.2 Processing

#### B.1.2.1 Reactant or Intermediate

Processing as a reactant or intermediate is the use of TCE as a feedstock in the production of another chemical product via a chemical reaction in which TCE is consumed to form the product. TCE is used as a feedstock in the production of HFCs alternatives to CFCs, specifically the HFC-134a alternative to CFC-12 (ATSDR, 2014a; Elsheikh et al., 2005; Snedecor et al., 2004b). The production of HFC-134a from TCE can be carried out in one of two processes (Elsheikh et al., 2005). In the first process, TCE is

fluorinated in either a gas- or liquid-phase reaction with hydrofluoric acid using a Lewis acid catalyst to produce the hydrochlorofluorocarbon, HCFC-133a, which is then subsequently fluorinated to produce HFC-134a by reaction with hydrofluoric acid using a catalyst (Elsheikh et al., 2005) (Smart and Fernandez, 2000). The second process involves fluorination of TCE using a chromium-based catalyst to form HCFC-133a as the major product and HFC-134a as the minor product (Elsheikh et al., 2005). The HFC-134a is then separated out using distillation and the HCFC-133a is recycled back through the reactor (Elsheikh et al., 2005).

#### B.1.2.2 Incorporating into a Formulation, Mixture or Reaction Product

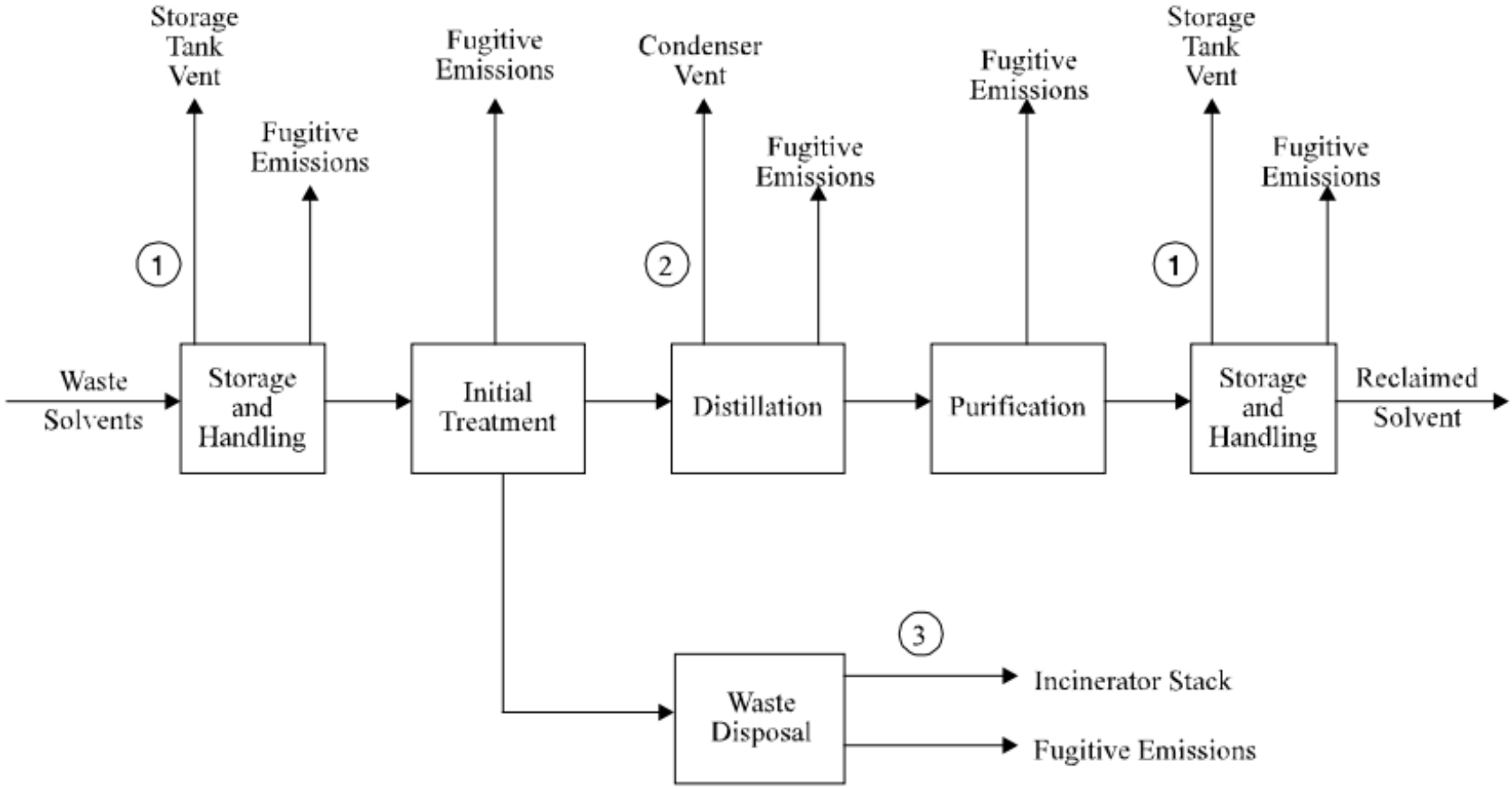
Incorporation into a formulation, mixture or reaction product refers to the process of mixing or blending of several raw materials to obtain a single product or preparation. The uses of TCE that may require incorporation into a formulation include adhesives, sealants, coatings and lubricants. TCE-specific formulation processes were not identified; however, several Emission Scenario Documents (ESDs) published by the OECD have been identified that provide general process descriptions for these types of products. The formulation of coatings typically involves dispersion, milling, finishing and filling into final packages (OECD, 2009b). Adhesive formulation involves mixing together volatile and non-volatile chemical components in sealed, unsealed or heated processes (OECD, 2009a). Sealed processes are most common for adhesive formulation because many adhesives are designed to set or react when exposed to ambient conditions (OECD, 2009a). Lubricant formulation typically involves the blending of two or more components, including liquid and solid additives, together in a blending vessel (OECD, 2004).

#### B.1.2.3 Repackaging

EPA has not identified specific information for the repackaging of TCE. EPA expects repackaging sites receive the chemical in bulk containers and transfer the chemical from the bulk container into another smaller container in preparation for distribution in commerce.

#### B.1.2.4 Recycling

TRI data from 2015 indicate that some sites ship TCE for off-site recycling. EPA did not identify TCE-specific information for recycling; however, a general description of waste solvent recovery processes was identified. Waste solvents are generated when the solvent stream becomes contaminated with suspended and dissolved solids, organics, water or other substance (U.S. EPA, 1980a). Waste solvents can be restored to a condition that permits reuse via solvent reclamation/recycling (U.S. EPA, 1980a). The recovery process involves an initial vapor recovery (e.g., condensation, adsorption and absorption) or mechanical separation (e.g., decanting, filtering, draining, setline and centrifuging) step followed by distillation, purification and final packaging (U.S. EPA, 1980a). Figure_Apx B-1 illustrates a typical solvent recovery process flow diagram (U.S. EPA, 1980a).




**Figure_Apx B-1. General Process Flow Diagram for Solvent Recovery Processes**

### B.1.3 Uses

EPA assessed inhalation risks from TCE in vapor and aerosol degreasing, spot cleaning at dry cleaning facilities and arts and craft uses (U.S. EPA, 2014c) and also completed four supplemental analyses as identified in Section 1.2. Based on these analyses, EPA published two proposed rules to address the unreasonable risks presented by TCE use in vapor degreasing and in commercial and consumer aerosol degreasing and for spot cleaning at dry cleaning facilities (82 FR 7432, January 19, 2017; 81 FR 91592, December 16, 2016). Scenarios previously examined in the 2014 publication will be considered in this risk evaluation to ensure previous assessments are in alignment with the Procedures for Chemical Risk Evaluation under the Amended Toxic Substances Control Act (40 CFR Part 702).

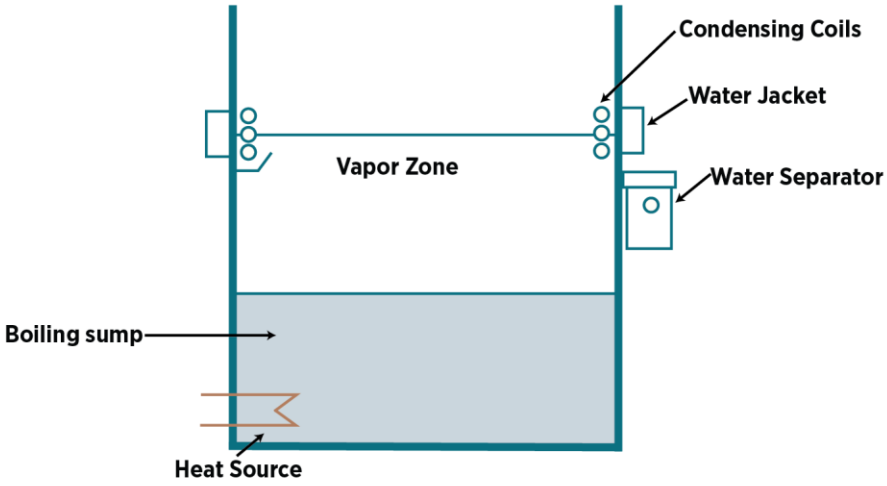
#### B.1.3.1 Solvent for Cleaning or Degreasing

***Vapor Degreasing***

This scenario was previously assessed in the 2014 risk assessment (U.S. EPA, 2014c). Vapor degreasing is a process used to remove dirt, grease and surface contaminants in a variety of metal cleaning industries. Vapor degreasing may take place in batches or as part of an in-line (i.e., continuous) system. Vapor degreasing equipment can generally be categorized into one of three degreaser types described below:

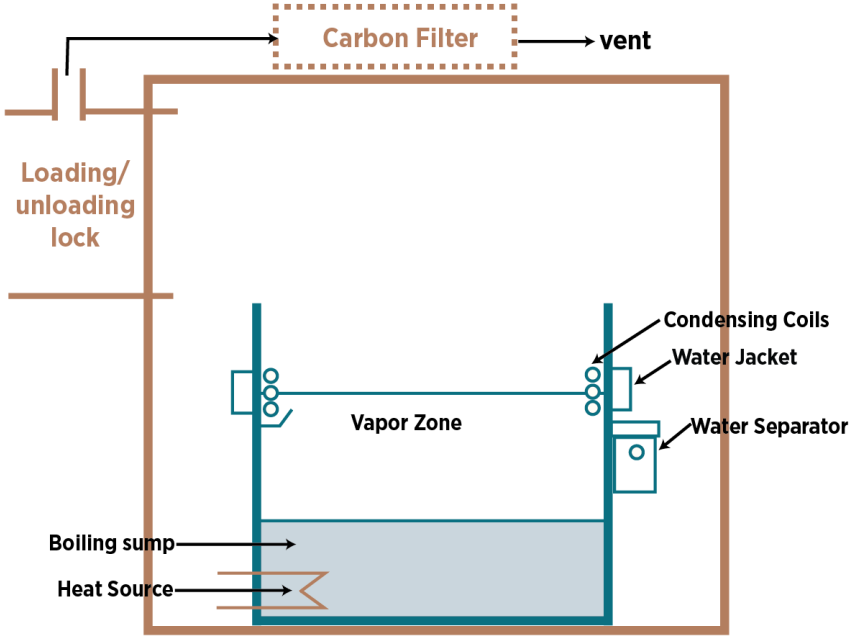
**Batch vapor degreasers:** In batch machines, each load (parts or baskets of parts) is loaded into the machine after the previous load is completed. Individual organizations, regulations and academic studies have classified batch vapor degreasers differently. For the purposes of the scope document (Scope Document), EPA categories the batch vapor degreasers into five types: open top vapor degreasers (OTVDs); OTVDs with enclosures; closed-loop degreasing systems (airtight); airless degreasing systems (vacuum drying); and airless vacuum-to-vacuum degreasing systems.

- Open top vapor degreasers (OTVD) – In OTVDs, a vapor cleaning zone is created by heating the liquid solvent in the OTVD causing it to volatilize. Workers manually load or unload fabricated parts directly into or out of the vapor cleaning zone. The tank usually has chillers along the side of the tank to prevent losses of the solvent to the air. However, these chillers are not able to eliminate emissions, and throughout the degreasing process significant air emissions of the solvent can occur. These air emissions can cause issues with both worker health and safety as well as environmental issues. Additionally, the cost of replacing solvent lost to emissions can be expensive (NEWMOA, 2001). Figure_Apx B-2 illustrates a standard OTVD.




**Figure_Apx B-2. Open Top Vapor Degreaser**

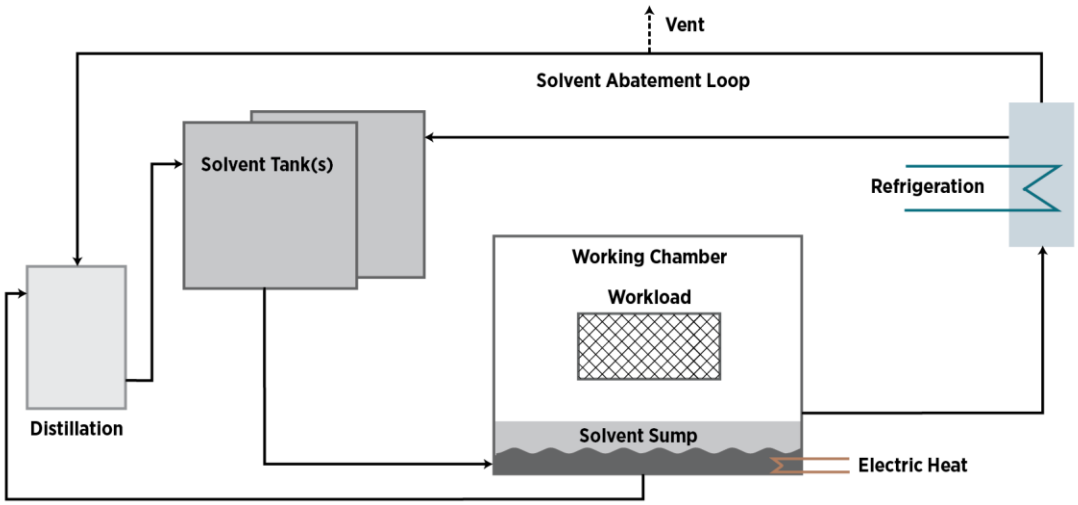
- OTVD with enclosure – OTVDs with enclosures operate the same as standard OTVDs except that the OTVD is enclosed on all sides during degreasing. The enclosure is opened and closed to add or remove parts to/from the machine, and solvent is exposed to the air when the cover is open. Enclosed OTVDs may be vented directly to the atmosphere or first vented to an external carbon filter and then to the atmosphere (EPA, 2004). Figure_Apx B-3 illustrates an OTVD with an enclosure. The dotted lines in Figure_Apx B-3 represent the optional carbon filter that may or may not be used with an enclosed OTVD.




**Figure_Apx B-3. Open Top Vapor Degreaser with Enclosure**

- Closed-loop degreasing system (Airtight) – In closed-loop degreasers, parts are placed into a basket, which is then placed into an airtight work chamber. The door is closed and solvent vapors are sprayed onto the parts. Solvent can also be introduced to the parts as a liquid spray or liquid

immersion. When cleaning is complete, vapors are exhausted from the chamber and circulated over a cooling coil where the vapors are condensed and recovered. The parts are dried by forced hot air. Air is circulated through the chamber and residual solvent vapors are captured by carbon adsorption. The door is opened when the residual solvent vapor concentration has reached a specified level (Kanegsberg and Kanegsberg, 2011). Figure_Apx B-4 illustrates a standard closed-loop vapor degreasing system.




**Figure_Apx B-4. Closed-loop/Vacuum Vapor Degreaser**

- Airless degreasing system (vacuum drying) – Airless degreasing systems are also sealed, closed-loop systems, but remove air at some point of the degreasing process. Removing air typically takes the form of drawing vacuum, but could also include purging air with nitrogen at some point of the process (in contrast to drawing vacuum, a nitrogen purge operates at a slightly positive pressure). In airless degreasing systems with vacuum drying only, the cleaning stage works similarly as with the airtight closed-loop degreaser. However, a vacuum is generated during the drying stage, typically below 5 torr (5 mmHg). The vacuum dries the parts and a vapor recovery system captures the vapors (EPA, 2001; (Kanegsberg and Kanegsberg, 2011); (NEWMOA, 2001).

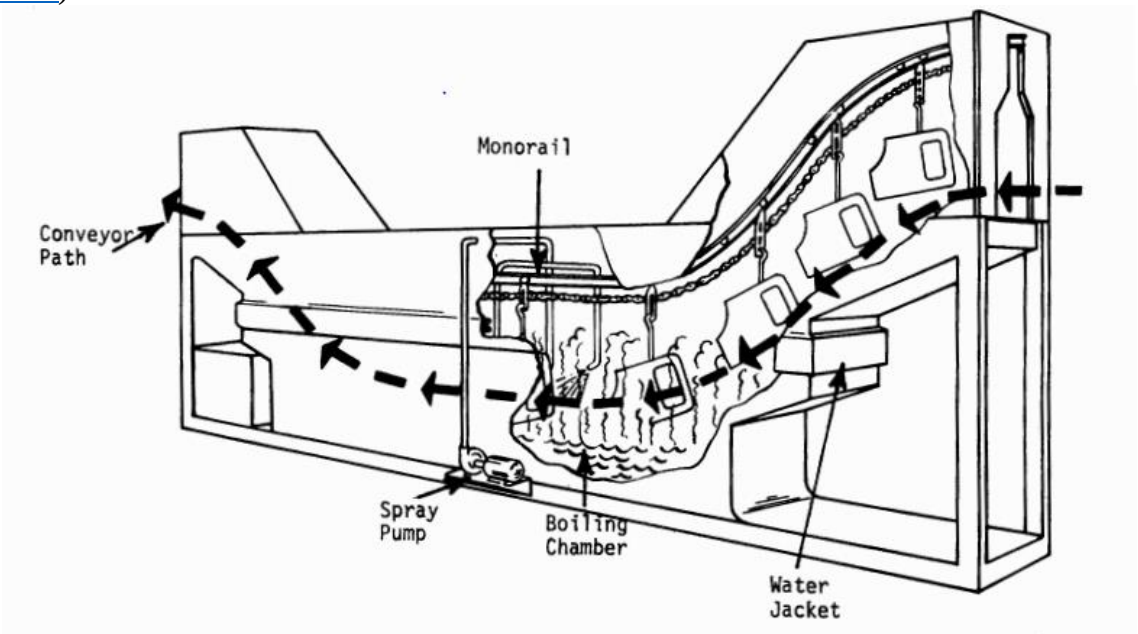
- Airless vacuum-to-vacuum degreasing system – Airless vacuum-to-vacuum degreasers are true "airless" systems because the entire cycle is operated under vacuum. Typically, parts are placed into the chamber, the chamber sealed, and then vacuum drawn within the chamber. The typical solvent cleaning process is a hot solvent vapor spray. The introduction of vapors in the vacuum chamber raises the pressure in the chamber. The parts are dried by again drawing vacuum in the chamber. Solvent vapors are recovered through compression and cooling. An air purge then purges residual vapors over an optional carbon adsorber and through a vent. Air is then introduced in the chamber to return the chamber to atmospheric pressure before the chamber is opened (Durkee, 2014; NEWMOA, 2001).

The general design of vacuum vapor degreasers and airless vacuum degreasers is similar as illustrated in Figure_Apx B-7 for closed-loop systems except that the work chamber is under vacuum during various stages of the cleaning process.

***Conveyorized Vapor Degreasers***

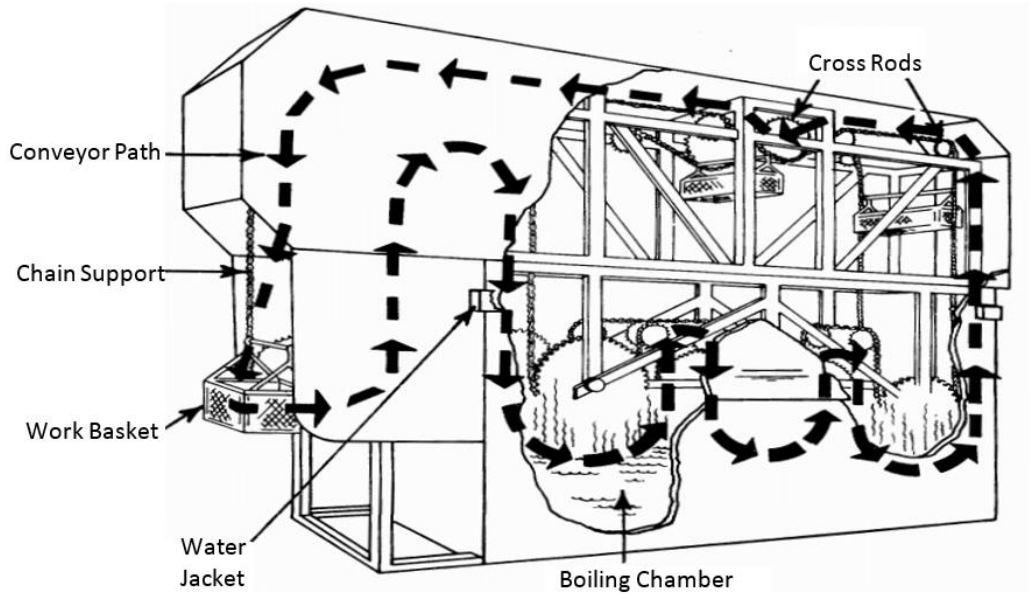
Conveyorized vapor degreasing systems are solvent cleaning machines that use an automated parts handling system, typically a conveyor, to automatically provide a continuous supply of parts to be cleaned. Conveyorized degreasing systems are usually fully enclosed except for the conveyor inlet and outlet portals. Conveyorized degreasers are likely used in similar shop types as batch vapor degreasers except for repair shops, where the number of parts being cleaned is likely not large enough to warrant the use of a conveyorized system. There are seven major types of conveyorized degreasers: monorail degreasers, cross-rod degreasers, vibra degreasers, ferris wheel degreasers, belt degreasers, strip degreasers and circuit board degreasers (U.S. EPA, 1977).

- Monorail Degreasers – Monorail degreasing systems are typically used when parts are already being transported throughout the manufacturing areas by a conveyor (U.S. EPA, 1977). They use a straight-line conveyor to transport parts into and out of the cleaning zone. The parts may enter one side and exit and the other or may make a 180° turn and exit through a tunnel parallel to the entrance (U.S. EPA, 1977). Figure_Apx B-5 illustrates a typical monorail degreaser (U.S. EPA, 1977).



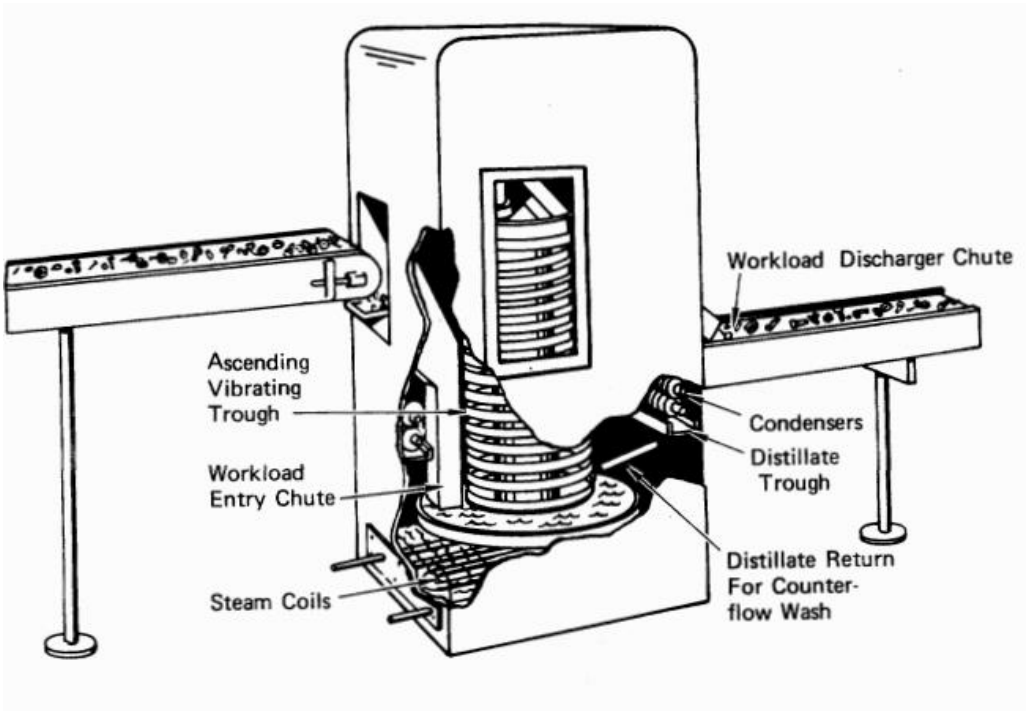

**Figure_Apx B-5. Monorail Conveyorized Vapor Degreasing System (U.S. EPA, 1977)**

- Cross-rod Degreasers – Cross-rod degreasing systems utilize two parallel chains connected by a rod that support the parts throughout the cleaning process. The parts are usually loaded into perforated baskets or cylinders and then transported through the machine by the chain support system. The baskets and cylinders are typically manually loaded and unloaded (U.S. EPA, 1977). Cylinders are used for small parts or parts that need enhanced solvent drainage because of crevices and cavities. The cylinders allow the parts to be tumbled during cleaning and drying and thus increase cleaning and drying efficiency. Figure_Apx B-6 illustrates a typical cross-rod degreaser (U.S. EPA, 1977).



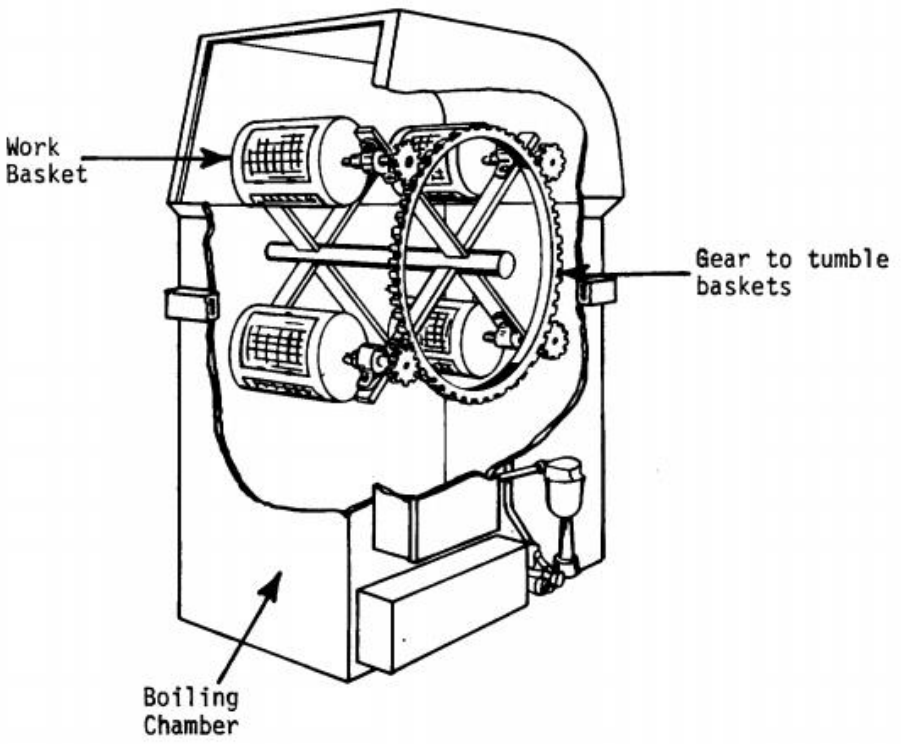

**Figure_Apx B-6. Cross-Rod Conveyorized Vapor Degreasing System (U.S. EPA, 1977)**

- Vibra Degreasers – In vibra degreasing systems, parts are fed by conveyor through a chute that leads to a pan flooded with solvent in the cleaning zone. The pan and the connected spiral elevator are continuously vibrated throughout the process causing the parts to move from the pan and up a spiral elevator to the exit chute. As the parts travel up the elevator, the solvent condenses and the parts are dried before exiting the machine (U.S. EPA, 1977). Figure_Apx B-7 illustrates a typical vibra degreaser (U.S. EPA, 1977).



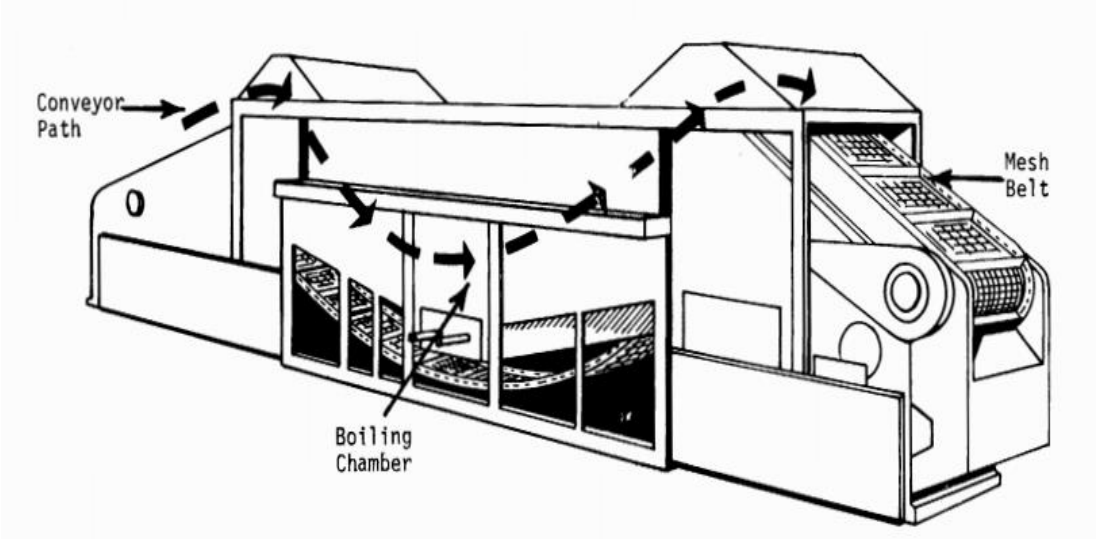

**Figure_Apx B-7. Vibra Conveyorized Vapor Degreasing System (U.S. EPA, 1977)**

- Ferris wheel degreasers – Ferris wheel degreasing systems are generally the smallest of all the conveyorized degreasers (U.S. EPA, 1977). In these systems, parts are manually loaded into perforated baskets or cylinders and then rotated vertically through the cleaning zone and back out. Figure_Apx B-8 illustrates a typical ferris wheel degreaser (U.S. EPA, 1977).




**Figure_Apx B-8. Ferris Wheel Conveyorized Vapor Degreasing System (U.S. EPA, 1977)**

- Belt degreasers – Belt degreasing systems (similar to strip degreasers; see next bullet) are used when simple and rapid loading and unloading of parts is desired (U.S. EPA, 1977). Parts are loaded onto a mesh conveyor belt that transports them through the cleaning zone and out the other side. Figure_Apx B-9 illustrates a typical belt or strip degreaser (U.S. EPA, 1977).

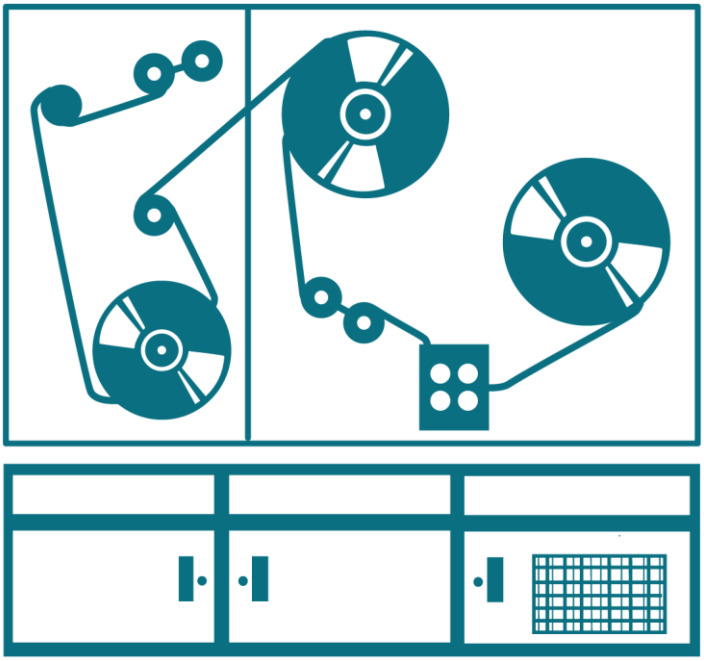



**Figure_Apx B-9. Belt/Strip Conveyorized Vapor Degreasing System (U.S. EPA, 1977)**

- Strip degreasers – Strip degreasing systems operate similar to belt degreasers except that the belt itself is being cleaned rather than parts being loaded onto the belt for cleaning. Figure_Apx B-9 illustrates a typical belt or strip degreaser (U.S. EPA, 1977).

- Circuit board cleaners – Circuit board degreasers use any of the conveyorized designs. However, in circuit board degreasing, parts are cleaned in three different steps due to the manufacturing processes involved in circuit board production (U.S. EPA, 1977).

**Continuous web vapor degreasers:** Continuous web cleaning machines are a subset of conveyorized degreasers but differ in that they are specifically designed for cleaning parts that are coiled or on spools such as films, wires and metal strips (Kanegsberg and Kanegsberg, 2011); U.S. EPA, 2006b). In continuous web degreasers, parts are uncoiled and loaded onto rollers that transport the parts through the cleaning and drying zones at speeds greater than 11 feet per minute (U.S. EPA, 2006c). The parts are then recoiled or cut after exiting the cleaning machine (Kanegsberg and Kanegsberg, 2011). Figure_Apx B-10 illustrates a typical continuous web cleaning machine.



**Figure_Apx B-10. Continuous Web Vapor Degreasing System**

***Cold Cleaners***

TCE can also be used as a solvent in cold cleaners, which are non-boiling solvent degreasing units. Cold cleaning operations include spraying, brushing, flushing and immersion; the use process and worker activities associated with cold cleaning have been previously described in EPA's TCE Risk Assessment (U.S. EPA, 2014a).

***Aerosol Spray Degreasers and Cleaners***

EPA assessed inhalation risks from TCE in vapor and aerosol degreasing, spot cleaning at dry cleaning facilities and arts and craft uses (U.S. EPA, 2014a)) and completed four supplemental analyses Table 1-11. Based on these analyses, EPA published two proposed rules to address the unreasonable risks presented by TCE use in vapor degreasing and in commercial and consumer aerosol degreasing and for

spot cleaning at dry cleaning facilities (82 FR 7432, January 19, 2017; 81 FR 91592, December 16, 2016).

Aerosol degreasing is a process that uses an aerosolized solvent spray, typically applied from a pressurized can, to remove residual contaminants from fabricated parts. Products containing TCE may be used in aerosol degreasing applications such as brake cleaning, engine degreasing and metal product cleaning. This use has been previously described in EPA's 1-BP Draft Risk Assessment (U.S. EPA, 2016g). Aerosol degreasing may occur at either industrial facilities or at commercial repair shops to remove contaminants on items being serviced. Aerosol degreasing products may also be purchased and used by consumers for various applications.

***Non-Aerosol Degreasing and Cleaning***

TCE can also be used as a solvent in non-aerosol degreasing and cleaning products. Non-aerosol cleaning products typically involve dabbing or soaking a rag with cleaning solution and then using the rag to wipe down surfaces or parts to remove contamination (U.S. EPA, 2014a). The cleaning solvent is usually applied in excess and allowed to air-dry (U.S. EPA, 2014a). Parts may be cleaned in place or removed from the service item for more thorough cleaning (U.S. EPA, 2014a).

#### B.1.3.2 Lubricants and Greases

The Use Document for TCE [EPA-HQ-OPPT-2016-0737-0003 (U.S. EPA, 2017c)] identified TCE in penetrating lubricants and tap and die fluids. EPA has not identified process information specific to tap and die fluids; however, the OECD ESD on Use of Metalworking Fluids provides a general process description for metalworking fluids. Metalworking fluids are unloaded, either diluted with water and transferred to the trough or directly transferred to the trough without dilution (OECD, 2011). The fluid is then pumped from the trough and applied to the metal parts, as needed, during shaping (OECD, 2011). Parts are then allowed to drip dry and the fluids are collected and treated with other process fluids (OECD, 2011). Parts may be rinsed down or wiped and then cleaned via alkaline cleaning or degreasing prior to the final finishing operations (OECD, 2011). Any metalworking fluid residue remaining on the part is removed during the cleaning or degreasing operation (OECD, 2011).

EPA has not identified process-specific information regarding the use of TCE in penetrating lubricants. More information on this use will be gathered through expanded literature searches in subsequent phases of the risk evaluation process.

#### B.1.3.3 Adhesive and Sealants

Based on products identified in EPA's Use Document, [EPA-HQ-OPPT-2016-0737-0003 (U.S. EPA, 2017c)], TCE may be used in adhesive and sealants for industrial, commercial and consumer applications. EPA did not identify TCE-specific information for adhesive and sealant use; however, the OECD ESD for Use of Adhesives provides general process descriptions and worker activities for industrial adhesive uses. Liquid adhesives are unloaded from containers into the coating reservoir, applied to a flat or three-dimensional substrate and the substrates are then joined and allowed to cure (OECD, 2013). The majority of adhesive applications include spray, roll, curtain, syringe or bead application (OECD, 2013). For solvent-based adhesives, the volatile solvent (in this case TCE) evaporates during the curing stage (OECD, 2013). Based on EPA's knowledge of the industry, overlap in process descriptions, worker activities and application methods are expected for sealant products.

EPA's Use Document, [EPA-HQ-OPPT-2016-0737-0003 (U.S. EPA, 2017c)] indicates that adhesives and sealants containing TCE may be used in both commercial and consumer applications. EPA did not identify process information for commercial and consumer use of adhesives and sealants; EPA

anticipates that the application methods for commercial and consumer uses may include spray, brush, syringe, eyedropper, roller and bead applications.

#### B.1.3.4 Functional Fluids (Closed Systems)

U.S. EPA (2017f) indicates TCE may be used as a heat transfer agent in industrial and commercial applications. EPA will further evaluate the use of TCE as a heat exchange fluid during the risk evaluation process.

#### B.1.3.5 Cleaning and Furniture Care Products

EPA interprets this reported commercial/consumer use category in CDR "Cleaning and Furniture Care Products" to include the use of TCE in spot cleaning and carpet cleaning applications. This use includes both professional spot cleaning (dry cleaning) and carpet cleaning activities as well as use in consumer purchased spot cleaning and carpet cleaning products.

Professional spot cleaning was previously assessed in the 2014 risk assessment (U.S. EPA, 2014c). Spot cleaning products can be applied to the garment either before or after the garment is dry cleaned. The process and worker activities associated with commercial dry cleaning and spot cleaning have been previously described in the 2014 risk assessment (U.S. EPA, 2014c).

#### B.1.3.6 Paints and Coatings

Based on products identified in EPA's Use Document, [EPA-HQ-OPPT-2016-0737-0003 (U.S. EPA, 2017c)], TCE may be used in various paints and coatings for industrial, commercial and consumer applications. EPA did not identify TCE specific information for paints and coating use; however, several OECD ESDs and EPA generic scenarios provide general process descriptions and worker activities for industrial and commercial uses. Typical coating applications include manual application with roller or brush, air spray systems, airless and air-assisted airless spray systems, electrostatic spray systems, electrodeposition/electrocoating and autodeposition, dip coating, curtain coating systems, roll coating systems and supercritical carbon dioxide systems (OECD, 2009b). After application, solvent-based coatings typically undergo a drying stage in which the solvent evaporates from the coating (OECD, 2009b).

#### B.1.3.7 Corrosion Inhibitors and Anti-Scaling Agents

In the 2016 CDR (U.S. EPA, 2016a), one submitter reported the use of TCE in corrosion inhibitors and anti-scaling agents in soap, cleaning compound, and toilet preparation manufacturing. The U.S. EPA Trichloroethylene Market and Use Report (U.S. EPA, 2017f) identified TCE as a component in commercial and consumer battery coat products. Battery coat products form a coating that protects against corrosion on battery terminals, cables, clamps, and hold-downs (U.S. EPA, 2017f).

#### B.1.3.8 Processing Aid

The U.S. EPA Trichloroethylene Market and Use Report (U.S. EPA, 2017f) identified uses of TCE as a process solvent in lithium ion battery manufacture, polymer fiber spinning, fluoroelastomer manufacture, Alacantara manufacture, and pulverized sulfur production; as a extractant in caprolactam manufacture, in the recovery of fat-free glues in tanneries, in wood resin extraction, in the recovery of wax and paraffin from refuse, for tin recovery from scrap metal, and phenol extraction from wastewater; and as a precipitant for beta-cyclodextrin manufacture (Baumann et al., 2008a) indicates TCE is used in the manufacture of microporous polyethylene battery separator material to remove excess oil from the extruded polyethylene sheets.

#### B.1.3.9 Ink, Toner and Colorant Products

Based on products identified in EPA's Use Document, EPA-HQ-OPPT-2016-0737-0003 (U.S. EPA, 2017c)] and the U.S. EPA Trichloroethylene Market and Use Report (U.S. EPA, 2017f), TCE may be used as a component in a toner aid to improve image opacity, develop higher resolutions, and enhance detail clarity. The GS for Use of PMN Component in Toner Used in Photocopiers (1992) provides general process description for the use of toner. Toners are received in plastic cartridges and workers remove seal on the cartridge and place it into the photocopier (U.S. EPA, 1992). Toner is applied to the image area of the paper through electrostatic transfer (U.S. EPA, 1992). Waste toner is disposed to municipal landfills and spent cartridges are sent back to the manufacturer or distributor for reuse (U.S., 1992).

#### B.1.3.10 Other Uses

Based on products identified in EPA's Use Document, [EPA-HQ-OPPT-2016-0737-0003 (U.S. EPA, 2017c)], a variety of other uses may exist for TCE, including use in hoof polish, pepper spray and as a toner aide. It is unclear at this time the total volume of TCE used in any of these applications. EPA has not identified any information to further refine the use of TCE in these products at this time; more information on these uses will be gathered through expanded literature searches in subsequent phases of the risk evaluation process.

### B.1.4 Disposal

Federal regulations prevent land disposal of various chlorinated solvents (including TCE) (ATSDR, 2014a). The recommended disposal method is mixing with a combustible fuel followed by incineration (ATSDR, 2014a). In incineration, complete combustion is necessary to prevent phosgene or other toxic byproduct formation (ATSDR, 2014a).

## B.2 Occupational Exposure Data

EPA presents below an example of occupational exposure-related information from the preliminary data gathering. EPA will consider this information and data in combination with other data and methods for use in the risk evaluation.

Table_Apx B-1 summarizes the TCE OSHA CEHD data by NAICS code and Table_Apx B-2 summarizes NIOSH HHE data.

**Table_Apx B-1. Mapping of Scenarios to Industry Sectors with TCE Personal Monitoring Air Samples Obtained from OSHA Inspections Conducted Between 2002 and 2017**

| Release/ Exposure Scenario | NAICS Code | NAICS Description |
|---|---|---|
| Unknown, company inspected is an excavation contractor, possibly from contact with soil contaminated with TCE | 236220 | Commercial and Institutional Building Construction |
| Textile pre-treatment, textile dyeing, or textile finishing | 313312 | Textile and Fabric Finishing (except Broadwoven Fabric) Mills |
| Textile pre-treatment or textile finishing | 313320 | Fabric Coating Mills |
| Textile pre-treatment, textile dyeing, or textile finishing | 314999 | All Other Miscellaneous Textile Product Mills |
| Manufacture of large, rigid plastic products (as vapor degreaser) | 325212 | Synthetic Rubber Manufacturing |
| Formulation of aerosol and non-aerosol products | 325520 | Adhesive Manufacturing |
| Aerosol use of mold release or other miscellaneous industrial, commercial, and consumer uses (Foam Blowing Agent) | 326150 | Urethane and Other Foam Product (except Polystyrene) Manufacturing |
| Manufacture of large, rigid plastic products (likely as adhesive or vapor degreaser) or Aerosol use of mold release | 326199 | All Other Plastics Product Manufacturing |
| Manufacture of large, rigid plastic products | 326211 | Tire Manufacturing (except Retreading) |
| Manufacture of large, rigid plastic products (as a vapor degreaser or paint/coating) | 326299 | All Other Rubber Product Manufacturing |
| Vapor degreasing or cold cleaning | 331210 | Iron and Steel Pipe and Tube Manufacturing from Purchased Steel |
| Vapor degreasing or cold cleaning | 331491 | Nonferrous Metal (except Copper and Aluminum) Rolling, Drawing, and Extruding |
| Vapor degreasing or cold cleaning | 331512 | Steel Investment Foundries |
| Vapor degreasing or cold cleaning | 331528 | Beryllium castings (except die-castings), unfinished manufacturing |
| Vapor degreasing or cold cleaning | 332116 | Metal stampings (except automotive, cans, cooking, closures, crowns), unfinished, manufacturing |
| Vapor degreasing or cold cleaning | 332439 | Other Metal Container Manufacturing |
| Vapor degreasing or cold cleaning or metalworking fluids | 332710 | Machine Shops |
| Vapor degreasing or cold cleaning | 332721 | Precision Turned Product Manufacturing |
| Vapor degreasing or cold cleaning | 332722 | Bolt, Nut, Screw, Rivet, and Washer Manufacturing |
| Vapor degreasing or cold cleaning | 332811 | Metal Heat Treating |
| Vapor degreasing or cold cleaning | 332813 | Electroplating, Plating, Polishing, Anodizing, and Coloring |
| Vapor degreasing or cold cleaning | 332991 | Ball and Roller Bearing Manufacturing |
| Vapor degreasing or cold cleaning | 332994 | Small Arms, Ordnance, and Ordnance Accessories Manufacturing |
| Vapor degreasing or cold cleaning | 332996 | Fabricated Pipe and Pipe Fitting Manufacturing |
| Vapor degreasing or cold cleaning | 332999 | All Other Miscellaneous Fabricated Metal Product Manufacturing |
| Vapor degreasing or cold cleaning | 333111 | Farm Machinery and Equipment Manufacturing |
| Vapor degreasing or cold cleaning | 333513 | Arbor presses, metalworking, manufacturing |
| Vapor degreasing or cold cleaning | 334412 | Bare Printed Circuit Board Manufacturing |
| Vapor degreasing or cold cleaning | 334419 | Other Electronic Component Manufacturing |

| Release/ Exposure Scenario | NAICS Code | NAICS Description |
|---|---|---|
| Vapor degreasing or cold cleaning | 334513 | Instruments and Related Products Manufacturing for Measuring, Displaying, and Controlling Industrial Process Variables |
| Vapor degreasing or cold cleaning | 335311 | Power, Distribution, and Specialty Transformer Manufacturing |
| Vapor degreasing or cold cleaning | 336370 | Motor Vehicle Metal Stamping |
| Vapor degreasing or cold cleaning | 339114 | Dental Equipment and Supplies Manufacturing |
| Industrial adhesive (unknown application type) | 339950 | Sign Manufacturing |
| Vapor degreasing or cold cleaning | 339991 | Gasket, Packing, and Sealing Device Manufacturing |
| Paints and Coatings (application method unknown) | 423830 | Industrial Machinery and Equipment Merchant Wholesalers |
| Commercial automotive repair/servicing | 424610 | Plastics Materials and Basic Forms and Shapes Merchant Wholesalers |
| Spot cleaning | 812320 | Drycleaning and Laundry Services (except Coin-Operated) |
| Spot cleaning | 812332 | Industrial Launderers |
| Unknown – this seems to be for OSHA inspectors which could have been collected during site inspections | 926150 | Regulation, Licensing, and Inspection of Miscellaneous Commercial Sectors |
| Other miscellaneous industrial, commercial, and consumer uses (atmospheric chamber cleaner) | 927110 | Space Research and Technology |

**Table_Apx B-2. Summary of Exposure Data from NIOSH HHEs [a]**

| Data Source | Report Number | Exposure/Release Scenario | Facility Description | Number of Exposure Samples | Minimum of Exposure Values (ppm) | Maximum of Exposure Values (ppm) | Comments |
|---|---|---|---|---|---|---|---|
| NIOSH, 1991 | HETA-1990-0344-2159 | Vapor degreasing | Brass and stainless steel valve manufacture | 7 | 1.1 | 5.3 | Two PBZ full-shift samples and five area full-shift samples |
| NIOSH, 1992a | HETA-1990-0029-2212 | Adhesive application | Automotive headliner production | 4 | 2.7 | 21.4 | PBZ samples |
| NIOSH, 1992b | HETA-1990-0223-2211 | Vapor degreasing | Television picture tubes (i.e., cathode ray tubes) | 11 | ND | 50 | Partial shift PBZ and area samples |
| NIOSH, 1995 | HETA-1994-0298-2499 | Rubber stock mixing | Automotive vibration control and vibration sealing manufacture | Unknown | Trace | | Exact use of TCE is not specified and is only detected at trace levels. |
| NIOSH, 1998 | HETA-1997-0214-2689 | Vapor degreasing | Hydraulic door closer manufacturing | 2 | 0.71 | 3.5 | Partial shift PBZ samples |
| NIOSH, 2003 | HETA-2002-0184-2888 | Vapor degreasing | Aluminum oil coolers (for use in army battle tank) manufacture | 2 | 7.1 | 7.6 | TCE vapor degreaser was not in operation at time of site visit. PBZ full-shift samples taken of welders; exposure likely residual TCE on parts that vaporized during welding. |
| NIOSH, 2004 | HETA-2003-0029-2923 | Wipe cleaning | Musical instrument repair | 6 | Trace (>0.0143 and <0.0477) | 0.99 | Two PBZ and four area samples. |
| NIOSH, 2005 | HETA-2003-0203-2952 | Wipe cleaning | Printing press operations | 26 | ND (<0.00005) | 25 | 20 full-shift PBZ and six task-based PBZ samples. |
| NIOSH, 2008 | HETA-2004-0372-3054 | Battery manufacturing | Oil extraction during battery separator manufacturing | 274 | 1.7 | 130 | Full shift PBZ samples |

ND = not detected

PBZ = personal breathing zone

[a] Table includes HHEs identified to date

## B.3 References Related to Risk Evaluation – Environmental Release and Occupational Exposure

**Table_Apx B-3. Potentially Relevant Data Sources for Process Description Related Information for TCE[2]**

| Bibliography | url |
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**Table_Apx B-6. Potentially Relevant Data Sources for Engineering Controls and Personal Protective Equipment Information for TCE[4]**

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[4] The data sources identified are based on preliminary results to date of the full-text screening step of the SR process. Further screening and quality control are on-going.

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# Appendix C SUPPORTING TABLES FOR INDUSTRIAL AND COMMERCIAL ACTIVITIES CONCEPTUAL MODEL

**Table_Apx C-1. Supporting Table for Industrial and Commercial Activities Conceptual Model**
(Note that rows shaded in gray are not proposed for further analysis)

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Manufacture | Domestic Manufacture | Domestic Manufacture | Manufacture of TCE via chlorination, oxychlorination, and as a byproduct | Liquid Contact | Dermal | Workers | Yes | Although the potential for dermal exposure exists, EPA expects the relative contribution of dermal to overall exposure to be relatively small (0.8% absorption and 99.2% volatilization based on modeling from IHSKinPerm) for non-occluded conditions. An occluded scenario, wherein liquid TCE is not able to readily evaporate, may result in higher dermal exposures and a larger contribution to the overall exposure or effects on the skin (e.g. dermal sensitization). |
| | | | | Vapor | Inhalation | Workers | Yes | Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during Manufacturing |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Manufacture | Import | Import | Repackaging of import containers | Liquid Contact | Dermal | Workers | Yes | Although the potential for dermal exposure exists, EPA expects the relative contribution of dermal to overall exposure to be relatively small (0.8% absorption and 99.2% volatilization based on modeling from IHSKinPerm) for non-occluded conditions. An occluded scenario, wherein liquid TCE is not able to readily evaporate, may result in higher dermal exposures and a larger contribution to the overall exposure or effects on the skin (e.g. dermal sensitization). Exposure will only occur in the event the imported material is repackaged. |
| | | | | Vapor | Inhalation | Workers | Yes | Exposure expected only in the event the imported material is repackaged into different sized containers. Exposure frequency may be low. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | Exposure expected only in the event the imported material is repackaged into different sized containers. Exposure frequency may be low. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during import |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Processing | Processing as a reactant | Intermediate in industrial gas manufacturing; all other basic inorganic chemical manufacturing; and all other basic organic chemical manufacturing | Manufacture of HFCs, HCl and muriatic acid | Liquid Contact | Dermal | Workers | Yes | Although the potential for dermal exposure exists, EPA expects the relative contribution of dermal to overall exposure to be relatively small (0.8% absorption and 99.2% volatilization based on modeling from IHSKinPerm) for non-occluded conditions. An occluded scenario, wherein liquid TCE is not able to readily evaporate, may result in higher dermal exposures and a larger contribution to the overall exposure or effects on the skin (e.g. dermal sensitization). |
| | | | | Vapor | Inhalation | Workers | Yes | Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. However, potential for exposure may be low in scenarios where TCE is consumed as a chemical intermediate. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. However, potential for exposure may be low in scenarios where TCE is consumed as a chemical intermediate. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during processing as an intermediate |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Processing | Incorporated into formulation, mixture or reaction product | Solvent for cleaning or degreasing; adhesive and sealant chemicals; and solvents which become part of product formulation or mixture (e.g., lubricants and greases, paints and coatings, other uses) | Formulation of aerosol and non-aerosol products | Liquid Contact | Dermal | Workers | Yes | Although the potential for dermal exposure exists, EPA expects the relative contribution of dermal to overall exposure to be relatively small (0.8% absorption and 99.2% volatilization based on modeling from IHSKinPerm) for non-occluded conditions. An occluded scenario, wherein liquid TCE is not able to readily evaporate, may result in higher dermal exposures and a larger contribution to the overall exposure or effects on the skin (e.g. dermal sensitization). |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected at processing sites that formulate products containing TCE. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected at processing sites that formulate products containing TCE. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during processing/formulation operations. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Processing | Incorporated into articles | Solvents (becomes an integral components of articles) | Manufacture of large, rigid plastic products; industrial textile dyeing; and industrial textile finishing | Liquid Contact | Dermal | Workers | Yes | Although the potential for dermal exposure exists, EPA expects the relative contribution of dermal to overall exposure to be relatively small (0.8% absorption and 99.2% volatilization based on modeling from IHSKinPerm) for non-occluded conditions. An occluded scenario, wherein liquid TCE is not able to readily evaporate, may result in higher dermal exposures and a larger contribution to the overall exposure or effects on the skin (e.g. dermal sensitization). |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected at processing sites that incorporate TCE into articles. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected at processing sites that incorporate TCE into articles. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during processing operations. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Processing | Repackaging | Solvent for cleaning or degreasing | Repackaging into large and small containers | Liquid Contact | Dermal | Workers | Yes | Although the potential for dermal exposure exists, EPA expects the relative contribution of dermal to overall exposure to be relatively small (0.8% absorption and 99.2% volatilization based on modeling from IHSKinPerm) for non-occluded conditions. An occluded scenario, wherein liquid TCE is not able to readily evaporate, may result in higher dermal exposures and a larger contribution to the overall exposure or effects on the skin (e.g. dermal sensitization). |
| | | | | Vapor | Inhalation | Workers | Yes | Exposure frequency may be low; however, the number of workers exposed may be high per CDR (1 submission reporting 10-25 workers, 2 submissions reporting 50-100 workers, 4 submissions reporting 100-500 workers, 2 submissions reporting 500-1,000 workers, and 2 submissions reporting NKRA). |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | Exposure frequency may be low; however, the number of workers exposed may be high per CDR (1 submission reporting 10-25 workers, 2 submissions reporting 50-100 workers, 4 submissions reporting 100-500 workers, 2 submissions reporting 500-1,000 workers, and 2 submissions reporting NKRA). |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during repackaging. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Processing | Recycling | Recycling | Recycling of process solvents containing TCE | Liquid Contact | Dermal | Workers | Yes | Although the potential for dermal exposure exists, EPA expects the relative contribution of dermal to overall exposure to be relatively small (0.8% absorption and 99.2% volatilization based on modeling from IHSKinPerm) for non-occluded conditions. An occluded scenario, wherein liquid TCE is not able to readily evaporate, may result in higher dermal exposures and a larger contribution to the overall exposure or effects on the skin (e.g. dermal sensitization). |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected at recycling sites. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected at recycling sites. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during recycling. |
| Distribution in commerce | Distribution | Distribution | Distribution of bulk shipment of TCE; and distribution of formulated products | Liquid Contact, Vapor | Dermal/ Inhalation | Workers, ONU | No | These exposures will be assessed during other life-cycle stages such as loading/unloading. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Industrial / commercial / consumer use | Solvents (for cleaning or degreasing) | Batch vapor degreaser (e.g., open-top, closed-loop); and In-line vapor degreaser (e.g., conveyorized, web cleaner) | Open top vapor degreasing (OTVD); OTVD with enclosures; Conveyorized vapor degreasing; Cross-rod and ferris wheel vapor degreasing; Web vapor degreasing; Airtight closed-loop degreasing system; Airless vacuum-to-vacuum degreasing system; Airless vacuum drying degreasing system | Liquid Contact | Dermal | Workers | Yes | Although the potential for dermal exposure exists, EPA expects the relative contribution of dermal to overall exposure to be relatively small (0.8% absorption and 99.2% volatilization based on modeling from IHSKinPerm) for non-occluded conditions. An occluded scenario, wherein liquid TCE is not able to readily evaporate, may result in higher dermal exposures and a larger contribution to the overall exposure or effects on the skin (e.g. dermal sensitization). Additionally, repeat contact or dermal immersion may occur, especially while cleaning and maintaining degreasing equipment. Note: EPA proposed a rule to ban the use of TCE in vapor degreasing and will consider the proposed rule when evaluating this scenario. |
| | | | | Vapor | Inhalation | Workers | Yes | EPA has previously assessed OTVD in the 2014 RA and conveyorized degreasing in the subsequent Section 6 rulemaking and has a proposed rule to ban the use of TCE in vapor degreasing. EPA will forward the past assessments for this risk evaluation. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| | | | | Vapor | Inhalation | ONU | Yes | EPA has previously assessed OTVD in the 2014 RA and conveyorized degreasing in the subsequent Section 6 rulemaking and has a proposed rule to ban the use of TCE in vapor degreasing. EPA will forward the past assessments for this risk evaluation. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during this use scenario. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Industrial / commercial / consumer use | Solvents (for cleaning or degreasing) | Cold cleaner | Cold cleaning - maintenance (manual spray; spray sink; dip tank) | Liquid Contact | Dermal | Workers | Yes | Although the potential for dermal exposure exists, EPA expects the relative contribution of dermal to overall exposure to be relatively small (0.8% absorption and 99.2% volatilization based on modeling from IHSKinPerm) for non-occluded conditions. An occluded scenario, wherein liquid TCE is not able to readily evaporate, may result in higher dermal exposures and a larger contribution to the overall exposure or effects on the skin (e.g. dermal sensitization). Additionally, repeat contact or dermal immersion may occur. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected from cold cleaning operations. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected from cold cleaning operations. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | EPA will further evaluate to determine if mist generation is applicable. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Industrial / commercial / consumer use | Solvents (for cleaning or degreasing) | Aerosol spray degreaser/ cleaner | Aerosol use in degreasing/ cleaning | Liquid Contact | Dermal | Workers | No | Contact time with skin is expected to be <3 min due to rapid volatilization. However, repeat contact may occur. Note: EPA proposed a rule to ban the use of TCE in aerosol degreasing and will consider the proposed rule when evaluating this scenario. |
| | | | | Vapor | Inhalation | Workers | Yes | As a result of the 2014 RA, EPA previously assessed inhalation exposure from aerosol degreasing during the Section 6 rulemaking and has a proposed rule to ban the use of TCE in aerosol degreasing. EPA will forward the past assessments for this risk evaluation. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | As a result of the 2014 RA, EPA previously assessed inhalation exposure from aerosol degreasing during the Section 6 rulemaking and has a proposed rule to ban the use of TCE in aerosol degreasing. EPA will forward the past assessments for this risk evaluation. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | Mist generation expected for aerosol applications. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Industrial / commercial / consumer use | Solvents (for cleaning or degreasing) | Mold release | Aerosol use of mold release | Liquid Contact | Dermal | Workers | Yes | Although the potential for dermal exposure exists, EPA expects the relative contribution of dermal to overall exposure to be relatively small (0.8% absorption and 99.2% volatilization based on modeling from IHSKinPerm) for non-occluded conditions. An occluded scenario, wherein liquid TCE is not able to readily evaporate, may result in higher dermal exposures and a larger contribution to the overall exposure or effects on the skin (e.g. dermal sensitization). Additionally, repeat contact may occur. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected from use of aerosols. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected from use of aerosols. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | Mist generation expected for aerosol applications. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Industrial / commercial / consumer use | Lubricants and greases/ lubricants and lubricant additives | Tap and die fluid | Use of metalworking fluids (tap and die) | Liquid Contact | Dermal | Workers | Yes | Although the potential for dermal exposure exists, EPA expects the relative contribution of dermal to overall exposure to be relatively small (0.8% absorption and 99.2% volatilization based on modeling from IHSKinPerm) for non-occluded conditions. An occluded scenario, wherein liquid TCE is not able to readily evaporate, may result in higher dermal exposures and a larger contribution to the overall exposure or effects on the skin (e.g. dermal sensitization). Additionally, repeat contact may occur. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected from use of metalworking fluids. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected from use of metalworking fluids. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | Mist generation expected from use of metalworking fluids. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Industrial / commercial / consumer use | Lubricants and greases/ lubricants and lubricant additives | Penetrating lubricant | Aerosol application of lubricants to substrates | Liquid Contact | Dermal | Workers | Yes | Although the potential for dermal exposure exists, EPA expects the relative contribution of dermal to overall exposure to be relatively small (0.8% absorption and 99.2% volatilization based on modeling from IHSKinPerm) for non-occluded conditions. An occluded scenario, wherein liquid TCE is not able to readily evaporate, may result in higher dermal exposures and a larger contribution to the overall exposure or effects on the skin (e.g. dermal sensitization). Additionally, repeat contact may occur. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected from use of aerosols. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected from use of aerosols. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | Mist generation expected for aerosol applications. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Industrial / commercial / consumer use | Adhesives and sealants | Solvent-based adhesives and sealants; and mirror edge sealants | Industrial spray adhesive application; and other adhesive and sealant applications (e.g. roll) | Liquid Contact | Dermal | Workers | Yes | Although the potential for dermal exposure exists, EPA expects the relative contribution of dermal to overall exposure to be relatively small (0.8% absorption and 99.2% volatilization based on modeling from IHSKinPerm) for non-occluded conditions. An occluded scenario, wherein liquid TCE is not able to readily evaporate, may result in higher dermal exposures and a larger contribution to the overall exposure or effects on the skin (e.g. dermal sensitization). Additionally, repeat contact may occur. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected from use of adhesives and sealants. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected from use of adhesives and sealants. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | Mist generation expected for spray and roll applications. EPA will further evaluate to determine if mist generation is applicable for each adhesive/sealant product. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Industrial / commercial / consumer use | Adhesives and sealants | Tire repair cement/sealer | Commercial automotive repair/servicing | Liquid Contact | Dermal | Workers | Yes | Although the potential for dermal exposure exists, EPA expects the relative contribution of dermal to overall exposure to be relatively small (0.8% absorption and 99.2% volatilization based on modeling from IHSKinPerm) for non-occluded conditions. An occluded scenario, wherein liquid TCE is not able to readily evaporate, may result in higher dermal exposures and a larger contribution to the overall exposure or effects on the skin (e.g. dermal sensitization). Additionally, repeat contact may occur. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected from use of adhesives and sealants. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected from use of adhesives and sealants. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | Products identified in marker report show brush application; generation of mists not expected from brush applications. EPA will further evaluate if other application methods resulting in mist generation are applicable to this scenario |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Industrial / commercial / consumer use | Functional fluids (closed systems) | Heat exchange fluid | Refrigerant in air-conditioning installations; and low temperature heat transfer agent | Liquid Contact | Dermal | Workers | Yes | Although the potential for dermal exposure exists, EPA expects the relative contribution of dermal to overall exposure to be relatively small (0.8% absorption and 99.2% volatilization based on modeling from IHSKinPerm) for non-occluded conditions. An occluded scenario, wherein liquid TCE is not able to readily evaporate, may result in higher dermal exposures and a larger contribution to the overall exposure or effects on the skin (e.g. dermal sensitization). Additionally, repeat contact may occur. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected from initial charging and servicing/recharging of heat exchange fluid. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. However exposure frequency may be low. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected from initial charging and servicing/recharging of heat exchange fluid. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. However exposure frequency may be low. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during use of heat exchange fluid. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Industrial / commercial | Paints and coatings | Diluent in solvent-based paints and coatings | Industrial spray coating application; and other paint and coating applications (e.g. roll) | Liquid Contact | Dermal | Workers | Yes | Although the potential for dermal exposure exists, EPA expects the relative contribution of dermal to overall exposure to be relatively small (0.8% absorption and 99.2% volatilization based on modeling from IHSKinPerm) for non-occluded conditions. An occluded scenario, wherein liquid TCE is not able to readily evaporate, may result in higher dermal exposures and a larger contribution to the overall exposure or effects on the skin (e.g. dermal sensitization). Additionally, repeat contact may occur. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected from use of paints and coatings. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected from use of paints and coatings. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | Mist generation expected for spray and roll applications. EPA will further evaluate to determine if mist generation is applicable for each paint/coating product. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Industrial / commercial / consumer use | Cleaning and furniture care products | Carpet cleaner | Commercial carpet spotting and stain removers | Liquid Contact | Dermal | Workers | Yes | Although the potential for dermal exposure exists, EPA expects the relative contribution of dermal to overall exposure to be relatively small (0.8% absorption and 99.2% volatilization based on modeling from IHSKinPerm) for non-occluded conditions. An occluded scenario, wherein liquid TCE is not able to readily evaporate, may result in higher dermal exposures and a larger contribution to the overall exposure or effects on the skin (e.g. dermal sensitization). Additionally, repeat contact may occur. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected from carpet cleaning. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected from carpet cleaning. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | EPA will further evaluate to determine if mist generation is applicable. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Industrial / commercial / consumer use | Cleaning and furniture care products | Cleaning wipes | | Liquid Contact | Dermal | Workers | Yes | Although the potential for dermal exposure exists, EPA expects the relative contribution of dermal to overall exposure to be relatively small (0.8% absorption and 99.2% volatilization based on modeling from IHSKinPerm) for non-occluded conditions. An occluded scenario, wherein liquid TCE is not able to readily evaporate, may result in higher dermal exposures and a larger contribution to the overall exposure or effects on the skin (e.g. dermal sensitization). Additionally, repeat contact may occur. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected from wipe cleaning. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected from wipe cleaning. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during wipe cleaning. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Industrial / commercial / consumer use | Laundry and dishwashing products | Spot cleaner | Spot cleaning at dry cleaners | Liquid Contact | Dermal | Workers | No | Although the potential for dermal exposure exists, EPA expects the relative contribution of dermal to overall exposure to be relatively small (0.8% absorption and 99.2% volatilization based on modeling from IHSKinPerm) for non-occluded conditions. An occluded scenario, wherein liquid TCE is not able to readily evaporate, may result in higher dermal exposures and a larger contribution to the overall exposure or effects on the skin (e.g. dermal sensitization). Additionally, repeat contact may occur. Note: EPA proposed a rule to ban the use of TCE in spot cleaning and will consider the proposed rule when evaluating this scenario. |
| | | | | Vapor | Inhalation | Workers | Yes | EPA has previously assessed spot cleaning in the 2014 RA and in the subsequent Section 6 rulemaking and has a proposed rule to ban the use of TCE in spot cleaners. EPA will forward the past assessments for this risk evaluation. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | EPA has previously assessed OTVD in the 2014 RA and conveyorized degreasing in the subsequent Section 6 rulemaking and has a proposed rule to ban the use of TCE in vapor degreasing. EPA will forward the past assessments for this risk evaluation. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | Mist generation expected for spot cleaning. Note: EPA proposed a rule to ban the use of TCE in spot cleaning and will consider the proposed rule when evaluating this scenario. |
| Industrial / commercial / consumer use | Corrosion inhibitors and anti-scaling agents | Battery coat; and soap, cleaning compound, and toilet preparation manufacturing | Battery coat; and soap, cleaning compound, and toilet preparation manufacturing | Liquid Contact | Dermal | Workers | Yes | Although the potential for dermal exposure exists, EPA expects the relative contribution of dermal to overall exposure to be relatively small (0.8% absorption and 99.2% volatilization based on modeling from IHSKinPerm) for non-occluded conditions. An occluded scenario, wherein liquid TCE is not able to readily evaporate, may result in higher dermal exposures and a larger contribution to the overall exposure or effects on the skin (e.g. dermal sensitization). Additionally, EPA will need additional information to fully understand the use of TCE in this scenario to determine potential for dermal exposure. |
| | | | | Vapor | Inhalation | Workers | Yes | Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. However, EPA will need additional information to fully understand the use of TCE in this scenario to determine potential for inhalation exposure. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| | | | | Vapor | Inhalation | ONU | Yes | Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. However, EPA will need additional information to fully understand the use of TCE in this scenario to determine potential for inhalation exposure. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | EPA will further evaluate to determine if mist generation is applicable. |
| Industrial / commercial / consumer use | Processing aids | Industrial process solvent; industrial extraction solvent; and industrial precipitant | Process solvent for lithium ion battery manufacture; polymer fiber spinning; fluoroelastomer manufacture; Alcantara manufacture; pulverized sulfur production; and sulfur chloride and cellulose esters and ethers<br><br>Extraction solvent for caprolactam manufacture; recovery of fat-free glues in tanneries; wood resin extraction; | Liquid Contact | Dermal | Workers | Yes | Although the potential for dermal exposure exists, EPA expects the relative contribution of dermal to overall exposure to be relatively small (0.8% absorption and 99.2% volatilization based on modeling from IHSKinPerm) for non-occluded conditions. An occluded scenario, wherein liquid TCE is not able to readily evaporate, may result in higher dermal exposures and a larger contribution to the overall exposure or effects on the skin (e.g. dermal sensitization). Additionally, EPA will need additional information to fully understand the use of TCE in this scenario to determine potential for dermal exposure. |
| | | | | Vapor | Inhalation | Workers | Yes | Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. However, EPA will need additional information to fully understand the use of TCE in this scenario to determine potential for inhalation exposure. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| | | | recovery of wax and paraffin from refuse; tin recovery from scrap metal; and phenol extraction from wastewater<br><br>Precipitant for beta-cyclodextrin manufacture | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. However, EPA will need additional information to fully understand the use of TCE in this scenario to determine potential for inhalation exposure. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | No | Mist generation not expected during use of industrial processing aid. |
| Industrial / commercial / consumer use | Ink, toner and colorant products | Toner aid | Commercial printing and copying | Liquid Contact | Dermal | Workers | | Contact time with skin is expected to be <3 min due to rapid volatilization. Additionally, toner expected to be contained in cartridges thus reducing the potential for dermal exposures. |
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected from toner use. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected from toner use. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | EPA will further evaluate to determine if mist generation is expected. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| Industrial / commercial / consumer use | Automotive care products | Brake and parts cleaner | Aerosol degreasing use in commercial automotive servicing and brake servicing | Liquid Contact | Dermal | Workers | No | Contact time with skin is expected to be <3 min due to rapid volatilization. However, repeat contact may occur. Additionally, EPA may need to evaluate total exposure to TCE from multiple conditions of use in automotive servicing (degreasing and tire repair). Note: EPA proposed a rule to ban the use of TCE in aerosol degreasing and will consider the proposed rule when evaluating this scenario. |
| | | | | Vapor | Inhalation | Workers | Yes | As a result of the 2014 RA, EPA previously assessed inhalation exposure from aerosol degreasing during the Section 6 rulemaking and has a proposed rule to ban the use of TCE in aerosol degreasing. EPA will forward the past assessments for this risk evaluation. Additionally, EPA may need to evaluate total exposure to TCE from multiple conditions of use in automotive servicing (degreasing and tire repair). |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| | | | | Vapor | Inhalation | ONU | Yes | As a result of the 2014 RA, EPA previously assessed inhalation exposure from aerosol degreasing during the Section 6 rulemaking and has a proposed rule to ban the use of TCE in aerosol degreasing. EPA will forward the past assessments for this risk evaluation. Additionally, EPA may need to evaluate total exposure to TCE from multiple conditions of use in automotive servicing (degreasing and tire repair). |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | Mist generation expected for aerosol applications. Additionally, EPA may need to evaluate total exposure to TCE from multiple conditions of use in automotive servicing (degreasing and tire repair). Note: EPA proposed a rule to ban the use of TCE in aerosol degreasing and will consider the proposed rule when evaluating this scenario. |
| Industrial / commercial / consumer use | Apparel and footwear care products | Shoe polish | Commercial shoe polishing and repair | Liquid Contact | Dermal | Workers | Yes | Although the potential for dermal exposure exists, EPA expects the relative contribution of dermal to overall exposure to be relatively small (0.8% absorption and 99.2% volatilization based on modeling from IHSKinPerm) for non-occluded conditions. An occluded scenario, wherein liquid TCE is not able to readily evaporate, may result in higher dermal exposures and a larger contribution to the overall exposure or effects on the skin (e.g. dermal sensitization). Additionally, repeat contact may occur. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| | | | | Vapor | Inhalation | Workers | Yes | Inhalation exposure is expected from shoe polish use. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | Inhalation exposure is expected from shoe polish use. Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | EPA will further evaluate to determine if mist generation is applicable. |
| Industrial / commercial / consumer use | Other uses | Other miscellaneous industrial, commercial, and consumer uses | See Table XX for specific scenario corresponding to the condition of use. | Liquid Contact | Dermal | Workers | Yes | Although the potential for dermal exposure exists, EPA expects the relative contribution of dermal to overall exposure to be relatively small (0.8% absorption and 99.2% volatilization based on modeling from IHSKinPerm) for non-occluded conditions. An occluded scenario, wherein liquid TCE is not able to readily evaporate, may result in higher dermal exposures and a larger contribution to the overall exposure or effects on the skin (e.g. dermal sensitization). Additionally, repeat contact may occur for some miscellaneous conditions of use. |
| | | | | Vapor | Inhalation | Workers | Yes | Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |
| | | | | Vapor | Inhalation | ONU | Yes | Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Mist | Dermal/ Inhalation | Workers, ONU | Yes | EPA will further evaluate to determine if mist generation is applicable to specific conditions of use in this scenario. |
| Disposal | Waste Handling, Treatment and Disposal | Disposal of TCE wastes | Worker handling of wastes | Liquid Contact | Dermal | Workers | Yes | Although the potential for dermal exposure exists, EPA expects the relative contribution of dermal to overall exposure to be relatively small (0.8% absorption and 99.2% volatilization based on modeling from IHSKinPerm) for non-occluded conditions. An occluded scenario, wherein liquid TCE is not able to readily evaporate, may result in higher dermal exposures and a larger contribution to the overall exposure or effects on the skin (e.g. dermal sensitization). Additionally, the frequency of exposure and the potential for dermal immersion needs to be further analyzed. |
| | | | | Vapor | Inhalation | Workers | Yes | Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |
| | | | | Liquid Contact | Dermal | ONU | No | Dermal exposure is expected to be primarily to workers directly involved in working with the chemical |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor / Population | Proposed for Further Risk Evaluation | Rationale for Further Evaluation / No Further Evaluation |
|---|---|---|---|---|---|---|---|---|
| | | | | Vapor | Inhalation | ONU | Yes | Due to high volatility (VP = 73.46 mmHg) at room temperature, inhalation pathway should be further analyzed. |

# Appendix D SUPPORTING TABLE FOR CONSUMER ACTIVITIES AND USES CONCEPTUAL MODEL

**Table_Apx D-1. Consumer Activities and Uses Conceptual Model Supporting Table**
(Note that rows shaded in gray are not proposed for further analysis)

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| Use | Solvents (for cleaning or degreasing) | Liquid / non-spray application: Cold cleaner | Dermal contact with liquid product on the skin per event - shorter duration (direct) | Liquid Contact | Dermal | Consumers | Yes | CEM | TCE in direct contact with skin would be expected to evaporate before significant dermal absorption could occur. However, there may be effects on the skin (e.g., dermal sensitization), or certain scenarios with a higher dermal exposure potential, for example, an occluded scenario, wherein liquid TCE is not able to evaporate readily. Therefore, occluded scenarios will be evaluated for systemic and sensitization effects, whereas, non-occluded scenarios will be evaluated for sensitization effects alone. |
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct) | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct dermal exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Oral exposures may also occur through hand-to-mouth patterns following dermal contact with TCE. As described, any TCE present on surfaces of the home or skin surfaces is expected to volatilize rapidly – making it available for inhalation as a vapor before oral ingestion may occur through such patterns. |
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct oral exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| | | | Dermal vapor to skin | Vapor | Dermal | Consumers | No | NA | Mist not expected from this use pattern. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |
| | | | Dermal vapor to skin | | | Bystanders | No | NA | Mist not expected from this use pattern. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |
| | | | Evaporation from the surface (quick decay) | | Inhalation | Consumers | Yes | MCCEM, CEM | Inhalation is expected to be the primary route of exposure for users. |
| | | | Evaporation from the surface (quick decay) | | | Bystanders | Yes | MCCEM, CEM | Inhalation is expected to be the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Mist not expected from this use pattern. |
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Mist not expected from this use pattern. |
| Use | Solvents (for cleaning or degreasing) | Spray / aerosol application: Aerosol spray degreaser/cleaner, electronic degreaser, gun scrubber | Dermal contact with liquid product on the skin per event - shorter duration (direct) | Liquid Contact | Dermal | Consumers | Yes | CEM | This use assessed in the U.S. EPA (2014c) risk assessment will be considered in this evaluation to ensure previous assessments are in alignment with the Procedures for Chemical Risk Evaluation under the Amended Toxic Substances Control Act (40 CFR Part 702). TCE in direct contact with skin would be expected to evaporate before significant dermal absorption could occur. However, there may be effects on the skin (e.g., dermal sensitization), or |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | certain scenarios with a higher dermal exposure potential, for example, an occluded scenario, wherein liquid TCE is not able to evaporate readily. Therefore, occluded scenarios will be evaluated for systemic and sensitization effects, whereas, non-occluded scenarios will be evaluated for sensitization effects alone. |
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct) | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct dermal exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Oral exposures may also occur through hand-to-mouth patterns following dermal contact with TCE. As described, any TCE present on surfaces of the home or skin surfaces is expected to volatilize rapidly – making it available for inhalation as a vapor before oral ingestion may occur through such patterns. |
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct oral exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct); Dermal vapor to skin | Vapor / Mist | Dermal | Consumers | No | NA | Based on physical chemical properties, mists of TCE are expected to rapidly evaporate before being deposited on skin, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct); Dermal vapor to skin | | | Bystanders | No | NA | Based on physical chemical properties, mists of TCE are expected to rapidly evaporate before being deposited on skin, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |
| | | | Spray application (stationary) | | Inhalation | Consumers | Yes | MCCEM, CEM | This use assessed in the U.S. EPA (2014c) risk assessment will be considered in this evaluation to ensure previous assessments are in alignment with the Procedures for Chemical Risk Evaluation under the Amended Toxic Substances Control Act (40 CFR Part 702). Inhalation is expected to be the primary route of exposure for users. |
| | | | Spray application (stationary) | | | Bystanders | Yes | MCCEM, CEM | This use assessed in the U.S. EPA (2014c) risk assessment will be considered in this evaluation to ensure previous assessments are in alignment with the Procedures for Chemical Risk Evaluation under the Amended Toxic Substances Control Act (40 CFR Part 702). Inhalation is expected to be the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Based on physical chemical properties, mists of TCE are expected to be rapidly absorbed in the respiratory tract or evaporate before being introduced into the respiratory tract, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. |
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Based on physical chemical properties, mists of TCE are expected to be rapidly absorbed in the respiratory tract or evaporate before being introduced into the |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | respiratory tract, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. |
| Use | Lubricants and greases/ lubricants and lubricant additives | Liquid / non-spray application: Penetrating lubricant | Dermal contact with liquid product on the skin per event - shorter duration (direct) | Liquid Contact | Dermal | Consumers | Yes | CEM | TCE in direct contact with skin would be expected to evaporate before significant dermal absorption could occur. However, there may be effects on the skin (e.g., dermal sensitization), or certain scenarios with a higher dermal exposure potential, for example, an occluded scenario, wherein liquid TCE is not able to evaporate readily. Therefore, occluded scenarios will be evaluated for systemic and sensitization effects, whereas, non-occluded scenarios will be evaluated for sensitization effects alone. |
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct) | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct dermal exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Oral exposures may also occur through hand-to-mouth patterns following dermal contact with TCE. As described, any TCE present on surfaces of the home or skin surfaces is expected to volatilize rapidly – making it available for inhalation as a vapor before oral ingestion may occur through such patterns. |
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct oral exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |
| | | | Dermal vapor to skin | Vapor | Dermal | Consumers | No | NA | Mist not expected from this use pattern. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |
| | | | Dermal vapor to skin | | | Bystanders | No | NA | Mist not expected from this use pattern. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |
| | | | Evaporation from the surface (quick decay) | | Inhalation | Consumers | Yes | MCCEM, CEM | Inhalation is expected to be the primary route of exposure for users. |
| | | | Evaporation from the surface (quick decay) | | | Bystanders | Yes | MCCEM, CEM | Inhalation is expected to be the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Mist not expected from this use pattern. |
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Mist not expected from this use pattern. |
| Use | Lubricants and greases/ lubricants and lubricant additives | Spray / aerosol application: Penetrating lubricant | Dermal contact with liquid product on the skin per event - shorter duration (direct) | Liquid Contact | Dermal | Consumers | Yes | CEM | TCE in direct contact with skin would be expected to evaporate before significant dermal absorption could occur. However, there may be effects on the skin (e.g., dermal sensitization), or certain scenarios with a higher dermal exposure potential, for example, an occluded scenario, wherein liquid TCE is not able to evaporate readily. Therefore, occluded scenarios will be evaluated for systemic and sensitization effects, whereas, non-occluded scenarios will be evaluated for sensitization effects alone. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct) | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct dermal exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Oral exposures may also occur through hand-to-mouth patterns following dermal contact with TCE. As described, any TCE present on surfaces of the home or skin surfaces is expected to volatilize rapidly – making it available for inhalation as a vapor before oral ingestion may occur through such patterns. |
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct oral exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct); Dermal vapor to skin | Vapor / Mist | Dermal | Consumers | No | NA | Based on physical chemical properties, mists of TCE are expected to rapidly evaporate before being deposited on skin, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct); Dermal vapor to skin | | | Bystanders | No | NA | Based on physical chemical properties, mists of TCE are expected to rapidly evaporate before being deposited on skin, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |
| | | | Spray application (stationary) | | Inhalation | Consumers | Yes | MCCEM, CEM | Inhalation is expected to be the primary route of exposure for users. |
| | | | Spray application (stationary) | | | Bystanders | Yes | MCCEM, CEM | Inhalation is expected to be the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Based on physical chemical properties, mists of TCE are expected to be rapidly absorbed in the respiratory tract or evaporate before being introduced into the respiratory tract, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. |
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Based on physical chemical properties, mists of TCE are expected to be rapidly absorbed in the respiratory tract or evaporate before being introduced into the respiratory tract, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. |
| Use | Adhesives and sealants | Liquid / non-spray application: Mirror edge sealant | Dermal contact with liquid product on the skin per event - shorter duration (direct) | Liquid Contact | Dermal | Consumers | Yes | CEM | TCE in direct contact with skin would be expected to evaporate before significant dermal absorption could occur. However, there may be effects on the skin (e.g., dermal sensitization), or certain scenarios with a higher dermal exposure potential, for example, an occluded scenario, wherein liquid TCE is not able to evaporate readily. Therefore, occluded scenarios will be evaluated for systemic and sensitization effects, whereas, non-occluded scenarios will be evaluated for sensitization effects alone. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct) | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct dermal exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Oral exposures may also occur through hand-to-mouth patterns following dermal contact with TCE. As described, any TCE present on surfaces of the home or skin surfaces is expected to volatilize rapidly – making it available for inhalation as a vapor before oral ingestion may occur through such patterns. |
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct oral exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |
| | | | Dermal vapor to skin | Vapor | Dermal | Consumers | No | NA | Mist not expected from this use pattern. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |
| | | | Dermal vapor to skin | | | Bystanders | No | NA | Mist not expected from this use pattern. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |
| | | | Evaporation from the surface (slow decay) | | Inhalation | Consumers | Yes | MCCEM, CEM | Inhalation is expected to be the primary route of exposure for users. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| | | | Evaporation from the surface (slow decay) | | | Bystanders | Yes | MCCEM, CEM | Inhalation is expected to be the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Mist not expected from this use pattern. |
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Mist not expected from this use pattern. |
| Use | Adhesives and sealants | Spray / aerosol application: Mirror edge sealant | Dermal contact with liquid product on the skin per event - shorter duration (direct) | Liquid Contact | Dermal | Consumers | Yes | CEM | TCE in direct contact with skin would be expected to evaporate before significant dermal absorption could occur. However, there may be effects on the skin (e.g., dermal sensitization), or certain scenarios with a higher dermal exposure potential, for example, an occluded scenario, wherein liquid TCE is not able to evaporate readily. Therefore, occluded scenarios will be evaluated for systemic and sensitization effects, whereas, non-occluded scenarios will be evaluated for sensitization effects alone. |
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct) | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct dermal exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Oral exposures may also occur through hand-to-mouth patterns following dermal contact with TCE. As described, any TCE present on surfaces of the home or skin surfaces is expected to volatilize rapidly – making it available for inhalation as a vapor before oral ingestion may occur through such patterns. |
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct oral exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct); Dermal vapor to skin | Vapor / Mist | Dermal | Consumers | No | NA | Based on physical chemical properties, mists of TCE are expected to rapidly evaporate before being deposited on skin, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct); Dermal vapor to skin | | | Bystanders | No | NA | Based on physical chemical properties, mists of TCE are expected to rapidly evaporate before being deposited on skin, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |
| | | | Spray application (stationary) | | Inhalation | Consumers | Yes | MCCEM, CEM | Inhalation is expected to be the primary route of exposure for users. |
| | | | Spray application (stationary) | | | Bystanders | Yes | MCCEM, CEM | Inhalation is expected to be the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Based on physical chemical properties, mists of TCE are expected to be rapidly absorbed in the respiratory tract or evaporate before being introduced into the respiratory tract, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Based on physical chemical properties, mists of TCE are expected to be rapidly absorbed in the respiratory tract or evaporate before being introduced into the respiratory tract, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. |
| Use | Cleaning and furniture care products | Liquid / non-spray application: Carpet cleaner, cleaning wipes, spot remover | Dermal contact with liquid product on the skin per event - shorter duration (direct) | Liquid Contact | Dermal | Consumers | Yes | CEM | TCE in direct contact with skin would be expected to evaporate before significant dermal absorption could occur. However, there may be effects on the skin (e.g., dermal sensitization), or certain scenarios with a higher dermal exposure potential, for example, an occluded scenario, wherein liquid TCE is not able to evaporate readily. Therefore, occluded scenarios will be evaluated for systemic and sensitization effects, whereas, non-occluded scenarios will be evaluated for sensitization effects alone. |
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct) | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct dermal exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Oral exposures may also occur through hand-to-mouth patterns following dermal contact with TCE. As described, any TCE present on surfaces of the home or skin surfaces is expected to volatilize rapidly – making it available for inhalation as a vapor before oral ingestion may occur through such patterns. |
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct oral exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |
| | | | Dermal vapor to skin | Vapor | Dermal | Consumers | No | NA | Mist not expected from this use pattern. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| | | | Dermal vapor to skin | | | Bystanders | No | NA | Mist not expected from this use pattern. |
| | | | Evaporation from the surface (quick decay) | | Inhalation | Consumers | Yes | MCCEM, CEM | Inhalation is expected to be the primary route of exposure for users. |
| | | | Evaporation from the surface (quick decay) | | | Bystanders | Yes | MCCEM, CEM | Inhalation is expected to be the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Mist not expected from this use pattern. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Mist not expected from this use pattern. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |
| | | | Dermal contact with liquid product on the skin (direct) | Contact with treated surface | Dermal | Bystanders | No | NA | There is potential for bystanders to have indirect dermal contact via contact with a surface upon which TCE has been applied (e.g., counter, floor). Based on the expectation that TCE would evaporate from a surface rapidly (i.e., likely before such indirect contact occurs), this route is unlikely to contribute significantly to overall exposure to bystanders. |
| | | | Oral swallowing the product directly | | Oral | Bystanders | No | NA | Oral exposures may also occur through hand-to-mouth patterns following dermal contact with TCE. As described, dermal contact would not be expected for bystanders, and any TCE present on surfaces of the home or skin surfaces is |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | expected to volatilize rapidly – making it available for inhalation as a vapor before oral ingestion may occur through such patterns. |
| Use | Cleaning and furniture care products | Spray / aerosol application: Carpet cleaner, spot remover | Dermal contact with liquid product on the skin per event - shorter duration (direct) | Liquid Contact | Dermal | Consumers | Yes | CEM | TCE in direct contact with skin would be expected to evaporate before significant dermal absorption could occur. However, there may be effects on the skin (e.g., dermal sensitization), or certain scenarios with a higher dermal exposure potential, for example, an occluded scenario, wherein liquid TCE is not able to evaporate readily. Therefore, occluded scenarios will be evaluated for systemic and sensitization effects, whereas, non-occluded scenarios will be evaluated for sensitization effects alone. |
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct) | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct dermal exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Oral exposures may also occur through hand-to-mouth patterns following dermal contact with TCE. As described, any TCE present on surfaces of the home or skin surfaces is expected to volatilize rapidly – making it available for inhalation as a vapor before oral ingestion may occur through such patterns. |
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct oral exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct); Dermal vapor to skin | Vapor / Mist | Dermal | Consumers | No | NA | Based on physical chemical properties, mists of TCE are expected to rapidly evaporate before being deposited on skin, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct); Dermal vapor to skin | | | Bystanders | No | NA | Based on physical chemical properties, mists of TCE are expected to rapidly evaporate before being deposited on skin, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |
| | | | Spray application (stationary) | | Inhalation | Consumers | Yes | MCCEM, CEM | Inhalation is expected to be the primary route of exposure for users. |
| | | | Spray application (stationary) | | | Bystanders | Yes | MCCEM, CEM | Inhalation is expected to be the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Based on physical chemical properties, mists of TCE are expected to be rapidly absorbed in the respiratory tract or evaporate before being introduced into the respiratory tract, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Based on physical chemical properties, mists of TCE are expected to be rapidly absorbed in the respiratory tract or evaporate before being introduced into the respiratory tract, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. |
| | | | Dermal contact with liquid product on the skin (direct) | Contact with treated surface | Dermal | Bystanders | No | NA | There is potential for bystanders to have indirect dermal contact via contact with a surface upon which TCE has been applied (e.g., counter, floor). Based on the expectation that TCE would evaporate from a surface rapidly (i.e., likely before such indirect contact occurs), this route is unlikely to contribute significantly to overall exposure to bystanders. |
| | | | Oral swallowing the product directly | | Oral | Bystanders | No | NA | Oral exposures may also occur through hand-to-mouth patterns following dermal contact with TCE. As described, dermal contact would not be expected for bystanders, and any TCE present on surfaces of the home or skin surfaces is expected to volatilize rapidly – making it available for inhalation as a vapor before oral ingestion may occur through such patterns. |
| Use | Arts, crafts and hobby materials | Spray / aerosol application: Fixatives and coatings | Dermal contact with liquid product on the skin per event - shorter duration (direct) | Liquid Contact | Dermal | Consumers | Yes | CEM | This use assessed in the U.S. EPA (U.S. EPA, 2014c) risk assessment will be considered in this evaluation to ensure previous assessments are in alignment with the Procedures for Chemical Risk Evaluation under the Amended Toxic Substances Control Act (40 CFR Part 702). TCE in direct contact with skin would be expected to evaporate before significant dermal absorption could occur. However, there may be effects on the skin (e.g., dermal sensitization), or certain scenarios with a higher dermal exposure potential, for example, an occluded scenario, wherein liquid TCE is not able to evaporate readily. Therefore, occluded scenarios will be evaluated for systemic |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
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| | | | | | | | | | and sensitization effects, whereas, non-occluded scenarios will be evaluated for sensitization effects alone. |
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct) | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct dermal exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Oral exposures may also occur through hand-to-mouth patterns following dermal contact with TCE. As described, any TCE present on surfaces of the home or skin surfaces is expected to volatilize rapidly – making it available for inhalation as a vapor before oral ingestion may occur through such patterns. |
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct oral exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct); Dermal vapor to skin | Vapor / Mist | Dermal | Consumers | No | NA | Based on physical chemical properties, mists of TCE are expected to rapidly evaporate before being deposited on skin, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct); Dermal vapor to skin | | | Bystanders | No | NA | Based on physical chemical properties, mists of TCE are expected to rapidly evaporate before being deposited on skin, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |
| | | | Spray application (stationary) | | Inhalation | Consumers | Yes | MCCEM, CEM | This use assessed in the U.S. EPA (2014c) risk assessment will be considered in this evaluation to ensure previous assessments are in alignment with the Procedures for Chemical Risk Evaluation under the Amended Toxic Substances Control Act (40 CFR Part 702). Inhalation is expected to be the primary route of exposure for users. |
| | | | Spray application (stationary) | | | Bystanders | Yes | MCCEM, CEM | This use assessed in the U.S. EPA (2014c) risk assessment will be considered in this evaluation to ensure previous assessments are in alignment with the Procedures for Chemical Risk Evaluation under the Amended Toxic Substances Control Act (40 CFR Part 702). Inhalation is expected to be the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Based on physical chemical properties, mists of TCE are expected to be rapidly absorbed in the respiratory tract or evaporate before being introduced into the respiratory tract, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. |
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Based on physical chemical properties, mists of TCE are expected to be rapidly absorbed in the respiratory tract or evaporate before being introduced into the |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
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| | | | | | | | | | respiratory tract, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. |
| Use | Automotive care products | Liquid / non-spray application: Brake and parts cleaner | Dermal contact with liquid product on the skin per event - shorter duration (direct) | Liquid Contact | Dermal | Consumers | Yes | CEM | TCE in direct contact with skin would be expected to evaporate before significant dermal absorption could occur. However, there may be effects on the skin (e.g., dermal sensitization), or certain scenarios with a higher dermal exposure potential, for example, an occluded scenario, wherein liquid TCE is not able to evaporate readily. Therefore, occluded scenarios will be evaluated for systemic and sensitization effects, whereas, non-occluded scenarios will be evaluated for sensitization effects alone. |
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct) | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct dermal exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Oral exposures may also occur through hand-to-mouth patterns following dermal contact with TCE. As described, any TCE present on surfaces of the home or skin surfaces is expected to volatilize rapidly – making it available for inhalation as a vapor before oral ingestion may occur through such patterns. |
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct oral exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |
| | | | Dermal vapor to skin | Vapor | Dermal | Consumers | No | NA | Mist not expected from this use pattern. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
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| | | | | | | | | | IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |
| | | | Dermal vapor to skin | | | Bystanders | No | NA | Mist not expected from this use pattern. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |
| | | | Evaporation from the surface (quick decay) | | Inhalation | Consumers | Yes | MCCEM, CEM | Inhalation is expected to be the primary route of exposure for users. |
| | | | Evaporation from the surface (quick decay) | | | Bystanders | Yes | MCCEM, CEM | Inhalation is expected to be the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Mist not expected from this use pattern. |
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Mist not expected from this use pattern. |
| Use | Automotive care products | Spray / aerosol application: Brake and parts cleaner | Dermal contact with liquid product on the skin per event - shorter duration (direct) | Liquid Contact | Dermal | Consumers | Yes | CEM | TCE in direct contact with skin would be expected to evaporate before significant dermal absorption could occur. However, there may be effects on the skin (e.g., dermal sensitization), or certain scenarios with a higher dermal exposure potential, for example, an occluded scenario, wherein liquid TCE is not able to evaporate readily. Therefore, occluded scenarios will be evaluated for systemic and sensitization effects, whereas, non-occluded scenarios will be evaluated for sensitization effects alone. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct) | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct dermal exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Oral exposures may also occur through hand-to-mouth patterns following dermal contact with TCE. As described, any TCE present on surfaces of the home or skin surfaces is expected to volatilize rapidly – making it available for inhalation as a vapor before oral ingestion may occur through such patterns. |
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct oral exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct); Dermal vapor to skin | Vapor / Mist | Dermal | Consumers | No | NA | Based on physical chemical properties, mists of TCE are expected to rapidly evaporate before being deposited on skin, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct); Dermal vapor to skin | | | Bystanders | No | NA | Based on physical chemical properties, mists of TCE are expected to rapidly evaporate before being deposited on skin, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
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| | | | | | | | | | dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |
| | | | Spray application (stationary) | | Inhalation | Consumers | Yes | MCCEM, CEM | Inhalation is expected to be the primary route of exposure for users. |
| | | | Spray application (stationary) | | | Bystanders | Yes | MCCEM, CEM | Inhalation is expected to be the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Based on physical chemical properties, mists of TCE are expected to be rapidly absorbed in the respiratory tract or evaporate before being introduced into the respiratory tract, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. |
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Based on physical chemical properties, mists of TCE are expected to be rapidly absorbed in the respiratory tract or evaporate before being introduced into the respiratory tract, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. |
| Use | Other uses | Liquid / non-spray application: Hoof polish, film cleaner | Dermal contact with liquid product on the skin per event - shorter duration (direct) | Liquid Contact | Dermal | Consumers | Yes | CEM | TCE in direct contact with skin would be expected to evaporate before significant dermal absorption could occur. However, there may be effects on the skin (e.g., dermal sensitization), or certain scenarios with a higher dermal exposure potential, for example, an occluded scenario, wherein liquid TCE is not able to evaporate readily. Therefore, occluded scenarios will be evaluated for systemic and sensitization effects, whereas, non-occluded scenarios will be evaluated for sensitization effects alone. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct) | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct dermal exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Oral exposures may also occur through hand-to-mouth patterns following dermal contact with TCE. As described, any TCE present on surfaces of the home or skin surfaces is expected to volatilize rapidly – making it available for inhalation as a vapor before oral ingestion may occur through such patterns. |
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct oral exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |
| | | | Dermal vapor to skin | Vapor | Dermal | Consumers | No | NA | Mist not expected from this use pattern. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |
| | | | Dermal vapor to skin | | | Bystanders | No | NA | Mist not expected from this use pattern. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |
| | | | Evaporation from the surface (quick decay) | | Inhalation | Consumers | Yes | MCCEM, CEM | Inhalation is expected to be the primary route of exposure for users. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| | | | Evaporation from the surface (quick decay) | | | Bystanders | Yes | MCCEM, CEM | Inhalation is expected to be the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Mist not expected from this use pattern. |
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Mist not expected from this use pattern. |
| Use | Other uses | Spray / aerosol application: Pepper spray, film cleaner | Dermal contact with liquid product on the skin per event - shorter duration (direct) | Liquid Contact | Dermal | Consumers | Yes | CEM | TCE in direct contact with skin would be expected to evaporate before significant dermal absorption could occur. However, there may be effects on the skin (e.g., dermal sensitization), or certain scenarios with a higher dermal exposure potential, for example, an occluded scenario, wherein liquid TCE is not able to evaporate readily. Therefore, occluded scenarios will be evaluated for systemic and sensitization effects, whereas, non-occluded scenarios will be evaluated for sensitization effects alone. |
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct) | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct dermal exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Oral exposures may also occur through hand-to-mouth patterns following dermal contact with TCE. As described, any TCE present on surfaces of the home or skin surfaces is expected to volatilize rapidly – making it available for inhalation as a vapor before oral ingestion may occur through such patterns. |
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Generally, individuals that have contact with liquid TCE would be users and not bystanders. Therefore, direct oral exposures to liquid TCE are not expected and inhalation is the primary route of exposure for bystanders. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct); Dermal vapor to skin | Vapor / Mist | Dermal | Consumers | No | NA | Based on physical chemical properties, mists of TCE are expected to rapidly evaporate before being deposited on skin, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |
| | | | Dermal contact with liquid product on the skin per event - shorter duration (direct); Dermal vapor to skin | | | Bystanders | No | NA | Based on physical chemical properties, mists of TCE are expected to rapidly evaporate before being deposited on skin, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures are concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be evaluated in these cases. |
| | | | Spray application (stationary) | | Inhalation | Consumers | Yes | MCCEM, CEM | Inhalation is expected to be the primary route of exposure for users. |
| | | | Spray application (stationary) | | | Bystanders | Yes | MCCEM, CEM | Inhalation is expected to be the primary route of exposure for bystanders. |
| | | | Oral swallowing the product directly | | Oral | Consumers | No | NA | Based on physical chemical properties, mists of TCE are expected to be rapidly absorbed in the respiratory tract or evaporate before being introduced into the respiratory tract, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| | | | Oral swallowing the product directly | | | Bystanders | No | NA | Based on physical chemical properties, mists of TCE are expected to be rapidly absorbed in the respiratory tract or evaporate before being introduced into the respiratory tract, thus contributing to the amount of TCE vapor in the air available for inhalation exposure. |
| Disposal | Consumer Handling and Disposal of Waste | Disposal of TCE wastes | Consumer handling of spent consumer products | Liquid Contact | Dermal / Oral | Consumers | No | NA | Consumer products containing TCE are expected to be primarily disposed of in original containers, thus limiting direct exposures to TCE during disposal or handling. Disposal of spent products are expected to be taken to municipal landfill sites and collected and disposed of as part of their waste handling practices. Any exposures associated with TCE-containing consumer products are expected to be significantly higher during use than during disposal or handling. Therefore, evaluation of the use-associated exposures is anticipated to reflect the worst-case exposure scenario for a specific product. |
| | | | | | | Bystanders | No | NA | Consumer products containing TCE are expected to be primarily disposed of in original containers, thus limiting direct exposures to TCE during disposal or handling. Disposal of spent products are expected to be taken to municipal landfill sites and collected and disposed of as part of their waste handling practices. Any exposures associated with TCE-containing consumer products are expected to be significantly higher during use than during disposal or handling. Therefore, evaluation of the use-associated exposures is anticipated to reflect the worst-case exposure scenario for a specific product. |
| | | | | Vapor | Dermal / Oral | Consumers | No | NA | Consumer products containing TCE are expected to be primarily disposed of in original containers, thus limiting direct exposures to TCE during disposal or handling. Disposal of spent products are expected to be taken to municipal landfill |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | sites and collected and disposed of as part of their waste handling practices. Any exposures associated with TCE-containing consumer products are expected to be significantly higher during use than during disposal or handling. Therefore, evaluation of the use-associated exposures is anticipated to reflect the worst-case exposure scenario for a specific product. |
| | | | | | | Bystanders | No | NA | Consumer products containing TCE are expected to be primarily disposed of in original containers, thus limiting direct exposures to TCE during disposal or handling. Disposal of spent products are expected to be taken to municipal landfill sites and collected and disposed of as part of their waste handling practices. Any exposures associated with TCE-containing consumer products are expected to be significantly higher during use than during disposal or handling. Therefore, evaluation of the use-associated exposures is anticipated to reflect the worst-case exposure scenario for a specific product. |
| | | | | | Inhalation | Consumers | No | NA | Consumer products containing TCE are expected to be primarily disposed of in original containers, thus limiting direct exposures to TCE during disposal or handling. Disposal of spent products are expected to be taken to municipal landfill sites and collected and disposed of as part of their waste handling practices. Any exposures associated with TCE-containing consumer products are expected to be significantly higher during use than during disposal or handling. Therefore, evaluation of the use-associated exposures is anticipated to reflect the worst-case exposure scenario for a specific product. |

| Life Cycle Stage | Category | Subcategory | Release / Exposure Scenario | Exposure Pathway | Exposure Routes | Receptor / Population | Proposed for Further Risk Evaluation | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Bystanders | No | NA | Consumer products containing TCE are expected to be primarily disposed of in original containers, thus limiting direct exposures to TCE during disposal or handling. Disposal of spent products are expected to be taken to municipal landfill sites and collected and disposed of as part of their waste handling practices. Any exposures associated with TCE-containing consumer products are expected to be significantly higher during use than during disposal or handling. Therefore, evaluation of the use-associated exposures is anticipated to reflect the worst-case exposure scenario for a specific product. |

# Appendix E SUPPORTING TABLE FOR ENVIRONMENTAL RELEASES AND WASTES CONCEPTUAL MODEL

**Table_Apx E-1. Environmental Releases and Wastes Conceptual Model Supporting Table**

(Note that rows shaded in gray are not proposed for further analysis)

| Life Cycle Stage | Releases and Wastes from Industrial / Commercial / Consumer Uses | | Release / Exposure Scenario | Exposure Pathway | Exposure Route | Receptor | Proposed for Further Analysis | Applicable Modeling Approach | Rationale for Further Evaluation / no Further Evaluation |
|---|---|---|---|---|---|---|---|---|---|
| Manufacturing, Processing, Use, and/or Disposal | Wastewater or Liquid Wastes | Industrial pre-treatment or indirect discharge to POTW | Direct discharge to surface water | Surface water | Not applicable to ecological receptors | Aquatic Species | Yes | E-FAST, VVWM | Within the past ten years of surface water monitoring data from STORET, there are detections (e.g., maximum of 50 ppb and average of 4.5 ppb), that do not exceed the acute COC for TCE, 340 ppb, but do exceed the chronic COC, 3 ppb. |
| Manufacturing, Processing, Use, and/or Disposal | Wastewater or Liquid Wastes | Industrial pre-treatment or indirect discharge to POTW | Direct discharge to surface water | Surface water | Not applicable to ecological receptors | Terrestrial Species | No | NA | Review of hazard data for terrestrial organisms shows that there is likely to be hazard; however, physical chemical properties do not support an exposure pathway through water and soil pathways to these organisms. TCE has a predicted 81% wastewater treatment removal efficiency, predominately due to volatilization during aeration. |
| Manufacturing, Processing, Use, and/or Disposal | Wastewater or Liquid Wastes | Industrial pre-treatment or indirect discharge to POTW | Direct discharge to surface water | Sediment: surface water to sediment | Not applicable to ecological receptors | Aquatic Species | No | NA | TCE is released to surface water from ongoing industrial and/or commercial activities, as reported in recent TRI and DMR release and loading data. However, TCE released to surface water is expected to primarily volatilize; thus, it is not expected that a significant portion of TCE would be available to enter the sediment compartment. |
| Manufacturing, Processing, Use, and/or Disposal | Wastewater or Liquid Wastes | Industrial pre-treatment or indirect discharge to POTW | Partitioning to biosolids | Soil: biosolids to soil | Not applicable to ecological receptors | Terrestrial Species | No | NA | Based on TCE's fate properties, it is not anticipated to partition to biosolids during wastewater treatment. TCE has a predicted 81% wastewater treatment removal efficiency, predominately due to volatilization during aeration. Any TCE present in the water portion of biosolids following wastewater treatment and land application would be expected to rapidly volatilize into air. Beyond these fate-based considerations, TCE is subject to RCRA land disposal restrictions under (40 CFR 268) and is considered a prohibited waste (organics toxicity characteristic) with land disposal restriction treatment standards that must be met prior to land disposal. |

# Appendix F INCLUSION AND EXCLUSION CRITERIA FOR FULL TEXT SCREENING

Appendix F contains the eligibility criteria for various data streams informing the TSCA risk evaluation: environmental fate; engineering and occupational exposure; exposure to consumers; and human health hazard. The criteria are applied to the *on-topic* references that were identified following title and abstract screening of the comprehensive search results published on June 22, 2017.

Systematic reviews typically describe the study eligibility criteria in the form of PECO statements or a modified framework. PECO stands for Population, Exposure, Comparator and Outcome and the approach is used to formulate explicit and detailed criteria about those characteristics in the publication that should be present in order to be eligible for inclusion in the review. EPA/OPPT adopted the PECO approach to guide the inclusion/exclusion decisions during full text screening.

Inclusion and exclusion criteria were also used during the title and abstract screening, and documentation about the criteria can be found in the *Strategy for Conducting Literature Searches* document published in June 2017 along with each of the TSCA Scope documents. The list of *on-topic* references resulting from the title and abstract screening is undergoing full text screening using the criteria in the PECO statements. The overall objective of the screening process is to select the most relevant evidence for the TSCA risk evaluation. As a general rule, EPA is excluding non-English data/information sources and will translate on a case by case basis.

The inclusion and exclusion criteria for ecotoxicological data have been documented in the ECOTOX SOPs. The criteria can be found at https://cfpub.epa.gov/ecotox/help.cfm?helptabs=tab4) and in the *Strategy for Conducting Literature Searches* document published along with each of the TSCA Scope documents.

## F.1 Inclusion Criteria for Data Sources Reporting Environmental Fate Data

EPA/OPPT developed a generic PESO statement to guide the full text screening of environmental fate data sources. PESO stands for Pathways and Processes, Exposure, Setting or Scenario, and Outcomes. Subsequent versions of the PESO statement may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the inclusion criteria in the PESO statement are eligible for inclusion, considered for evaluation, and possibly included in the environmental fate assessment. On the other hand, data sources are excluded if they do not meet the criteria in the PESO statement.

EPA describes the expected exposure pathways to human receptors from consumer uses of trichloroethylene that EPA plans to include in the risk evaluation in Section 2.5.2. EPA expects that the primary route of exposure for consumers will be via inhalation. There may also be dermal exposure. Environmental fate data will not be used to further assess these exposure pathways as they are expected to occur in the indoor environment.

During problem formulation, exposure pathways to human and ecological receptors from environmental releases and waste stream associated with industrial and commercial activities will not be further analyzed in risk evaluation. For a description of the rationale behind this conclusion, see Section 2.5.3.2 and Section 2.5.3.3 . In the absence of exposure pathways for further analysis, environmental fate data will not be further evaluated. Therefore, PESO statements describing fate endpoints, associated

processes, media and exposure pathways that were considered in the development of the environmental fate assessment for trichloroethylene will not be presented.

## F.2 Inclusion Criteria for Data Sources Reporting Engineering and Occupational Exposure Data

EPA/OPPT developed a generic RESO statement to guide the full text screening of engineering and occupational exposure literature (Table_Apx F-1). RESO stands for Receptors, Exposure, Setting or Scenario, and Outcomes. Subsequent versions of the RESO statement may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the inclusion criteria specified in the RESO statement will be eligible for inclusion, considered for evaluation, and possibly included in the environmental release and occupational exposure assessments, while those that do not meet these criteria will be excluded.

The RESO statement should be used along with the engineering and occupational exposure data needs table (Table_Apx F-2) when screening the literature.

**Table_Apx F-1. Inclusion Criteria for Data Sources Reporting Engineering and Occupational Exposure Data**

| RESO Element | Evidence |
|---|---|
| **R**eceptors | • **Humans:**<br>Workers, including occupational non-users<br><br>Please refer to the conceptual models for more information about the ecological and human receptors included in the TSCA risk evaluation. |
| **E**xposure | • Worker exposure to and relevant occupational environmental releases of the chemical substance of interest<br>  ○ Dermal and inhalation exposure routes (as indicated in the conceptual model)<br>  ○ Any relevant media/pathway [list included: water, land, air, incineration, and other(s)] as indicated in the conceptual model<br><br>Please refer to the conceptual models for more information about the routes and media/pathways included in the TSCA risk evaluation. |
| **S**etting or **S**cenario | • Any occupational setting or scenario resulting in worker exposure and relevant environmental releases (includes all manufacturing, processing, use, disposal indicated in Table A-3 below except (state none excluded or list excluded uses) |
| **O**utcomes | • Quantitative estimates* of worker exposures and of relevant environmental releases from occupational settings<br>• General information and data related and relevant to the occupational estimates* |

* Metrics (e.g., mg/kg/day or mg/m$^3$ for worker exposures, kg/site/day for releases) are determined by toxicologists for worker exposures and by exposure assessors for releases; also, the Engineering Data Needs (Table_Apx F-2) provides a list of related and relevant general information.
TSCA=Toxic Substances Control Act

| Table_Apx F-2. Engineering, Environmental Release and Occupational Data Necessary to Develop the Environmental Release and Occupational Exposure Assessments | |
|---|---|
| **Objective Determined during Scoping** | **Type of Data** |
| General Engineering Assessment (may apply for either or both Occupational Exposures and / or Environmental Releases) | 1. Description of the life cycle of the chemical(s) of interest, from manufacture to end-of-life (e.g., each manufacturing, processing, or use step), and material flow between the industrial and commercial life cycle stages. {Tags: Life cycle description, Life cycle diagram}[a]<br>2. The total annual U.S. volume (lb/yr or kg/yr) of the chemical(s) of interest manufactured, imported, processed, and used; and the share of total annual manufacturing and import volume that is processed or used in each life cycle step. {Tags: Production volume, Import volume, Use volume, Percent PV} [a]<br>3. Description of processes, equipment, unit operations, and material flows and frequencies (lb/site-day or kg/site-day and days/yr; lb/site-batch and batches/yr) of the chemical(s) of interest during each industrial/ commercial life cycle step. Note: if available, include weight fractions of the chemicals (s) of interest and material flows of all associated primary chemicals (especially water). {Tags: Process description, Process material flow rate, Annual operating days, Annual batches, Weight fractions (for each of above, manufacture, import, processing, use)} [a]<br>4. Basic chemical properties relevant for assessing exposures and releases, e.g., molecular weight, normal boiling point, melting point, physical forms, and room temperature vapor pressure. {Tags: Molecular weight, Boiling point, Melting point, Physical form, Vapor pressure, Water solubility} [a]<br>5. Number of sites that manufacture, process, or use the chemical(s) of interest for each industrial/ commercial life cycle step and site locations. {Tags: Numbers of sites (manufacture, import, processing, use), Site locations} [a] |
| Occupational Exposures | 6. Description of worker activities with exposure potential during the manufacture, processing, or use of the chemical(s) of interest in each industrial/commercial life cycle stage. {Tags: Worker activities (manufacture, import, processing, use)} [a]<br>7. Potential routes of exposure (e.g., inhalation, dermal). {Tags: Routes of exposure (manufacture, import, processing, use)} [a]<br>8. Physical form of the chemical(s) of interest for each exposure route (e.g., liquid, vapor, mist) and activity. {Tags: Physical form during worker activities (manufacture, import, processing, use)} [a]<br>9. Breathing zone (personal sample) measurements of occupational exposures to the chemical(s) of interest, measured as time-weighted averages (TWAs), short-term exposures, or peak exposures in each occupational life cycle stage (or in a workplace scenario similar to an occupational life cycle stage). {Tags: PBZ measurements (manufacture, import, processing, use)} [a]<br>10. Area or stationary measurements of airborne concentrations of the chemical(s) of interest in each occupational setting and life cycle stage (or in a workplace scenario similar to the life cycle stage of interest). {Tags: Area measurements (manufacture, import, processing, use)} [a]<br>11. For solids, bulk and dust particle size characterization data. {Tags: PSD measurements (manufacture, import, processing, use)} [a]<br>12. Dermal exposure data. {Tags: Dermal measurements (manufacture, import, processing, use)}<br>13. Data needs associated with mathematical modeling (will be determined on a case-by-case basis). {Tags: Worker exposure modeling data needs (manufacture, import, processing, use)} [a]<br>14. Exposure duration (hr/day). {Tags: Worker exposure durations (manufacture, import, processing, use)} [a]<br>15. Exposure frequency (days/yr). {Tags: Worker exposure frequencies (manufacture, import, processing, use)} [a]<br>16. Number of workers who potentially handle or have exposure to the chemical(s) of interest in each occupational life cycle stage. {Tags: Numbers of workers exposed (manufacture, import, processing, use)} [a]<br>17. Personal protective equipment (PPE) types employed by the industries within scope. {Tags: Worker PPE (manufacture, import, processing, use)} [a]<br>18. Engineering controls employed to reduce occupational exposures in each occupational life cycle stage (or in a workplace scenario similar to the life cycle stage of interest), and associated data or estimates of exposure reductions. {Tags: Engineering controls (manufacture, import, processing, use), Engineering control effectiveness data} [a] |

| Table_Apx F-2. Engineering, Environmental Release and Occupational Data Necessary to Develop the Environmental Release and Occupational Exposure Assessments | |
|---|---|
| **Objective Determined during Scoping** | **Type of Data** |
| Environmental Releases | 19. Description of relevant sources of potential environmental releases, including cleaning of residues from process equipment and transport containers, involved during the manufacture, processing, or use of the chemical(s) of interest in each life cycle stage. {Tags: Release sources (manufacture, import, processing, use)} [a]<br>20. Estimated mass (lb or kg) of the chemical(s) of interest released from industrial and commercial sites to relevant environmental medium (water) and treatment and disposal methods (POTW), including releases per site and aggregated over all sites (annual release rates, daily release rates) {Tags: Release rates (manufacture, import, processing, use)} [a]<br>21. Relevant release or emission factors. {Tags: Emission factors (manufacture, import, processing, use)} [a]<br>22. Number of release days per year. {Tags: Release frequencies (manufacture, import, processing, use)} [a]<br>23. Data needs associated with mathematical modeling (will be determined on a case-by-case basis). {Tags: Release modeling data needs (manufacture, import, processing, use)} [a]<br>24. Waste treatment methods and pollution control devices employed by the industries within scope and associated data on release/emission reductions. {Tags: Treatment/ emission controls (manufacture, import, processing, use), Treatment/ emission controls removal/ effectiveness data} [a] |

**Notes:**

[a] These are the tags included in the full text screening form. The screener makes a selection from these specific tags, which describe more specific types of data or information.

**Abbreviations:**

hr=Hour
kg=Kilogram(s)
lb=Pound(s)
yr=Year
PV=Production Volume
PBZ= Personal Breathing Zone
POTW=Publicly Owned Treatment Works
PPE=Personal Protective Equipment
PSD=Particle Size Distribution
TWA=Time-Weighted Average

## F.3 Inclusion Criteria for Data Sources Reporting Exposure Data on Consumers and Ecological Receptors

EPA/OPPT developed PECO statements to guide the full text screening of exposure data/information for human (i.e., consumers potentially exposure or susceptible subpopulations) and ecological receptors. Subsequent versions of the PECO statements may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the inclusion criteria in the PECO statement are eligible for inclusion, considered for evaluation, and possibly included in the exposure assessment. On the other hand, data sources are excluded if they do not meet the criteria in the PECO statement. The TCE-specific PECO is provided in Table_Apx F-3.

| Table_Apx F-3. Inclusion Criteria for the Data Sources Reporting Trichloroethylene Exposure Data on Consumers and Ecological Receptors | |
|---|---|
| **PECO Element** | **Evidence** |
| **P**opulation | **Human:** Consumers (i.e., receptors who use a product directly) and bystanders (i.e., receptors who are non-product users that are incidentally exposed to the product or article), including |

| | |
|---|---|
| | PESS such as infants, children, pregnant women, lactating women, women of child bearing age, and high-end consumers |
| | **Ecological:** Aquatic species, aquatic plants |
| **E**xposure | **Expected Primary Exposure Sources, Pathways, Routes:** *See Figures 2-3 and 2-4*<br>• Sources: Consumer uses in the home producing releases of TCE to air and dermal contact; industrial and commercial activities producing releases to surface water<br>• Pathways: Indoor air and dermal contact with TCE in consumer products; surface water<br>• Routes of Exposure: Inhalation via indoor air (consumer and bystander populations) and dermal exposure via direct contact with consumer products containing TCE; surface water |
| **C**omparator (Scenario) | **Human:** Consumer and bystander exposure via use of TCE-containing consumer products in the home |
| | **Ecological:** Aquatic species and plants exposed via releases to or presence in surface water |
| **O**utcomes for Exposure Concentration or Dose | **Human:** Acute, subchronic, and/or chronic external dose estimates (mg/kg/day); acute, subchronic, and/or chronic air concentration estimates (µg/$m^3$, mg/$m^3$). Both external potential dose and internal dose based on biomonitoring and reverse dosimetry mg/kg/day will be considered. |
| | **Ecological:** A wide range of ecological receptors will be considered (range depending on available ecotoxicity data) using surface water concentration(s) (µg/l, mg/L) |
| **Abbreviations:**<br>Kg=Kilogram(s)<br>Mg=Milligram(s)<br>$M^3$=Cubic meter<br>L=Liter(s) | |

## F.4 Inclusion Criteria for Data Sources Reporting Human Health Hazards

EPA/OPPT developed a TCE-specific PECO statement to guide the full text screening of the human health hazard literature. Subsequent versions of the PECOs may be produced throughout the process of screening and evaluating data for the chemicals undergoing TSCA risk evaluation. Studies that comply with the criteria specified in the PECO statement will be eligible for inclusion, considered for evaluation, and possibly included in the human health hazard assessment, while those that do not meet these criteria will be excluded according to the exclusion criteria.

In general, the PECO statements were based on (1) information accompanying the TSCA Scope document, and (2) preliminary review of the health effects literature from authoritative sources cited in the TSCA Scope documents. When applicable, these authoritative sources (e.g., IRIS assessments, EPA/OPPT's Work Plan Problem Formulations or risk assessments) will serve as starting points to identify PECO-relevant studies.

**Table_Apx F-4. Inclusion and Exclusion Criteria for the Data Sources Reporting Human Health Hazards Related to TCE Exposure[a]**

| PECO Element | Evidence Stream | Papers/Features Included | Papers/Features Excluded |
|---|---|---|---|
| **Population** | *Human* | • Any population<br>• All lifestages<br>• Study designs:<br>  ○ Controlled exposure, cohort, case-control, cross-sectional, case-crossover for all endpoints<br>  ○ Case studies, case series and ecological studies only related to deaths and respiratory distress | • Case studies, case series and ecological studies for all endpoints ***other than*** death and respiratory distress |
| | *Animal* | • All non-human whole-organism mammalian species<br>• All lifestages | • Non-mammalian species |
| | *Mechanistic/ Alternative Methods* | • Human or animal cells (including nonmammalian model systems), tissues, or biochemical reactions (e.g., ligand binding assays) with *in vitro* exposure regimens; bioinformatics pathways of disease analysis; or high throughput screening data. | |
| ***Exposure*** | *Human* | • Exposure based on administered dose or concentration of TCE, biomonitoring data (e.g., urine, blood or other specimens), environmental or occupational-setting monitoring data (e.g., air, water levels), job title or residence<br>• Primary metabolites of interest (e.g., trichloroacetic acid) as identified in biomonitoring studies<br>• Exposure identified as ***or presumed to be*** from oral, dermal, inhalation routes<br>• Any number of exposure groups<br>• Quantitative, semi-quantitative or qualitative estimates of exposure<br>• Exposures to multiple chemicals/mixtures only if TCE or related metabolites were independently measured and analyzed | • Route of exposure ***not*** by inhalation, oral or dermal type (e.g., intraperitoneal, injection)<br>• Multiple chemical/mixture exposures with no independent measurement of or exposure to TCE (or related metabolite) |
| | *Animal* | • A minimum of 2 quantitative dose or concentration levels of TCE plus a negative control group [a]<br>• Acute, subchronic, chronic exposure from oral, dermal, inhalation routes<br>• Exposure to TCE only (no chemical mixtures)<br>• Quantitative and/or qualitative relative/rank-order estimates of exposure | • Only 1 quantitative dose or concentration level in addition to the control [a]<br>• Route of exposure ***not*** by inhalation, oral or dermal type (e.g., intraperitoneal, injection)<br>• No duration of exposure stated<br>• Exposure to TCE in a chemical mixture |
| | *Mechanistic/ Alternative Methods* | • A minimum of 2 quantitative concentrations of TCE plus a negative control group [a]<br>• Exposure to TCE only (no chemical mixtures) | • Only 1 quantitative dose or concentration level in addition to the control [a]<br>• Exposure to TCE in a chemical mixture |
| **Comparator** | *Human* | • A comparison population [not exposed, | • No comparison population for |

**Table_Apx F-4. Inclusion and Exclusion Criteria for the Data Sources Reporting Human Health Hazards Related to TCE Exposure[a]**

| | | | |
|---|---|---|---|
| | | exposed to lower levels, exposed below detection] for endpoints ***other than*** death or respiratory distress<br>• Any or no comparison for exposures associated with death or respiratory distress | endpoints other than death or respiratory distress from acute exposure |
| | *Animal* | • Negative controls that are vehicle-only treatment and/or no treatment | • Negative controls ***other than*** vehicle-only treatment or no treatment |
| | *Mechanistic/ Alternative Methods* | • Negative controls that are vehicle-only treatment and/or no treatment | • Negative controls ***other than*** vehicle-only treatment or no treatment |
| **Outcome** | *Human* | • Endpoints described in the methylene chloride scope document [b]:<br>o Acute toxicity<br>o Liver toxicity<br>o Kidney toxicity<br>o Reproductive/developmental Toxicity<br>o Neurotoxicity<br>o Immunotoxicity<br>o Sensitization<br>o Cancer<br>• Other endpoints [c] | |
| | *Animal* | | |
| | *Mechanistic/ Alternative Methods* | • All data that may inform mechanisms of developmental toxicity | • Data that inform mechanisms of toxicity for endpoints ***other than*** developmental toxicity |
| **General Considerations** | | **Papers/Features Included** | **Papers/Features Excluded** |
| | | • Written in English [d]<br>• Reports primary data or meta-analysis [a]<br>• Full-text available<br>• Reports both TCE exposure ***and*** a health outcome or mechanism of action | • Not written in English [d]<br>• Reports secondary data (e.g., review papers) [a]<br>• No full-text available (e.g., only a study description/abstract, out-of-print text)<br>• Reports a TCE-related exposure ***or*** a health outcome/mechanism of action, but not both (e.g. incidence, prevalence report) |

[a] Some of the studies that are excluded based on the PECO statement may be considered later during the systematic review process. For TCE, EPA will evaluate studies related to susceptibility and may evaluate, toxicokinetics and physiologically based pharmacokinetic models after other data (e.g., human and animal data identifying adverse health outcomes) are reviewed. EPA may also review other data as needed (e.g., animal studies using one concentration, review papers).
[b] EPA will review key and supporting studies in the IRIS assessment that were considered in the dose-response assessment for non-cancer and cancer endpoints as well as studies published after the IRIS assessment.
[c] EPA may screen for hazards other than those listed in the scope document if they were identified in the updated literature search that accompanied the scope document.
[d] EPA may translate studies as needed.

# Appendix G List of Retracted Papers

The following reference was retracted by the journal:

HERO ID: 647007
Zhao, B; Zhu, L. (2006). Solubilization of DNAPLs by mixed surfactant: synergism and solubilization capacity. J Hazard Mater 136: 513-519. http://dx.doi.org/10.1016/j.jhazmat.2005.08.03

United States
Environmental Protection Agency

EPA Document# 740-P1-8001
Office of Chemical Safety and
Pollution Prevention

# APPLICATION OF SYSTEMATIC REVIEW IN TSCA RISK EVALUATIONS

***MAY 2018***

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# ACKNOWLEDGEMENTS

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**Docket**

This document can be found in EPA docket number EPA-HQ-OPPT-2018-0210. A copy of the document is also placed in the following dockets:

| Chemical Substance | Docket Number |
|---|---|
| Asbestos | EPA-HQ-OPPT-2016-0736 |
| 1-Bromopropane (1-BP) | EPA-HQ-OPPT-2016-0741 |
| Carbon Tetrachloride ($CCl_4$) | EPA-HQ-OPPT-2016-0733 |
| 1,4-Dioxane | EPA-HQ-OPPT-2016-0723 |
| Cyclic Aliphatic Bromide Cluster (HBCD) | EPA-HQ-OPPT-2016-0735 |
| Methylene Chloride | EPA-HQ-OPPT-2016-0742 |
| N-Methylpyrolidone (NMP) | EPA-HQ-OPPT-2016-0743 |
| Perchloroethylene (PERC) | EPA-HQ-OPPT-2016-0732 |
| Pigment Violet 29 (Anthra[2,1,9-def:6,5,10-d'e'f']diisoquinoline-1,3,8,10(2H,9H)-tetrone; PV29) | EPA-HQ-OPPT-2016-0725 |
| Trichloroethylene (TCE) | EPA-HQ-OPPT-2016-0737 |

# 1 PURPOSE OF THE DOCUMENT

The U.S. EPA's Office of Pollution Prevention and Toxics (EPA/OPPT) generally intends to apply systematic review principles[1] in the development of risk evaluations under the amended Toxic Substances Control Act (TSCA). This internal guidance sets out general principles to guide EPA's application of systematic review in the risk evaluation process for the first ten chemicals (Table 3-2), which EPA/OPPT initiated on December 19, 2016, as well as future evaluations. Integrating systematic review principles into the TSCA risk evaluation process is critical to develop transparent, reproducible and scientifically credible risk evaluations.

EPA/OPPT plans to implement a structured process of identifying, evaluating and integrating evidence for both the hazard and exposure assessments developed during the TSCA risk evaluation process. It is expected that new approaches and/or methods will be developed to address specific assessment needs for the relatively large and diverse chemical space under TSCA. Thus, EPA/OPPT expects to document the progress of implementing systematic review in the draft risk evaluations and through revisions of this document and publication of supplemental documents. EPA invites the public to provide input on this document at www.regulations.gov, docket# EPA-HQ-OPPT-2018-0210. The public can also contact EPA about questions about this document at TSCA-systematicreview@epa.gov.

Supplemental documents, released in June 2017, already document the data collection and screening activities for the first ten chemicals (Table 3-2). This document is the next supplemental publication containing details about the general principles that will guide EPA/OPPT in carrying out the systematic review process along with the strategy for assessing data quality that EPA/OPPT generally plans to use for the TSCA risk evaluations. This document only provides the general expectations for evidence synthesis and integration. Additional details on the approach for the evidence synthesis and integration will be included with the publication of the draft TSCA risk evaluations. Figure 1-1 displays a general roadmap for implementing systematic review in the TSCA risk evaluation process for the first ten chemicals. Ultimately, the goal is to establish an efficient systematic review process that generates high-quality, fit-for-purpose risk evaluations that rely on the best available science and the weight of the scientific evidence within the context of TSCA.

The information and procedures set forth in this document are intended as a technical resource to those conducting TSCA risk evaluations for existing chemicals. This internal guidance does not constitute rulemaking by the U.S. EPA, and cannot be relied on to create a substantive or procedural right enforceable by any party in litigation with the United States. Non-mandatory language such as "should" provides recommendations and does not impose any legally binding requirements. Similarly, statements about what EPA expects or intends to do reflect general principles to guide EPA's activities and not judgments or determinations as to what EPA will do

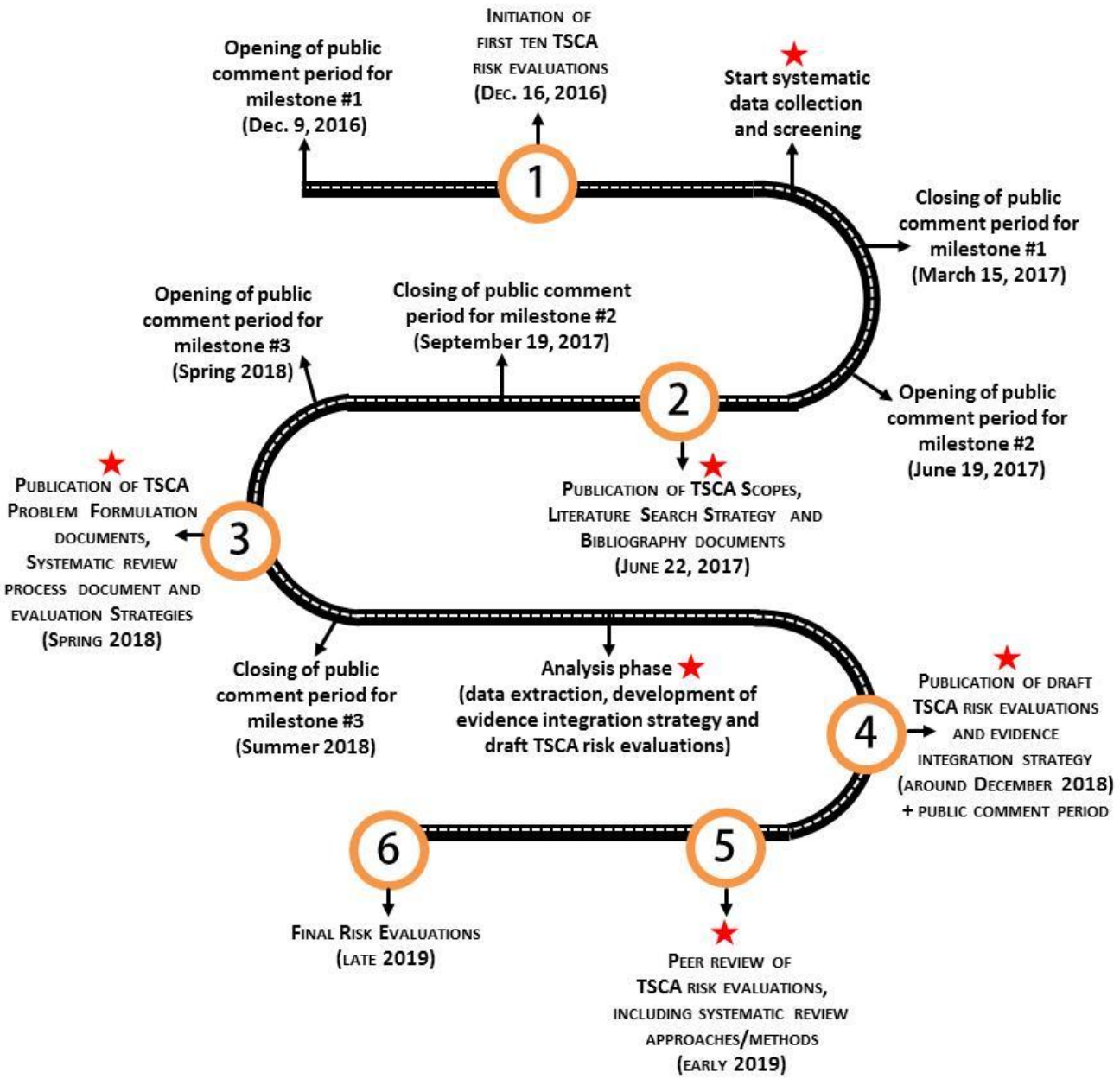
[1] This document refers to "*principle*" as a key concept or element guiding the series of steps (or *processes*) to achieve incorporation of systematic review approaches and/or methods in TSCA risk evaluations.

in any particular case. This document is not necessarily applicable to risk assessments developed to support other EPA's statutes or programs.

EPA expects to make changes to this living document at any time and therefore this document may be revised periodically. EPA welcomes public input on this document at any time.

Reference herein to any specific commercial products, process, or service by trade name, trademark, manufacturer, or otherwise, does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government.

**Figure 1-1. Road Map for Implementing Systematic Review for the First Ten TSCA Risk Evaluations**




**Notes for Figure 1-1:**

- Important milestones are numbered and depicted in upper case letters. Although dates would be different, milestones are also applicable for the future TSCA risk evaluations.
- Star symbols are next to those activities or technical documents that are related to the implementation of systematic review.
- Activities between milestones #3 and #6 show estimated timelines that are subject to change.
- There are multiple points in the process for public input.

# 2 SCOPING AND PROBLEM FORMULATION: ANALYTICAL FRAMEWORK GUIDING SYSTEMATIC REVIEW IN *TSCA* RISK EVALUATIONS

Scoping and problem formulation are important steps in providing the analytical framework for the systematic review efforts supporting the TSCA risk evaluations. Scoping and problem formulation are the first stages of the TSCA risk evaluation process and are intended to convey EPA/OPPT's expectations regarding the overall scope, level of detail, and approach for the risk evaluation. This initial planning effort is critical to developing clear objectives and assessment questions to support quantitative risk analyses, and to defining the steps that EPA/OPPT expects to take to conduct the different components of the risk evaluation. Scoping and problem formulation helps shape the systematic review approaches and/or methods that will be used to identify, evaluate, analyze, and integrate evidence. For example, the outcomes of scoping and problem formulation are used to tailor a data search and screening strategy (including eligibility criteria) to identify relevant data and information while winnowing out those that are irrelevant for the risk evaluation.

TSCA requires EPA to publish the scope for any risk evaluation it will conduct. Further, TSCA requires the scope to include the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations[2] that EPA expects to consider. To communicate and visually convey the relationships between these components, the final rule *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act* (40 CFR Part 702) requires including a conceptual model and an analysis plan for each risk evaluation. Under EPA's risk assessment guidance, the conceptual model and the analysis plan are the outcomes of conducting problem formulation (U.S. EPA, 2014, 1998, 1992).

Through the conceptual model and the analysis plan, problem formulation describes the exposure pathways, receptors and health endpoints that EPA/OPPT expects to consider in the risk evaluations (U.S. EPA, 2014, 1998, 1992). The conceptual model(s) illustrate the exposure pathways, receptor populations and effects that EPA expects to consider in the risk evaluation. An analysis plan presents the proposed approach for the risk evaluation. Hence, problem formulation has essentially the same function as scoping under the amended TSCA, thereby aligning the requirements of the scope for a TSCA risk evaluation with the components of a problem formulation in EPA guidance (U.S. EPA, 2014, 1998, 1992).

[2] Potentially exposed or susceptible subpopulation means a group of individuals within the general population identified by the Agency who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly (15 U.S.C. 2602 or 40 CFR Part 702.33).

With this context in mind, the systematic review activities for the TSCA risk evaluations will be guided by the results of problem formulation, as documented in the TSCA scope documents[3]. It is expected that the systematic review principles and general processes remain relatively the same across risk evaluations. However, systematic review methods and/or approaches, including criteria, will be customized, as necessary, to meet the assessment needs of each risk evaluation. Details about the fit-for-purpose systematic review methods and/or approaches will be in the draft risk evaluation and its supporting documents.

EPA/OPPT is currently implementing systematic review methods and/or approaches in a step-wise fashion in parallel with conducting the phases of the risk evaluation. The phased approach is necessary given the statutory timeframes imposed on EPA. Each of the steps of systematic review is being published in parallel, as supplemental documents, along with steps in the risk evaluation. EPA/OPPT may consolidate the information made available through the various supplemental documents in the future.

# 3 INTEGRATION OF SYSTEMATIC REVIEW PRINCIPLES INTO TSCA RISK EVALUATIONS

The Agency described systematic review in the preamble to the final rule *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act*, 82 FR 33726 (July 20, 2017), and in the preamble to the proposed rule, 82 FR 7562 (Jan. 19, 2017). The following two paragraphs are an excerpt from the final rule.

> As defined by the Institute of Medicine, systematic review "is *a scientific investigation that focuses on a specific question and uses explicit, pre-specified scientific methods to identify, select, assess, and summarize the findings of similar but separate studies*" (National Academy of Sciences, 2017). The goal of systematic review methods is to ensure that the review is complete, unbiased, reproducible, and transparent (Bilotta et al., 2014).
>
> The principles of systematic review have been well developed in the context of evidence-based medicine (e.g., evaluating efficacy in clinical trials) (Higgins and Green, 2011) and are being adapted for use across a more diverse array of systematic review questions, through the use of a variety of computational tools. For instance, the National Academies' National Research Council (NRC) has encouraged EPA to move towards systematic review processes to enhance the transparency of scientific literature review that support chemical-specific risk assessments to inform regulatory decision making (Process et al., 2014). Key elements of systematic review include:
>
> - A clearly stated set of objectives (defining the question)
> - Developing a protocol that describes the specific criteria and approaches that will

[3] TSCA problem formulation documents were developed for the first ten chemicals undergoing risk evaluation and refine the scope of the initial TSCA scope documents. They were published as an additional interim step prior to publication of the draft risk evaluations for the first ten chemicals.

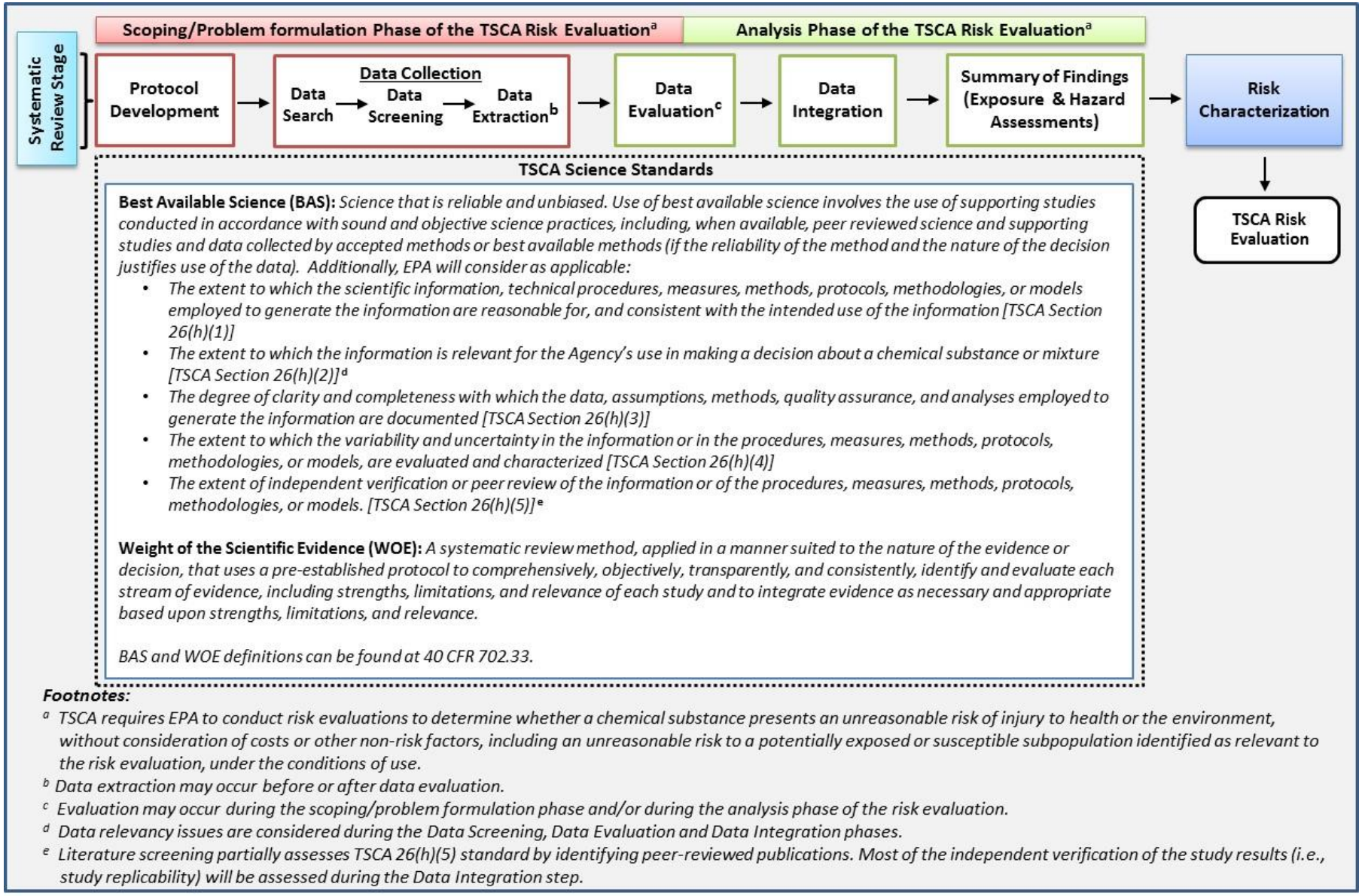
be used throughout the process
- Applying the search strategy in a literature search
- Selecting the relevant papers using predefined criteria
- Assessing the quality of the studies using predefined criteria
- Analyzing and synthesizing the data using the predefined methodology
- Interpreting the results and presenting a summary of findings

TSCA requires that EPA use data and/or information (hereinafter referred to as data/information) in a manner consistent with the best available science and that EPA base decisions on the weight of the scientific evidence. To meet the TSCA science standards, EPA/OPPT will be guided by the systematic review process described in Figure 3-1. This process complements the risk evaluation process in that the data collection, data evaluation and data integration stages of the systematic review process are used to develop the exposure and hazard assessments. As risk is a function of exposure and hazard, the exposure and hazard assessments are combined to support the integrative risk characterization, which ultimately supports the risk determination.

Although not shown in Figure 3-1, iteration is a natural component of the systematic review and risk evaluation processes. There could be different reasons triggering iteration such as the failure of retrieving relevant data and information after the initial search and screening activities, which would require repeating the data collection stage of the systematic review process, or refinements to the initial search, screening and extraction strategies.

A short description of each stage of the systematic review process is provided in sections 3.1 through 3.4. Table 3-1 describes EPA's general expectations for the planning, execution and assessment activities related to each stage of the systematic review process. The activities are general enough to be applied to multiple data/information streams supporting the TSCA risk evaluations.

**Figure 3-1. TSCA Systematic Review Process[4]**




[4] Diagram depicts systematic review process to guide the first ten TSCA risk evaluations. It is anticipated that the same basic process will be used to guide future risk evaluations with some potential refinements reflecting efficiencies and other adjustments adopted as EPA/OPPT gains experience in implementing systematic review methods and/or approaches to support risk evaluations within statutory deadlines (e.g., aspects of protocol development would be better defined prior to starting scoping/problem formulation).

| Table 3-1. Planning, Execution and Assessment Activities Supporting the Systematic Review Process of TSCA Risk Evaluations | |
|---|---|
| **Phase** | **Process Steps** |
| **Data Search[a]** | |
| **Planning phase** | • Define specific objectives for the searches.<br>• Develop search strategies. This includes describing all information sources to be searched, specification of search strings for each data/information source, search instructions, date range, filters, limits or other details to ensure reproducibility of search by an independent party. |
| **Execution phase** | • Execute search based on the approach described in the Literature Search Strategy documents.<br>• Store search results.<br>• Document date(s) the searches were conducted.<br>• Document refinements to the protocol as part of the iterative process of improving the literature search strategy.<br>• Finalize files using a bibliographic management tool and other documentation related to the literature search protocol. |
| **Assessment phase**<br>**(Quality Assurance (QA)/ Quality Control (QC))** | • Describe the mechanisms for QA including management review processes.<br>• Describe the mechanisms for QC including data quality testing procedures. For example, demonstration that the search strategy retrieves a set of known relevant records. |
| **Data Screening (Title/Abstract) [a]** | |
| **Planning phase** | • Develop/refine inclusion/exclusion criteria for the title/abstract screening.<br>• Develop/refine screening categories ("tags") to categorize information.<br>• Develop pilot plan to test criteria for the title/abstract screening and tagging.<br>• Describe strategy used to identify and resolve screening conflicts.<br>• If natural language processing or other electronic processing is used, describe the methodology and specify the terms to be used for electronic screening and how groups of references will be reviewed. |
| **Execution phase** | • Conduct pilot study to test the criteria for title/abstract screening and tagging and conflict resolution strategy. Unless major changes are made, piloting may only need to be conducted once and not after each update.<br>• Refine the screening and tagging criteria before application.<br>• Conduct title/abstract screening and tagging for the remaining references.<br>• Document date(s) the screening was conducted and who conducted the screening. |
| **Assessment phase**<br>**(QA/QC)** | • Describe the mechanisms for QA including management review processes.<br>• Describe the mechanisms for QC including the following:<br>– Number of screeners and their technical skill background<br>– Process for pilot testing the clarity of inclusion and exclusion criteria on a set of studies<br>– Process for comparing results and resolving screening conflicts between screeners |

| Table 3-1. Planning, Execution and Assessment Activities Supporting the Systematic Review Process of TSCA Risk Evaluations | |
|---|---|
| **Phase** | **Process Steps** |
| **Data Screening (Full Text)** [a] | |
| **Planning phase** | • Develop/refine inclusion/exclusion criteria for the full text screening.<br>• Develop/refine screening categories ("tags") to categorize information.<br>• Develop pilot plan to test criteria for the full text data screening and tagging.<br>• Describe strategy used to identify and resolve screening conflicts.<br>• If natural language processing or other electronic processing is used, describe the methodology and specify the terms to be used for electronic screening and how groups of references will be reviewed. |
| **Execution phase** | • Conduct pilot study to test the criteria for full text screening and tagging and conflict resolution strategy. Unless major changes are made, piloting may only need to be conducted once and not after each update.<br>• Refine the screening and tagging criteria before application.<br>• Conduct full text screening and tagging for the remaining references.<br>• Document date(s) the screening was conducted and who conducted the screening. |
| **Assessment phase (QA/QC)** | • Describe the mechanisms for QA including management review processes.<br>• Describe the mechanisms for QC including the following:<br>– Number of screeners and their technical skill background<br>– Process for pilot testing the clarity of inclusion and exclusion criteria on a set of studies<br>– Process for comparing results and resolving screening conflicts between screeners |
| **Data Extraction**[a] | |
| **Planning Phase** | • Develop extraction templates preferably from existing examples (e.g., graphical or tabular displays) that capture specific attributes or data elements relevant for disciplines within the risk assessment. Templates should be designed to facilitate evaluation of the data and their synthesis with minimal reference to the original reference. Data/information will need to be tracked with unique identifies.<br>• Use an extraction process that ensures access to the extracted information by EPA and the public.<br>• Develop instructions and decision rules (e.g., what to extract/not extract under certain conditions) to be included in the template form to facilitate data extraction.<br>• Specify number and expertise of reviewers involved in the data extraction process.<br>• Select initial set of citations for training to promote data extraction in a consistent manner across reviewers.<br>• Identify tool(s) for managing extracted data and decisions (e.g., spreadsheet, database). |
| **Execution Phase** | • Conduct pilot study to test the extraction process and conflict resolution strategy. Unless major changes are made, piloting may only need to be conducted once and not after each update.<br>• Extract data/information using pre-defined templates. |
| **Assessment phase (QA/QC)** | • Describe the mechanisms for QA for data extraction process including management review processes.<br>• Describe the mechanisms for QC including the following:<br>– Number of data extraction staff and their technical skill background<br>– Process for pilot testing the data extraction and conflict resolution |

| Table 3-1. Planning, Execution and Assessment Activities Supporting the Systematic Review Process of TSCA Risk Evaluations | |
|---|---|
| **Phase** | **Process Steps** |
| **Data Evaluation** | |
| **Planning Phase** | • Develop/refine evaluation strategy to assess quality of studies.<br>• For large databases, develop prioritization strategy about how studies will be reviewed.<br>• Develop instructions and decision rules for the evaluation process.<br>• Specify number and expertise of reviewers involved in the data evaluation.<br>• Select initial set of citations for training to promote data evaluation in a consistent manner across reviewers.<br>• Identify tool(s) for managing evaluated data and decisions (e.g., spreadsheet, database). This should be ideally designed in a way that the tools facilitate the synthesis and integration of data in the subsequent phases of systematic review. |
| **Execution Phase** | • Conduct pilot study to test the evaluation criteria conflict resolution strategy. Unless major changes are made, piloting may only need to be conducted once and not after each update.<br>• Evaluate and document the quality of the study based on the pre-defined criteria documented in the protocol. |
| **Assessment phase (QA/QC)** | • Describe the mechanisms for QA including management review processes.<br>• Describe the mechanisms for QC including the following:<br>– Number of staff evaluating data/information sources and their technical skill background<br>– Process for pilot testing the data evaluation process<br>– Process for conflict resolution |
| **Data Integration Using the Weight of the Scientific Evidence** | |
| **Planning Phase** | • Develop and document strategy for analyzing and summarizing data/information across studies within each evidence stream, including strengths, limitations and relevance of the evidence.<br>• Develop and document strategy for weighing and integrating evidence across evidence streams, including strengths, limitations and relevance of the evidence. |
| **Execution Phase** | • Conduct and document the analysis and synthesis of the evidence.<br>• Document the conclusions within each evidence stream.<br>• Weigh and document results across evidence streams to develop weight of evidence conclusions.<br>• Document any professional judgment, including underlying assumptions that are used to support the risk evaluation. |
| **Assessment phase (QA/QC)** | • Specify process for assuring quality of the data being analyzed, synthesized and integrated. |

**Notes:**

[a] EPA/OPPT uses the ECOTOX infrastructure for the data searching, screening and extractions of ecological effects data to support the TSCA risk evaluations. The planning, execution and assessment phases for the data search, screening and extraction phases are comparable to those outlined in Table 3-1 for the other data/information streams (i.e., exposure, fate, animal toxicology, *in vitro*, and epidemiological data).

**Abbreviations:**

TSCA=Toxic Substances Control Act
EPA/OPPT=Environmental Protection Agency, Office of Pollution Prevention and Toxics
ECOTOX=ECOTOXicology knowledgebase
QA/QC=Quality Assurance/Quality Control
HERO=Health and Environmental Research Online

## 3.1 Protocol Development

*Protocol Development* is intended to pre-specify the criteria, approaches and/or methods for data collection, data evaluation and data integration. It is important to plan the systematic review approaches and methods in advance to reduce the risk of introducing bias into the risk evaluation process.

TSCA requirements and the results of scoping/problem formulation (i.e., conceptual model(s), analysis plan) frame the specific scientific risk assessment questions to be addressed in each TSCA risk evaluation. Likewise, the statutory requirements and scoping/problem formulation inform how the data are searched, evaluated and integrated in the assessment. The TSCA Scope and Problem Formulation documents for the first ten risk evaluations contain the analytical framework guiding the systematic review process and should be consulted to understand the context of this document.

The timeframe for development of the TSCA Scope documents has been very compressed. The first ten chemical substances were not subject to prioritization, the process through which EPA expects to collect and screen much of the relevant information about chemical substances that will be subject to the risk evaluation process. As a result, EPA had limited ability to develop a protocol document detailing the systematic review approaches and/or methods prior to the initiation of the risk evaluation process for the first ten chemical substances. For these reasons, the protocol development is staged in phases while conducting the assessment work.

Figure 1-1 and Table 3-2 provide information about those components of the systematic review process released to the public and those that are in the pipeline for development (e.g., data integration). Data integration activities for the first ten TSCA risk evaluation are anticipated to occur after the TSCA Problem Formulation documents are released (Figure 1-1). EPA/OPPT will provide further details about the data integration strategy along with the publication of the draft TSCA risk evaluations.

## 3.2 Data Collection

### 3.2.1 Data Search

Data are collected under a defined literature search strategy that is developed to fit the needs of the different disciplines supporting the risk evaluation (e.g., physical/chemical properties, environmental fate, engineering processes across the full life cycle of the chemical substance, exposure, human health hazard, environmental hazard). This step includes developing strategies for searching and identifying relevant data that are published in public databases (e.g., PubMed) and other sources containing unpublished or published data. The process steps are generally described in Table 3-1, which lists the planning, execution and assessment activities supporting the data search activities for the TSCA risk evaluation process.

Table 3-2 provides web links to the *Strategy for Conducting Literature Searches* and *Bibliography* documents published in June 2017 along with each of the first ten TSCA Scope documents. EPA/OPPT's initial methods for identifying, compiling, and screening publicly available information are described in the *Strategy for Conducting Literature Searches* supporting each of the TSCA Scope documents for the first ten chemicals. The literature search and screening strategy already published will be used for future risk evaluations.

**Table 3-2. Supplemental Documents on Systematic Review Activities Published with the TSCA Scope Documents on June 22, 2017**

| Chemical Name | CASRN | Docket Number | Web link to TSCA Scope, Literature Search Strategy and Bibliography Documents |
|---|---|---|---|
| Asbestos | 1332-21-4 | EPA-HQ-OPPT-2016-0736 | Link |
| 1-Bromopropane (1-BP) | 106-94-5 | EPA-HQ-OPPT-2016-0741 | Link |
| Carbon Tetrachloride ($CCl_4$) | 56-23-5 | EPA-HQ-OPPT-2016-0733 | Link |
| 1,4-Dioxane | 123-91-1 | EPA-HQ-OPPT-2016-0723 | Link |
| Cyclic Aliphatic Bromide Cluster (HBCD) | 25637-99-4; 3194-55-6; and 3194-57-8 | EPA-HQ-OPPT-2016-0735 | Link |
| Methylene Chloride | 75-09-2 | EPA-HQ-OPPT-2016-0742 | Link |
| N-Methylpyrolidone (NMP) | 872-50-4 | EPA-HQ-OPPT-2016-0743 | Link |
| Perchloroethylene (PERC) | 127-18-4 | EPA-HQ-OPPT-2016-0732 | Link |
| Pigment Violet 29 (Anthra[2,1,9-def:6,5,10-d'e'f']diisoquinoline-1,3,8,10(2H,9H)-tetrone; PV29) | 81-33-4 | EPA-HQ-OPPT-2016-0725 | Link |
| Trichloroethylene (TCE) | 79-01-6 | EPA-HQ-OPPT-2016-0737 | Link |

EPA/OPPT uses the infrastructure of the ECOTOXicology knowledgebase (U.S. EPA, 2018a) to identify single chemical toxicity data for aquatic life and terrestrial life. It uses a comprehensive chemical-specific literature search of the open literature that is conducted according to Standard Operating Procedures (SOPs)[5], including specific SOPs to fit the needs of the TSCA risk

[5] The ECOTOX SOPs can be found at https://cfpub.epa.gov/ecotox/help.cfm?helptabs=tab4.

evaluations[6]. The search strategy is revised on a regular basis to ensure that high quality ecological effects data are retrieved to support the risk assessment needs of various EPA programs. Due to its well-established methods to gather high quality data, ECOTOX processes and data are widely accepted and used by a variety of domestic and international organizations and researchers. The ECOTOX literature search strategy is documented in the *Strategy for Conducting Literature Searches* documents for each of the ten TSCA risk evaluations (Table 3-2).

EPA/OPPT also plans to search its internal databases for data and information submitted under TSCA (e.g., unpublished industry data). EPA will consider these data in the risk evaluations where relevant and whether or not they are claimed as confidential business information (CBI). If data/information are CBI, EPA/OPPT plans to use it in a manner that protects the confidentiality of the information from public disclosure.

The results of the literature search are entered into the EPA's Health Environmental Research Online (HERO) database[7] where the literature results are stored in chemical-specific pages. HERO also allows categorizing and sorting references by pre-defined topic areas. EPA/OPPT anticipates that the HERO project pages will be accessible to the public by the publication date of the draft risk evaluations.

EPA/OPPT plans to consider relevant data/information that are submitted by the public or peer reviewers. EPA/OPPT may conduct targeted supplemental searches to support the analytical approaches and/or methods in the TSCA risk evaluation (e.g., to locate specific information for exposure modeling) or identify new data/information published after the date limits of the initial search. In addition, retracted studies may be also identified during the process of developing the risk evaluations. EPA/OPPT does not plan to use retracted studies in the TSCA risk evaluations.

#### 3.2.1.1 *Summary of the Literature Search Strategy for the First Ten TSCA Risk Evaluations*

EPA/OPPT conducted chemical-specific searches for data and information on: physical and chemical properties; environmental fate and transport; conditions of use information; environmental and human exposures, including potentially exposed or susceptible subpopulations; ecological and human health hazard, including potentially exposed or susceptible subpopulations.

EPA/OPPT designed its initial data search to be broad enough to capture a comprehensive set of sources containing data/information potentially relevant to the risk evaluation process. Generally, the search was conducted on a wide range of data/information sources, including

[6] The ECOTOX SOPs for TSCA work can be found at https://cfpub.epa.gov/ecotox/blackbox/help/OPPTRADCodingGuidelinesSOP.pdf and https://cfpub.epa.gov/ecotox/blackbox/help/OPPTRADReportsSOP.pdf.

[7] HERO=Health and Environmental Research Online, https://hero.epa.gov/hero/index.cfm/content/home

but not limited to peer-reviewed and grey literature[8]. When available, EPA/OPPT relied on the search strategies from recent assessments (e.g., EPA Integrated Risk Information System (IRIS) assessments) as a starting point to identify relevant references and supplemented these searches to identify relevant information published after the end date of the previous search to capture more recent literature. For human health hazards, the literature search strategy was designed to identify relevant data/information in favor (e.g., positive study) or against (e.g., negative study) a given hypothesis within the context of the assessment question(s) being evaluated in the risk evaluation.

Following the initial search of data for the first ten risk evaluations, EPA/OPPT searched for data submitted to EPA under TSCA sections 4, 5, 8(e), and 8(d), as well as for your information (FYI) submissions, to find additional data relevant to human health and environmental hazard, exposure, fate, engineering, physical-chemical properties, and TSCA conditions of use. Searches were conducted of CBI and non-CBI databases followed by a duplicate identification step. Many of the non-CBI data submissions were captured in the initial search published on June 22, 2017, but some were found and added to the pool of new references to undergo data screening.

### 3.2.2 Data Screening

EPA/OPPT develops and applies inclusion and exclusion criteria during title/abstract and full text screening to identify information potentially relevant for the risk evaluation process. This step also classifies the references into useful categories (e.g., *on-topic* versus *off-topic*, human versus animal hazard) to facilitate the sorting of information through the systematic review process.

Below are examples of data characteristics, generally chemical-specific, that are used as indicators of relevance based on the scope of the assessments. These data characteristics are the basis for the development of inclusion and exclusion criteria for the title/abstract and full text screening.

- Data on environmental fate, transport, partitioning and degradation behavior across environmental media of interest.
- Data on environmental exposure of ecological receptors (i.e., aquatic and terrestrial organisms) to the chemical substance of interest and/or its degradation products and metabolites.
- Data on environmental exposure of human receptors (general population, consumers), including any potentially exposed or susceptible subpopulations, to the substance of interest and/or its degradation products and metabolites.
- Data on any setting or scenario resulting in releases of the chemical substance of interest into the natural or built environment (e.g., buildings including homes or workplaces) that

[8] *Grey literature* refers to sources of scientific information that are not formally published and distributed in peer-reviewed journal articles. These references are still valuable and consulted in the TSCA risk evaluation process. Examples of grey literature are theses and dissertations, technical reports, guideline studies, conference proceedings, publicly-available industry reports, unpublished industry data, trade association resources, and government reports.

would expose ecological (i.e., aquatic and terrestrial organisms) or human receptors (i.e., general population, and potentially exposed or susceptible subpopulation)
- Quantitative estimates of worker exposures and of environmental releases from occupational settings for the chemical of interest
- Data on human health and environmental hazards that meet minimum reporting elements (i.e., test chemical, species/organisms, effect(s), dose(s) or concentration(s), and duration).
- Data on human health hazards for potentially exposed or susceptible subpopulations.

#### 3.2.2.1 *Title/Abstract Screening*

Titles and abstracts of the retrieved literature are reviewed for relevance according to inclusion and exclusion criteria. Table 3-1 describes the planning, execution and assessment activities supporting the title/abstract screening activities for the TSCA risk evaluation process. These activities are consistent with those conducted and described in the *Strategy for Conducting Literature Searches* documents (Table 3-2).

Systematic reviews typically describe the study eligibility criteria in the form of PECO statements or a modified framework. PECO stands for Population, Exposure, Comparator and Outcome. The approach is used to formulate explicit and detailed criteria about those characteristics in the publication that should be present in order to be eligible for inclusion in the review (e.g., inclusion of studies reporting on the effects of chemical exposure to potentially exposed or susceptible subpopulations).

Each article is generally screened by two independent reviewers using specialized web-based software (i.e., DistillerSR)[9]. Screeners are assigned batches of references after conducing pilot testing. Screening forms are typically used to facilitate the screening process by asking a series of questions based on pre-determined inclusion and exclusion criteria. The screeners resolve conflicts by consensus, or consultation with an independent individual(s).

Ecological hazard references undergo a similar screening process following the ECOTOX SOPs. Search results, screening decisions and respective tags are stored electronically in the ECOTOX Knowledgebase. Please also refer to the ECOTOX SOPs[10] and the *Strategy for Conducting Literature Searches* (Table 3-2) documents to understand the screening process and criteria that are applied for the ecological hazard literature.

[9] In addition to using DistillerSR, EPA/OPPT is exploring automation and machine learning tools for data screening and prioritization activities (e.g., SWIFT-Review, SWIFT-Active Screener, Dragon, DocTER). SWIFT is an acronym for "*Sciome Workbench for Interactive Computer-Facilitated Text-mining*".

[10] See footnote 3.

#### *3.2.2.1.1 Summary of the Title/Abstract Screening Conducted for the First Ten TSCA Risk Evaluations*

One screener[11] conducted the screening and categorization of titles and abstracts. Relevant studies were identified according to inclusion and exclusion criteria as described in the *Strategy for Conducting Literature Searches* documents (Table 3-2). The categorization scheme (or tagging structure) varied by scientific discipline (i.e., physical and chemical properties; environmental fate and transport; chemical use/conditions of use information; environmental exposures; human exposures, including potentially exposed or susceptible subpopulations identified by virtue of greater exposure; human health hazard, including potentially exposed or susceptible subpopulations identified by virtue of greater susceptibility; and ecological hazard).

Within each data set, there were two broad categories or data tags: (1) *on-topic* references or (2) *off-topic* references. *On-topic* references are those that may contain data/information relevant to the risk evaluation. *Off-topic* references are those that do not appear to contain data or information relevant to the risk evaluation. Additional sub-categories (or sub-tags) were performed to facilitate further sorting of data/information - for example, identifying references by source type (e.g., published peer- reviewed journal article, government report); data type (e.g., primary data, review article); human health hazard (e.g., liver toxicity, cancer, reproductive toxicity); or chemical-specific and use-specific data or information.

The ECOTOX process and methodologies were used to screen the ecological hazard references. The ECOTOX literature screening strategy is discussed in the *Strategy for Conducting Literature Searches* documents for each of the ten TSCA risk evaluations (Table 3-2). Search results, screening decisions and respective tags were stored electronically in the ECOTOX Knowledgebase.

### 3.2.2.2 ***Full Text Screening***

The references identified during title/abstract screening are checked for relevance at the full-text level against specific eligibility criteria (e.g., PECO statements). Since EPA/OPPT is implementing systematic review methods and/or approaches in phases, the PECO approach was adopted during full text screening for the first ten TSCA risk evaluation. Future assessments will use PECOs from the start of the screening process (i.e., title/abstract screening).

The number of screeners, the process of reference assignment and conflict resolution are similar to those used for title/abstract screening. Table 3-1 describes the planning, execution and assessment activities supporting the full text screening activities for TSCA risk evaluations.

[11] Systematic review guidelines typically recommend at least two screeners to review each article to minimize bias. EPA had less than 6 months to conduct data collection and screening activities for 10 chemical substances; thus, one screener was used for the title/abstract screening to meet the statutory deadline in June 2017. However, full text screening generally used two independent screeners (see Section 3.2.2.2).

Like the title/abstract screening, the ECOTOX SOPs guide the title/abstract and full text screening of ecological hazard references. Please refer to the ECOTOX SOPs[12] to understand the screening process and criteria that are applied for the ecological hazard literature.

#### *3.2.2.2.1 Summary of the Full Text Screening Conducted for the First Ten TSCA Risk Evaluations*

The full text screening was conducted while EPA/OPPT refined the scope of the TSCA risk evaluations during problem formulation for the first ten chemical substances. PECO statements or a modified framework were used to describe the full-text inclusion and exclusion criteria for selecting relevant references. These criteria have been placed in each of the TSCA Problem Formulation documents as some criteria reflect chemical-specific issues that are better discussed in each chemical assessment. Refinements to the criteria may occur as EPA/OPPT delves into the analysis of relevant information.

Each article was generally screened by two independent reviewers using specialized web-based software (i.e., DistillerSR)[13]. Screeners were assigned batches of references after conducing pilot testing. Screening forms facilitated the reference review process by asking a series of questions based on pre-determined eligibility criteria. DistillerSR was used to manage the work flow of the screening process and document the eligibility decisions for each reference. The screeners resolved conflicts by consensus, or consultation with an independent individual(s).

As indicated in section 3.2.2.1, ecological hazard references underwent a similar screening process using the ECOTOX SOPs.

### 3.2.2.3 ***Data Extraction***

Data extraction is the process in which quantitative and qualitative data/information are identified from each relevant data/information source and extracted using structured forms or templates. Table 3-1 describes the planning, execution and assessment activities supporting the data extraction activities for TSCA risk evaluations.

When possible, the same reviewers used for the full-text screening will be used for data extraction, as these reviewers are already familiar with the references. EPA/OPPT will use various extraction tools to meet the needs of each chemical assessment. These may include specialized web-based software (e.g., DistillerSR, HAWC[14]).

Irrespective of whether data/information are extracted before or after evaluation, the general principle is that the extraction will occur for those sources containing relevant data/information

[12] See footnote 3.

[13] In addition to using DistillerSR, EPA/OPPT is exploring automation and machine learning tools for data screening and prioritization activities (e.g., SWIFT-Review, SWIFT-Active Screener, Dragon, DocTER). SWIFT is an acronym for "*Sciome Workbench for Interactive computer-Facilitated Text-mining*" [this is the same as footnote 6 above].

[14] EPA/OPPT is exploring HAWC for extracting data supporting TSCA risk evaluations. HAWC stands for Health Assessment Workspace Collaborative.

for the risk evaluation. EPA/OPPT is not planning to extract data/information from sources that exhibit serious flaws that would make the data unacceptable for use in the risk evaluation.

When applicable and feasible, EPA/OPPT will reach out to the authors of the data/information source to obtain raw data or missing elements that would be important to support the data evaluation and data integration steps. In such cases, the request(s) for additional data/information, number of contact attempts, and responses from the authors will be documented.

Data extraction activities for the first ten TSCA risk evaluation are anticipated to occur after the TSCA Problem Formulation documents are released Figure 1-1).

## 3.3 Data Evaluation

Data evaluation is the stage where the study quality of individual studies is assessed. Table 3-1 describes the planning, execution and assessment activities supporting the data evaluation activities for TSCA risk evaluations.

EPA/OPPT will use the evaluation strategies, including pre-determined criteria, documented in Appendices A through I. Refinements to the evaluation strategies are likely to occur and, in such case, any adjustments will be documented. Ideally, each data/information source will be screened by two reviewers but one reviewer may be used. The reviewers will resolve conflicts by consensus, or consultation with an independent individual(s).

Data evaluation activities for the first ten TSCA risk evaluation are anticipated to occur after the TSCA Problem Formulation documents are released in March 2018 (Figure 1-1).

## 3.4 Data Integration and Summary of Findings

Data integration is the stage where the analysis, synthesis and integration of data/information takes place by considering quality, consistency, relevancy, coherence and biological plausibility. It is in this stage where the weight of the scientific evidence approach is applied to evaluate and synthetize multiple evidence streams in order to support the chemical risk evaluation.

EPA/OPPT is required by TSCA to use the weight of the scientific evidence in TSCA risk evaluations. Application of weight of evidence analysis is an integrative and interpretive process that considers both data/information in favor (e.g., positive study) or against (e.g., negative study) a given hypothesis within the context of the assessment question(s) being evaluated in the risk evaluation. Table 3-1 describes the planning, execution and assessment activities supporting the data integration for TSCA risk evaluations.

Within the TSCA context, the weight of the scientific evidence is defined as "*a systematic review method, applied in a manner suited to the nature of the evidence or decision, that uses a pre-established protocol to comprehensively, objectively, transparently, and consistently identify and evaluate each stream of evidence, including strengths, limitations, and relevance of each*

*study and to integrate evidence as necessary and appropriate based upon strengths, limitations, and relevance*". 40 C.F.R. 702.33. In other words, it will involve assembling the relevant data and evaluating the data for quality and relevance, followed by synthesis and integration of the evidence to support conclusions (U.S. EPA, 2016). The significant issues, strengths, and limitations of the data and the uncertainties that require consideration will be presented, and the major points of interpretation will be highlighted. Professional judgment will be used at every step of the process and will be applied transparently, clearly documented, and to the extent possible, follow principles and procedures that are articulated prior to conducting the assessment (U.S. EPA, 2016).

The last step of the systematic review process is the summary of findings in which the evidence is summarized, the approaches or methods used to weigh the evidence are discussed, and the basis for the conclusion(s), recommendation(s), and any uncertainties are fully described. This step occurs in each of the components of the risk assessment (i.e., exposure assessment and hazard assessment) and is summarized in the risk characterization section of the TSCA risk evaluation.

Data integration activities for the first ten TSCA risk evaluation are anticipated to occur after the TSCA Problem Formulation documents are released (Figure 1-1). EPA/OPPT will provide further details about the data integration strategy along with the publication of the draft TSCA risk evaluations.

# 4 UPDATES TO THE DATA SEARCH AND SCREENING RESULTS FOR THE FIRST TEN RISK EVALUATIONS

## 4.1 Initial Data Search

EPA/OPPT identified additional environmental fate and exposure references that were not captured in the initial categorization of *the on-topic* references for the first ten risk evaluations published on June 22, 2017. Specifically, assessors identified references by checking the list of references of data sources frequently used to support EPA/OPPT's risk assessments (e.g., previous assessments cited in Table 1-1 of the TSCA Scope documents). This method, called backward reference searching (or snowballing), was not part of the initial literature search strategy. The inclusion of these additional *on-topic* references is not expected to change the information presented in the TSCA Scope and Problem Formulation documents. Also, EPA/OPPT anticipates targeted supplemental searches during the analysis phase (e.g., to locate specific information for exposure modeling). Backward reference searching will be included in the literature search strategy for supplemental searches.

Since the gathering of the initial literature search results, EPA/OPPT identified a list of *on-topic* and *off-topic* references that have been retracted from the scientific literature. Retracted references will not be considered in the development of TSCA risk evaluations. These references are listed in the pertinent TSCA Problem Formulation documents.

## 4.2 Initial Title/Abstract Screening

During the problem formulation phase, EPA/OPPT evaluated the performance of the initial title/abstract screening and tagging for the first ten risk evaluations to identify potentially misclassified *on-topic* and *off-topic* references. Misclassification was generally assessed by reviewing a small subset of references in the engineering/occupational exposure, exposure (e.g., general population, consumer exposure), environmental fate and human health hazard peer-reviewed literature. Once a misclassification was identified, EPA/OPPT initiated the process of updating the tags of the reference in HERO.

There were many *on-topic* references identified without readily available full text through the EPA library subscriptions or open sources. EPA/OPPT conducted a second title/abstract screening to confirm relevance of the data source and prioritize the decision of purchasing the full text in the case that the data source remained relevant after making refinements to the TSCA scope as the result from problem formulation. This ensured that EPA/OPPT would purchase the most relevant references for the risk evaluations.

Also, assessors questioned the usefulness of some *on-topic* references after closer inspection of the bibliographic citations. For instance, EPA/OPPT initially included a small subset of references reporting on the therapeutic or ameliorative properties of different drugs in carbon tetrachloride-treated animals. The references were re-classified as *off-topic* after updating the eligibility criteria and conducting a second title/abstract screening with the assistance of machine learning for literature prioritization (i.e., DocTER).

An exploratory exercise was conducted to identify *on-topic* references that were mischaracterized as *off-topic* references within the peer-reviewed human health hazard literature. Some *on-topic* references were identified using SWIFT-Review, but additional work is needed to further optimize the method. The second title/abstract screening for some of the references (see paragraph above) helped identify additional *off-topic* references that were originally tagged as *on-topic*. Based on performance checks, it is anticipated that very few on-topic references were misclassified as off-topic.

# 5 REFERENCES

*Note: This list contains the references cited in sections 1 through 3. References supporting the various evaluation strategies are listed in their respective appendices.*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# APPENDIX A: STRATEGY FOR ASSESSING THE QUALITY OF DATA/INFORMATION SUPPORTING TSCA RISK EVALUATIONS

The strategies for assessing the quality of data/information sources[15] use a structured framework with predefined criteria for each type of data/information source. EPA/OPPT developed a numerical scoring system to inform the characterization of the data/information sources during the data integration phase. The goal is to provide transparency and consistency to the evaluation process along with creating evaluation strategies that meet the TSCA science standards for various data/information streams. Further details about the data integration strategy will be provided with the publication of the draft TSCA risk evaluations, including how the scores will be considered.

In this document, the term data/information source is used in a broad way to capture the heterogeneity of data/information sources that are used in the TSCA risk evaluations. The data/information are intended to understand the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations as required by the amended TSCA. Thus, EPA/OPPT has developed evaluation strategies for various data/information streams:

- Physical-chemical properties (Appendix B);
- Environmental fate (Appendix C);
- Occupational exposure and release data (Appendix D)
- Exposures to general population and consumers as well as environmental exposures (Appendix E);
- Ecological hazard studies (Appendix F);
- Animal toxicity and *in vitro* toxicity (Appendix G);
- Epidemiological studies (Appendix H)

The process of developing the strategies involved reviewing various evaluation tools/frameworks and documents as well as getting input from scientists based on their expert knowledge about evaluating various data/information sources for risk assessment purposes. Criteria and/or evaluation tools/frameworks that were consulted during the development phase of the evaluation strategies were the following:

- Biomonitoring, Environmental Epidemiology, and Short-lived Chemicals (BEES-C) instrument (Lakind et al., 2014)
- Criteria used in EPA's ECOTOXicology knowledgebase (U.S. EPA, 2018a)
- Criteria for reporting and evaluating ecotoxicity data(CRED) (Moermond et al., 2016b)
- Systematic review practices in EPA's Integrated Risk Information System (IRIS) (U.S. EPA, 2018b)
- EPA's Guidelines for Exposure Assessment (U.S. EPA, 1992)

[15] The term data/information source is used in this document in a broad way to capture the heterogeneity of data/information in TSCA risk evaluations (e.g., experimental studies, data sets, published models, completed assessments, release data).

- EPA's Summary of General Assessment Factors for Evaluating the Quality of Scientific and technical information (U.S. EPA, 2003b)
- EPA's Exposure Factors Handbook (U.S. EPA, 2011b)
- *Handbook for Conducting a Literature-based Health Assessment Using OHAT Approach for Systematic Review and Evidence Integration* (NTP, 2015a)
- *NAS report on Human Biomonitoring for Environmental Chemicals* (NRC, 2006)
- Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement (Von Elm et al., 2008)
- ToxRTool (Toxicological data Reliability Assessment Tool) developed by the European Commission (EC, 2018)
- Various OECD guidance document on exposure, environmental fate and modeling data (see appendices more information) (EC, 2018; OECD, 2017; Cooper et al., 2016; ECHA, 2016; Lynch et al., 2016; Moermond et al., 2016a; Moermond et al., 2016b; Samuel et al., 2016; NTP, 2015a, b; Hooijmans et al., 2014; Koustas et al., 2014; Lakind et al., 2014; NRC, 2014; OECD, 2014; Kushman et al., 2013; Hartling et al., 2012; ECHA, 2011a, c; U.S. EPA, 2011a, b; Hooijmans et al., 2010; U.S. EPA, 2009; Von Elm et al., 2008; OECD, 2007; Barr et al., 2006; FTC, 2006; NRC, 2006; U.S. EPA, 2006; ATSDR, 2005; OECD, 2004, 2003; U.S. EPA, 2003a, b, c; Bower, 1999; OECD, 1998, 1997, 1995; U.S. EPA, 1992; NRC, 1991)

The general structure of the TSCA evaluation strategies is composed of evaluation domains, metrics and criteria. Evaluation domains represent general categories of attributes that are evaluated in each data/information source (e.g., test substance, test conditions, reliability, representativeness). Each domain contains a unique set of metrics, or sub-categories of attributes, intended to assess an aspect of the methodological conduct of the data/information source. Each metric specifies criteria expressing the relevant elements or conditions for assessing confidence that, along with professional judgement, will guide the identification of study strengths and limitations/deficiencies. EPA/OPPT plans to pilot the evaluation strategies for optimization purposes.

Reporting quality is an important aspect of a study that needs to be considered in the evaluation process. The challenge, in many cases, is to distinguish a deficit in reporting from a problem in the underlying methodological quality of the data/information source. The TSCA evaluation strategies incorporate reporting criteria within the existing domains rather than adding a separate reporting domain as recommended in some evaluation tools/frameworks. Since reporting contributes to the evaluation of each facet of the data source, EPA/OPPT assesses reporting and methodological quality simultaneously with the idea of untangling reporting from study conduct while the reviewer is assessing a particular metric for each domain. Developing a reporting checklist, guidance document or a separate reporting quality domain may be possible in the near future as EPA/OPPT uses and optimizes the evaluation strategies.

Data/information sources should also be evaluated for their relevance or appropriateness to support the risk evaluation. Specifically, data/information sources should support the

assessment questions, analytical approaches, methods, models and considerations that are laid out in the analysis plan of the TSCA Scope documents[16]. EPA/OPPT uses a tiered approach to check for relevance starting at the data search stage and continuing during the title/abstract and full text screening and evaluation and integration stages. By design, the TSCA systematic review process uses a fit-for-purpose literature search and relevance-driven eligibility criteria to end up evaluating the most relevant data/information sources for the TSCA risk evaluation. The reviewers also check for relevance while assessing the quality of the data/information source and are asked to document[17] any relevancy issues during the evaluation process. Refer to section 3.2.2 for data attributes that are included in the eligibility criteria to check for relevance.

The TSCA evaluation strategies in some cases refer to study guidelines along with professional judgement as a helpful guidance in determining the adequacy or appropriateness of certain study designs or analytical methods. This should not be construed to imply that non-guideline studies have lower confidence than guideline or Good Laboratory Practice (GLP) studies. EPA/OPPT will consider any and all available, relevant data and information that conform to the TSCA science standards when developing the risk evaluations irrespective of whether they were conducted in accordance with standardized methods (e.g., OECD test guidelines or GLP standards).

Some data sources may be evaluated under different evaluation strategies. For instance, exposure assessors may evaluate an epidemiological study for estimating exposure via direct measurements or modeling. In addition, a human health hazard assessor may evaluate the same study for hazards and effects in the human population related to the exposure of a particular chemical substance. Although this may be cumbersome, EPA/OPPT's approach is justifiable since the data source is supporting different assessment questions. EPA/OPPT recognizes that this approach may be refined in the future to adopt efficiencies, if lessons learned indicate that it needs to be changed.

EPA/OPPT will consider data and information from alternative test methods and strategies (or new approach methodologies or NAMs), as applicable and available, to support TSCA risk evaluations. This is consistent with EPA/OPPT's *Strategic Plan to Promote the Development and Implementation of Alternative Test Methods (Draft)* to reduce, refine or replace vertebrate animal testing (U.S. EPA, 2018c). Since these NAMs may support the analyses for the exposure and hazard assessments, the data/information quality criteria may need to be optimized or new criteria may need to be developed as part of evaluating and integrating NAMs in the TSCA risk evaluation process.

[16] Refer to the TSCA Problem Formulation documents to obtain refined analysis plans for the first ten chemical assessments.

[17] Relevancy issues will be documented in the reviewer's comments.

## A.1 Evaluation Method

Based on the strengths, limitations, and deficiencies of each data/information source, the reviewer assigns a confidence level score of 1 (high confidence), 2 (medium confidence), 3 (low confidence) or 4 (unacceptable) for each individual metric that is evaluating a particular aspect of the methodological conduct of the data/information source. Although many metrics have criteria for all four bins (i.e., *High, Medium, Low, and Unacceptable*), there are some metrics with dichotomous or trichotomous criteria to fit better the nature of the criteria.

The confidence levels and corresponding scores at the metric level are defined as follows:

- **High:** No notable deficiencies or concerns are identified in the domain metric that are likely to influence results [score of 1].
- **Medium:** Minor uncertainties or limitations are noted in the domain metric that are unlikely to have a substantial impact on results [score of 2].
- **Low:** Deficiencies or concerns are noted in the domain metric that are likely to have a substantial impact on results [score of 3].
- **Unacceptable:** Serious flaws are noted in the domain metric that consequently make the data/information source unusable. [score of 4].
- **Not rated/applicable:** Rating of this metric is not applicable to the data/information source being evaluated [no score]. *Not rated/applicable* will also be used in cases in which studies cite a literature source for their test methodology instead of providing detailed descriptions. In these circumstances, EPA will score the metric as *Not rated/not applicable* and capture it in the reviewer's notes. If the data/information source is not classified as "unacceptable" in the initial review, the cited literature source will be reviewed during a subsequent evaluation step and the metric will be rated at that time.

A numerical scoring method is used to convert the confidence level for each metric into the overall quality level for the data/information source. The overall study score is equated to an overall quality level (*High*, *Medium*, or *Low*) using the level definitions and scoring scale shown in Table A-1. The scoring scale was obtained by calculating the difference between the highest possible score of 3 and the lowest possible score of 1 (i.e., 3-1= 2) and dividing into three equal parts (2 ÷ 3 = 0.67). This results in a range of approximately 0.7 for each overall data quality level, which was used to estimate the transition points (cut-off values) in the scale between *High* and *Medium* scores, and *Medium* and *Low* scores. These transition points between the ranges of 1 and 3 were calculated as follows:

- Cut-off values between *High* and *Medium*: 1 + 0.67= 1.67, rounded up to 1.7 (scores lower than 1.7 will be assigned an overall quality level of *High*)
- Cut-off values between *Medium* and *Low*: 1.67 + 0.67= 2.34, rounded up to 2.3 (scores between 1.7 and lower than 2.3 will be assigned an overall quality level of *Medium)*

A study is disqualified from further consideration if the confidence level of one or more metrics is rated as *Unacceptable* [score of 4]. EPA/OPPT plans to use data with an overall quality level of *High, Medium*, or *Low* confidence to quantitatively or qualitatively support the risk evaluations, but does not plan to use data rated as *Unacceptable*. Data or information from *Unacceptable*

studies might be useful qualitatively and such use of unacceptable studies may be done on a case-by-case basis.

**Table A-1. Definition of Overall Quality Levels and Corresponding Quality Scores**

| Overall Quality Level | Definition | Overall Quality Score |
|---|---|---|
| **High** | No notable deficiencies or concerns are identified and the data therefore could be used in the assessment with a high degree of confidence. | ≥ 1 and < 1.7 |
| **Medium** | Possible deficiencies or concerns are noted and the data therefore could be used in the assessment with a medium degree of confidence. | ≥ 1.7 and < 2.3 |
| **Low** | Deficiencies or concerns are noted and the data therefore could be used in the assessment with a low degree of confidence. | ≥ 2.3 and ≤ 3 |
| **Unacceptable** | Serious flaw(s) are identified and therefore, the data cannot be used for the assessment. | 4 |

After the overall score is applied to determine an overall quality level, professional judgment may be used to adjust the quality level obtained by the weighted score calculation. The reviewer must have a compelling reason to invoke the adjustment of the overall score and written justification must be provided. This approach has been used in other established tools such as the ToxRTool (Toxicological data Reliability Assessment Tool) developed by the European Commission (https://eurl-ecvam.jrc.ec.europa.eu/about-ecvam/archive-publications/toxrtool).

Domain definitions, evaluation metrics, and details about the numerical scoring method can be found in the appendices for each data/information stream (Appendices B to H).

## A.2 Documentation and Instructions for Reviewers

Data evaluation is conducted in a tool (e.g., Excel, DistillerSR) that tracks and records the evaluation for each data/information source. The following basic information will be generally recorded for each data/information source that is reviewed.

**Table A-2. Documentation Template for Reviewer and Data/Information Source**

**Reviewer Information:**

| | |
|---|---|
| **Name:** | |
| **Affiliation:** | |
| **Qualifications (area of expertise):** | |
| **Date of Review:** | |

**Data/Information Source:**

| | |
|---|---|
| **Reference citation:** | |
| **HERO ID:** | |
| **HERO Link:** | |
| **Study or Data Type (if publication reports multiple studies or data types):** | |

A confidence level is assigned for each relevant metric within each domain by following the confidence level specifications provided in section A.1, along with professional judgment, to identify study strengths and limitations. The assigned confidence level is indicated by placing a score between 1 and 4 in the column labeled *Selected Score*. In some cases, reference to study guidelines (in addition to professional judgement) may be helpful in determining the adequacy or appropriateness of certain study designs or analytical methods. This should not be construed to imply that non-guideline studies necessarily have lower confidence than guideline studies. If a publication reports more than one study or endpoint, each study and, as needed, each endpoint will be evaluated separately.

Some metrics may not be applicable to all study types. If a metric is not applicable to the study under review, *NR* (not rated) will be placed in the *Selected Score* column for this metric.

After scoring of the individual metrics within each domain, the overall study score is calculated and assigned to the corresponding bin (*High*, *Medium*, *Low*, or *Unacceptable*).

In the *Reviewer's Comments* field, the reviewer documents concerns, uncertainties, strengths, limitations, deficiencies and any additional comments observed for each metric, when necessary. For instance, EPA may not always provide a comment for a metric that has been categorized as *High*. However, a reviewer is strongly encouraged to provide a comment for metrics categorized as *Medium* or *Low* to improve transparency. The reviewer also records any relevance issues with the data/information source (e.g., study is not useful to answer assessment questions).

## A.3 Important Caveats

The following is a discussion of important caveats for the data quality evaluation method that EPA/OPPT intends to use in the TSCA risk evaluations:

- Although specifications for the data quality evaluation metrics have been developed, professional judgment is required to assess the metrics.
- Data evaluation is a qualitative assessment of confidence in a study or data set. A scoring system is being applied to ascertain a qualitative rating in order to provide consistency and transparency to the evaluation process. Scores will be used for the purpose of assigning the confidence level rating of *High, Medium, Low, or Unacceptable*, and inform the characterization of data/information sources during the data integration phase. The system is not intended to imply precision and/or accuracy of the scoring results.
- Every study or data set is unique and therefore the individual metrics and domains may have various degrees of importance (e.g., more or less important). The weighting approach for some of the strategies may need to be adjusted as EPA/OPPT tests the evaluation method with different types of studies.
- The metrics developed are intended to be indicators of data quality. They were selected because they are generally considered common and important for a broad range of

studies. Other metrics not listed may also be important and added if necessary. Also, there is the possibility of deviating from the calculated overall confidence level score in case the metric criteria are unable to capture professional judgement. A reviewer must provide a justification for the score adjustment to ensure transparency for the decision.

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# APPENDIX B: DATA QUALITY CRITERIA FOR PHYSICAL/CHEMICAL PROPERTY DATA

Table B-1 describes the general approach that EPA/OPPT uses to assess the quality of physical-chemical property data.

**Table B-1. Evaluation Metrics and Ratings for Physical-Chemical Property Data**

| Domain/Metric | Description/ Definition | Ratings and Criteria |
|---|---|---|
| Representativeness | The information or data reflects the data and chemical substance type. | *High:* Data are measured for the subject chemical substance.<br><br>*Medium:* Data are measured for a structural analog of the subject chemical substance.<br><br>*Low:* Data are estimated (modeled) for the subject chemical substance.<br><br>*Not rated:* Rating of this factor is not applicable to this kind of information. |
| Appropriateness | The information or data reflects anticipated results based on chemical structural features or behaviors. | *High:* Measured data are consistent with the subject chemical substance structural features (e.g., presence of certain functional groups).<br><br>*Medium:* Data measured for a structural analog of the subject chemical substance or estimated (modeled) for the subject chemical substance are consistent with what is expected for the subject chemical substance structural features or behaviors.<br><br>*Low:* Data measured for a structural analog of the subject chemical substance or estimated (modeled) for the subject chemical substance are not consistent with the subject chemical substance structural features or behaviors, or the structural features or behaviors of the subject chemical substance are uncertain.<br><br>*Unacceptable:* Measured data for a structural analog of the subject chemical substance are not appropriate because the analog is not appropriate (e.g., analog is a neutral molecule and the subject chemical substance is a salt). Estimated (modeled) data for the subject chemical substance are not appropriate because the estimation tool is not appropriate (e.g., estimation tool is not able to estimate class 2 and polymeric substances).<br><br>*Not rated:* Rating of this factor is not applicable to this kind of information. |

| Domain/Metric | Description/ Definition | Ratings and Criteria |
|---|---|---|
| Evaluation/Review | The information or data reported has reliable review. | *High:* The information or data is from a recognized data collection/repository where data are peer-reviewed by experts in the field, are broadly available to the public for review and use, and include references to the original sources.<br><br>*Medium:* From a source that is not described as High above but is known.<br><br>*Low:* From a source that is uncertain (unknown primary source).<br><br>*Not rated:* Rating of this factor is not applicable to this kind of information. |
| Reliability/Unbiased (Method Objectivity) | The method for producing the data/information is not biased towards a particular product or outcome. | *High*: Methodology for producing the information is designed to answer a specific question, and the methodology's objective is clear.<br><br>*Medium*: Method bias appears unlikely.<br><br>*Low*: Method bias appears likely or is highly uncertain.<br><br>*Unacceptable:* Method bias is so severe as to be unacceptable.<br><br>*Not rated*: Rating of this factor is not applicable to this kind of information. |
| Reliability/Analytic Method | The information or data reported is from a reliable method. | *High*: Data are obtained by accepted standard analytic methods.<br><br>*Medium*: Analytic method is non-standard but is expected to be appropriate.<br><br>*Low:* From a source that is uncertain. Analytic method is not known.<br><br>*Unacceptable:* Analytic method is not appropriate.<br><br>Not rated: Rating of this factor is not applicable to this kind of information. |

# APPENDIX C: DATA QUALITY CRITERIA FOR FATE DATA

## C.1 Types of Fate Data Sources

The quality of fate data, which includes mass transport, chemical partitioning, and chemical or biological transformations in soil, surface waters, groundwater, and air (e.g., biodegradation, hydrolysis, photolysis), will be evaluated for four different data sources: experimental data, field studies, modeling data, and monitoring data. Generally experimental fate data is preferred over modeled data; however, fate data from all data sources will be evaluated using the data criteria in this section. Definitions for these data types are shown in Table C-1. Since the availability of information varies considerably for different chemicals, it is anticipated that some study types will not be available while others may be identified beyond those listed in Table C-1.

**Table C-1. Types of Fate Data**

| Type of Data Source | Definition |
|---|---|
| Experimental Data | Data obtained from experimental studies conducted in a controlled environment with pre-defined testing conditions. Examples include data from laboratory tests such as those conducted for ready biodegradation (e.g., MITI test) or hydrolysis (i.e., following OECD TG 111), among others. |
| Field Studies | Data collected from incidental sampling of environmental media, especially to provide information on partitioning, bioconcentration, or long-term environmental fate. |
| Modeling Data | Calculated values derived from computational models for estimating environmental fate and property data including degradation, bioconcentration, and partitioning. |
| Monitoring Data | Measured chemical concentration(s) obtained from systematic sampling of environmental media (e.g., air, water, soil, and biota) to observe and study the effect of environment conditions on the fate of chemicals. Monitoring data may include studies of chemical(s) after a known exposure/release of test substance as well as measured chemical concentrations over a period of time to provide direct evidence about fate in environment. |

Notes:
MITI = Ministry of International Trade and Industry
OECD TG = Organisation for Economic Co-operation and Development (OECD) Testing Guideline (TG)

## C.2 Data Quality Evaluation Domains

The quality of fate data sources will be evaluated against metrics and criteria grouped into eight evaluation domains: Test Substance; Test Design; Test Conditions; Test Organisms (does not apply to abiotic studies); Outcome Assessment; Confounding/Variable Control; Data Presentation and Analysis; and Other. These domains, as defined in Table C-2, address elements of the TSCA Science Standards 26(h)(1) through 26(h)(5). The evaluation strategies are intended to apply to all fate data, although certain domains, metrics, and criteria may not apply to all studies. For example, there are evaluation strategy considerations for organisms in biodegradation, bioconcentration, or bioaccumulation studies that do not apply to abiotic studies.

**Table C-2. Data Evaluation Domains and Definitions for Fate Data**

| Evaluation Domain | Definition |
|---|---|
| Test Substance | Metrics in this domain evaluate whether the information provided in the study provides a reliable[18] confirmation that the test substance used in a study has the same (or sufficiently similar) identity, purity, and properties as the test substance of interest. |
| Test Design | Metrics in this domain evaluate whether the experimental design enables the study to distinguish the behavior of the test substance from other factors. This domain includes metrics related to the use of control groups. |
| Test Conditions | Metrics in this domain assess the reliability of methods used to measure or characterize test substance behavior. These metrics evaluate whether presence of the test substance was characterized using method(s) that provide reliable results over the duration of the experiment. |
| Test Organisms | Metrics in this domain pertain to some fate studies[19]. These metrics assess the appropriateness of the population or organism(s) to assess the outcome of interest. |
| Outcome Assessment | Metrics in this domain assess the reliability of methods, including sensitivity, that are used to measure or otherwise characterize outcomes. Outcomes may include physical/chemical properties or fate parameters. |
| Confounding/ Variable Control | Metrics in this domain assess the potential impact of factors other than presence of test substance that may affect the risk of outcome. The metrics evaluate whether studies identify and account for factors that are related to presence of the test substance and independently related to outcome (confounding factors) and whether appropriate experimental or analytical (statistical) methods are used to control for factors unrelated to the presence of test substance that may affect the risk of outcome (variable control). |
| Data Presentation and Analysis | Metrics in this domain assess whether appropriate experimental or analytical methods were used and if all outcomes are presented. |
| Other | Metrics in this domain are added as needed to incorporate chemical- or study-specific evaluations (i.e., QSAR models). |

## C.3 Data Quality Evaluation Metrics

Table C-3 lists the data evaluation domains and metrics for fate studies. Each domain has between two and four metrics; however, some metrics may not apply to all fate data. A general domain for other considerations is available for metrics that are specific to a given test substance or study type (i.e., QSAR models).

As with all evaluation criteria, EPA may modify the metrics used for fate data as more experience is acquired with the evaluation tools, to support fit-for-purpose TSCA risk evaluations. Any modifications will be documented.

[18] Reliability is defined as "the inherent property of a study or data, which includes the use of well-founded scientific approaches, the avoidance of bias within the study or data collection design and faithful study or data collection conduct and documentation" (ECHA, 2011b).

[19] This domain does not apply to abiotic studies.

**Table C-3. Summary of Metrics for the Fate Data Evaluation Domains**

| Evaluation Domain | Number of Metrics Overall | Metrics (Metric Number and Description) |
|---|---|---|
| Test Substance | 2 | • Metric 1: Test Substance Identity<br>• Metric 2: Test Substance Purity |
| Test Design | 2 | • Metric 3: Study Controls<br>• Metric 4: Test Substance Stability |
| Test Conditions | 4 | • Metric 5: Test Method Suitability<br>• Metric 6: Testing Conditions<br>• Metric 7: Testing Consistency<br>• Metric 8: System Type and Design |
| Test Organisms[20] | 2 | • Metric 9: Test Organism – Degradation<br>• Metric 10: Test Organism – Partitioning |
| Outcome Assessment | 2 | • Metric 11: Outcome Assessment Methodology<br>• Metric 12: Sampling Methods |
| Confounding/ Variable Control | 2 | • Metric 13: Confounding Variables<br>• Metric 14: Outcomes Unrelated to Exposure |
| Data Presentation and Analysis | 2 | • Metric 15: Data Presentation<br>• Metric 16: Statistical Methods & Kinetic Calculations |
| Other | 2 | • Metric 17: Verification or Plausibility of Results<br>• Metric 18: QSAR Models |

## C.4 Scoring Method and Determination of Overall Data Quality Level

Appendix A provides information about the evaluation method that will be applied across the various data/information sources being assessed to support TSCA risk evaluations. This section provides details about the scoring system that will be applied to fate data/information, including the weighting factors assigned to each metric score of each domain.

Some metrics may be given greater weights than others, if they are regarded as key or critical metrics based on expert judgment (Moermond et al., 2016a). Thus, EPA will use a weighting approach to reflect that some metrics are more important than others when assessing the overall quality of the data.

[20] This domain does not apply to abiotic studies.

### C.4.1 Weighting Factors

Each metric was assigned a weighting factor of 1 or 2, with the higher weighting factor (2) given to metrics deemed critical for the evaluation. The critical metrics were identified based on factors that are most frequently included in other study quality and/or risk of bias tools (reviewed by (Lynch et al., 2016); (Samuel et al., 2016)). In selecting critical metrics, EPA recognized that the relevance of an individual fate study to the risk analysis for a given substance is determined by its ability to inform hazard identification and/or exposure. Thus, the critical metrics are those that determine how well a study supports the risk analysis. The rationale for selection of the critical metrics for fate studies is presented in Table C-4.

**Table C-4. Fate Metrics with Greater Importance in the Evaluation and Rationale for Selection**

| Domain | Critical Metrics with Weighting Factor of 2 (Metric Number) [a] | Rationale |
|---|---|---|
| Test Substance | Test Substance Identity (Metric 1) | The test substance must be identified and characterized definitively to ensure that the study is relevant to the substance of interest. |
| Test Design | Study Controls (Metric 3) | Controls, with all conditions equal excluding exposure to the degradation pathway (e.g., sunlight, test organism, reductant, etc.) or partitioning surface, are required to ensure that any observed effects are attributable to the outcome of interest. |
| Test Conditions | Testing Conditions (Metric 6) | Testing conditions must be defined without ambiguity to enable valid comparisons across studies. |
| Test Organisms[21] | Test Organism – Degradation (Metric 9)<br><br>Test Organism – Partitioning (Metric 10) | The test organism information must be reported to enable assessment of whether they are suitable for the endpoint of interest and whether there are species, strain, sex, or age/life-stage differences within or between different studies. |
| Data Presentation and Analysis | Data Presentation (Metric 15) | Detailed reports are necessary to determine if the study authors' conclusions are valid. |

Note:

[a] A weighting factor of 1 is assigned for the following metrics: test substance purity (metric 2); test substance stability (metric 4); test method suitability (metric 5); testing consistency (metric 7); system type and design (metric 8); outcome assessment methodology (metric 11); sampling methods (metric 12); confounding variables (metric 13); outcomes unrelated to exposure (metric 14); statistical methods and kinetic calculations (metric 16); Verification or Plausibility of Results (metric 17); QSAR models (metric 18)

[21] This domain does not apply to abiotic studies.

### C.4.2 Calculation of Overall Study Score

To determine the overall study score, the first step is to multiply the score for each metric (1, 2, or 3 for high, medium, or low confidence, respectively) by the appropriate weighting factor, as shown in Table C-5, to obtain a weighted metric score. The weighted metric scores are then summed and divided by the sum of the weighting factors (for all metrics that are scored) to obtain an overall study score between 1 and 3. The equation for calculating the overall score is shown below:

$$\textit{Overall Score (range of 1 to 3)} = \sum (\textit{Metric Score} \times \textit{Weighting Factor}) / \sum (\textit{Weighting Factors})$$

Scoring examples for fate studies are given in Tables C-6 to C-8.

Studies with any single metric scored as unacceptable (score = 4) will be automatically assigned an overall quality score of 4 (unacceptable) and further evaluation of the remaining metrics is not necessary. An unacceptable score means that serious flaws are noted in the domain metric that consequently make the data unusable (or invalid). EPA/OPPT plans to use data with an overall quality level of *High, Medium*, or *Low* confidence to quantitatively or qualitatively support the risk evaluations, but does not plan to use data rated as *Unacceptable*.

Any metrics that are *not rated/not applicable* to the study under evaluation will not be considered in the numerator or calculation of the study's overall quality score. These metrics will not be included in the nominator or denominator of the *overall score* equation. The overall score will be calculated using only those metrics that receive a numerical score. In addition, if a publication reports more than one study or endpoint, each study and, as needed, each endpoint will be evaluated separately.

Detailed tables showing quality criteria for the metrics are provided in Tables C-9 through C-10, including a table that summarizes the serious flaws that would make the data unacceptable for use in the environmental fate assessment.

**Table C-5. Metric Weighting Factors and Range of Weighted Metric Scores for Scoring the Quality of Environmental Fate Data**

| Domain Number/ Description | Metric Number/Description | Range of Metric Scores[a] | Metric Weighting Factor | Range of Weighted Metric Scores[b] |
|---|---|---|---|---|
| 1. Test Substance | 1. Test Substance Identity | 1 to 3 | 2 | 2 to 6 |
| | 2. Test Substance Purity | 1 to 3 | 1 | 1 to 3 |
| 2. Test Design | 3. Study Controls | 1 to 3 | 2 | 2 to 6 |
| | 4. Test Substance Stability | 1 to 3 | 1 | 1 to 3 |
| 3. Test Conditions | 5. Test Method Suitability | 1 to 3 | 1 | 1 to 3 |
| | 6. Testing Conditions | 1 to 3 | 2 | 2 to 6 |
| | 7. Testing Consistency | 1 to 2 | 1 | 1 to 3 |
| | 8. System Type and Design | 1 to 2 | 1 | 1 to 3 |
| 4. Test Organisms[22] | 9. Test Organism - Degradation | 1 to 3 | 2 | 2 to 6 |
| | 10. Test Organism - Partitioning | 1 to 3 | 2 | 2 to 6 |
| 5. Outcome Assessment | 11. Outcome Assessment Methodology | 1 to 3 | 1 | 1 to 3 |
| | 12. Sampling Methods | 1 to 3 | 1 | 1 to 3 |
| 6. Confounding/ Variable Control | 13. Confounding Variables | 1 to 3 | 1 | 1 to 3 |
| | 14. Outcomes Unrelated to Exposure[23] | 1 to 2 | 1 | 1 to 3 |
| 7. Data Presentation and Analysis | 15. Data Reporting | 1 to 3 | 2 | 2 to 6 |
| | 16. Statistical Methods & Kinetic Calculations | 1 to 3 | 1 | 1 to 3 |
| 8. Other | 17. Verification or Plausibility of Results | 1 to 3 | 1 | 1 to 3 |
| | 18. QSAR Models | 1 | 1 | 1 to 3 |
| | | | Sum= 24 | Sum= 24 to 72 |
| Range of Overall Scores after using equation<br>Overall Score = ∑ (Metric Score × Metric Weighting Factor)/∑ (Metric Weighting Factors)<br>High: ≥1 and <1.7 \| Medium: ≥1.7 and <2.3 \| Low: ≥2.3 and ≤3 | | | | 24/24= 1;<br>72/24=3<br><br>Range of overall score = 1 to 3[d] |

Notes:

[a] For the purposes of calculating an overall study score, the range of possible metric scores is 1 to 3 for each metric, corresponding to high and low confidence. No calculations will be conducted if a study receives an "unacceptable" rating (score of "4") for any metric.

[b] The range of weighted scores for each metric is calculated by multiplying the range of metric scores (1 to 3) by the weighting factor for that metric.

[c] The sum of weighting factors and the sum of the weighted scores will differ if some metrics are not scored (not applicable).

[d] The range of possible overall scores is 1 to 3. If a study receives a score of 1 for every metric, then the overall study score will be 1. If a study receives a score of 3 for every metric, then the overall study score will be 3.

[22] This domain does not apply to abiotic studies.

[23] This metric does not apply to abiotic studies.

**Table C-6. Scoring Example for Abiotic Fate Data (i.e., hydrolysis data) with All Applicable Metrics Scored**

| Domain | Metric | Metric Score | Metric Weighting Factor | Weighted Metric Score |
|---|---|---|---|---|
| 1. Test Substance | 1. Test Substance Identity | 1 | 2 | 2 |
| | 2. Test Substance Purity | 2 | 1 | 2 |
| 2. Test Design | 3. Study Controls | 1 | 2 | 2 |
| | 4. Test Substance Stability | 3 | 1 | 3 |
| 3. Test Conditions | 5. Test Method Suitability | 1 | 1 | 1 |
| | 6. Testing Conditions | 1 | 2 | 2 |
| | 7. Testing Consistency | 1 | 1 | 1 |
| | 8. System Type and Design | 1 | 1 | 1 |
| 4. Test Organisms | 9. Test Organism - Degradation | N/A | | |
| | 10. Test Organism - Partitioning | N/A | | |
| 5. Outcome Assessment | 11. Outcome Assessment Methodology | 2 | 1 | 2 |
| | 12. Sampling Methods | 1 | 1 | 1 |
| 6. Confounding/ Variable Control | 13. Confounding Variables | 1 | 1 | 1 |
| | 14. Outcomes Unrelated to Exposure | N/A | | |
| 7. Data Presentation and Analysis | 15. Data Reporting | 2 | 2 | 4 |
| | 16. Statistical Methods & Kinetic Calculations | 1 | 1 | 1 |
| 8. Other | 17. Verification or Plausibility of Results | 1 | 1 | 1 |
| | 18. QSAR Models | N/A | | |
| | | Sum | 18 | 24 |
| N/A = not applicable to abiotic data | | Overall Study Score | **1.3333** | **= High** |

Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factor

| High | Medium | Low |
|---|---|---|
| ≥1 and <1.7 | ≥1.7 and <2.3 | ≥2.3 and ≤3 |

**Table C-7. Scoring Example for Abiotic Fate Data (i.e., hydrolysis data) with Some Metrics Not Rated/Not Applicable**

| Domain | Metric | Metric Score | Metric Weighting Factor | Weighted Metric Score |
|---|---|---|---|---|
| 1. Test Substance | 1. Test Substance Identity | 1 | 2 | 2 |
| | 2. Test Substance Purity | 2 | 1 | 2 |
| 2. Test Design | 3. Study Controls | 1 | 2 | 2 |
| | 4. Test Substance Stability | 3 | 1 | 3 |
| 3. Test Conditions | 5. Test Method Suitability | 1 | 1 | 1 |
| | 6. Testing Conditions | 1 | 2 | 2 |
| | 7. Testing Consistency | NR | | |
| | 8. System Type and Design | NR | | |
| 4. Test Organisms | 9. Test Organism - Degradation | N/A | | |
| | 10. Test Organism - Partitioning | N/A | | |
| 5. Outcome Assessment | 11. Outcome Assessment Methodology | 2 | 1 | 2 |
| | 12. Sampling Methods | 1 | 1 | 1 |
| 6. Confounding/ Variable Control | 13. Confounding Variables | NR | | |
| | 14. Outcomes Unrelated to Exposure | N/A | | |
| 7. Data Presentation and Analysis | 15. Data Reporting | 2 | 2 | 4 |
| | 16. Statistical Methods & Kinetic Calculations | 1 | 1 | 1 |
| 8. Other | 17. Verification or Plausibility of Results | 1 | 1 | 1 |
| | 18. QSAR Models | N/A | | |
| NR = not rated<br>N/A = not applicable to abiotic data | | Sum | 15 | 21 |
| | | Overall Study Score | **1.4 = High** | |

Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factor

| High | Medium | Low |
|---|---|---|
| ≥1 and <1.7 | ≥1.7 and <2.3 | ≥2.3 and ≤3 |

**Table C-8. Scoring Example for QSAR Data**

| Domain Number/ Description | Metric Number/Description | Metric Score [a] | Metric Weighting Factor | Weighted Metric Score [b] |
|---|---|---|---|---|
| 1. Test Substance | 1. Test Substance Identity | NR | N/A | N/A |
| | 2. Test Substance Purity | NR | N/A | N/A |
| 2. Test Design | 3. Study Controls | NR | N/A | N/A |
| | 4. Test Substance Stability | NR | N/A | N/A |
| 3. Test Conditions | 5. Test Method Suitability | NR | N/A | N/A |
| | 6. Testing Conditions | NR | N/A | N/A |
| | 7. Testing Consistency | NR | N/A | N/A |
| | 8. System Type and Design | NR | N/A | N/A |
| 4. Test Organisms[24] | 9. Test Organism - Degradation | NR | N/A | N/A |
| | 10. Test Organism - Partitioning | NR | N/A | N/A |
| 5. Outcome Assessment | 11. Outcome Assessment Methodology | NR | N/A | N/A |
| | 12. Sampling Methods | NR | N/A | N/A |
| 6. Confounding/ Variable Control | 13. Confounding Variables | NR | N/A | N/A |
| | 14. Outcomes Unrelated to Exposure[25] | NR | N/A | N/A |
| 7. Data Presentation and Analysis | 15. Data Reporting | NR | N/A | N/A |
| | 16. Statistical Methods & Kinetic Calculations | NR | N/A | N/A |
| 8. Other | 17. Verification or Plausibility of Results | 2 | 1 | 2 |
| | 18. QSAR Models | 1 | 1 | 1 |
| | Sum (of all metrics scored)[b] | | 2 | 3 |
| Overall Score = ∑ (Metric Score × Metric Weighting Factor)/∑ (Metric Weighting Factors) | Range of Overall Scores after using equation | | | 3/2=1.5<br>1.5<br>(High) |

| High | Medium | Low |
|---|---|---|
| ≥1 and <1.7 | ≥1.7 and <2.3 | ≥2.3 and ≤3 |

Notes:

[a] For the purposes of calculating an overall study score, the range of possible metric scores is 1 to 3 for each metric, corresponding to high and low confidence. No calculations will be conducted if a study receives an *unacceptable* rating (score of "4") for any metric.

[b] The sum of weighting factors and the sum of the weighted scores will differ if some metrics are not scored (not rated/ applicable).

NR: Not rated

N/A: Not applicable

[24] This domain does not apply to abiotic studies.

[25] This metric does not apply to abiotic studies.

## C.5 Data Quality Criteria

**Table C-9. Serious Flaws that Would Make Fate Data Unacceptable for Use in the Fate Assessment**

Optimization of the list of serious flaws may occur after pilot calibration exercises.

| Domain Number/ Description | Metric Number | Description of Serious Flaw(s) in Data Source |
|---|---|---|
| 1. Test Substance | 1 | The test substance identity could not be determined from the information provided. |
| | 2 | The nature and quantity of reported impurities were such that study results were unduly influenced by one or more of the impurities. |
| 2. Test Design | 3 | The study did not include or report control groups that consequently made the study unusable (e.g., no positive control data for a non-guideline biodegradation study with a novel media and/or inoculum, reporting 0% removal). |
| | | The vehicle (e.g., oil or carrier solvent) used in the study was likely to unduly influence the study results. |
| | 4 | There were problems with test substance stability, homogeneity, preparation, or storage conditions that had an impact on concentration or dose estimates and interfered with interpretation of study results. |
| 3. Test Conditions | 5 | The test method was not reported or not suitable for the test substance. |
| | 6 | The testing conditions were not reported and sufficient data were not provided to interpret results. |
| | | Testing conditions were not appropriate for the method (e.g., a biodegradation study at temperatures that inhibit the microorganisms) resulting in serious flaws that make the study unusable. |
| | 7 | Critical exposure details across samples or study groups were not reported and these omissions resulted in serious flaws that had a substantial impact on the overall confidence, consequently making the study unusable. |
| | 8 | Equilibrium was not established or reported preventing meaningful interpretation of study results<br>**OR**<br>The system type and design (i.e., static, semi-static, and flow-through; sealed, open) were not capable of appropriately maintaining substance concentrations preventing meaningful interpretation of study results. These are serious flaws that make the study unusable. |
| 4. Test Organisms | 9 | The test organism, species, or inoculum source was not reported. |
| | 10 | The test organism was not reported. |
| 5. Outcome Assessment | 11 | The assessment methodology did not address or report the outcome(s) of interest. |
| | 12 | Serious uncertainties or limitations were identified in sampling methods of the outcome(s) of interest and these were likely to have a substantial impact on the results, resulting in serious flaws which make the study unusable. |
| 6. Confounding / Variable Control | 13 | There were sources of variability and uncertainty in the measurements and statistical techniques or between study groups resulting in serious flaws that make the study unusable. |
| | 14 | Attrition or health outcomes were not reported and this omission was likely to have a substantial impact on study results. |
| | | One or more study groups experienced disproportionate organism attrition or health outcomes that influenced the outcome assessment. |

| Domain Number/ Description | Metric Number | Description of Serious Flaw(s) in Data Source |
|---|---|---|
| 7. Data Presentation and Analysis | 15 | The analytical method used was not suitable for detection of the test substance. |
| | 16 | Statistical methods or kinetic calculations used were likely to provide biased results. |
| 8. Other | 17 | Reported value was completely inconsistent with reference substance data, related physical chemical properties, or analog data, or was otherwise implausible, suggesting that an unidentified serious study deficiency exists. |
| | 18 | The QSAR model did not have a defined endpoint, unambiguous endpoint |
| | | The model performance was not known or $r^2 < 0.7$, $q^2 < 0.5$ or SE > 0.3 (ECHA, 2016). |

## Table C-10. Data Quality Criteria for Fate Data

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 1. Test Substance** | | |
| **Metric 1: Test substance identity**<br>Was the test substance identified definitively? | | |
| High (score = 1) | The test substance was identified definitively (i.e., established nomenclature, CASRN, or structure reported, including information on the specific form tested [particle characteristics for solid-state materials, salt or base, valence state, isomer, etc.] for materials that may vary in form, or submitting company's code name with supporting confirmatory documentation) and the specific form characterized, where applicable. | |
| Medium (score = 2) | The test substance was identified by trade name or other internal designation, but characterization details were omitted that could affect interpretation of study results; however, the omission was not likely to have a substantial impact on the study results. | |
| Low (score = 3) | The test substance was identified; however, it lacked specific characteristics such as stereochemistry or valence state<br>**OR**<br>there were some uncertainties or conflicting information regarding test substance identification or characterization that were likely to have a substantial impact on the study results. | |
| Unacceptable (score = 4) | The test substance identity could not be determined from the information provided (e.g., nomenclature was unclear and CASRN or structure was not reported). This is a serious flaw that makes the study unusable. | |
| Not rated/ applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Metric 2: Test substance purity**<br>Was the source of the test substance reported? If the test substance was synthesized or extracted (as part of the synthesis or from a substrate), was the test substance identity verified by analytical methods? Were the purity, grade or hydration state (e.g., analytical, technical) of the test substance reported? If the test substance was tested as part of a finished or formulated product, was the full chemical composition of the formulation reported? | | |
| High<br>(score = 1) | The source or purity of the test substance was reported or the test substance identity and purity were verified by analytical means (chemical analysis, etc.)<br>**OR**<br>if the test substance was tested as part of a finished or formulated product, the full chemical composition of the formulation was reported<br>**AND**<br>any observed effects were likely due to the nominal test substance itself (e.g., pure, analytical grade, technical grade test substance, or other substances in the formulation were inert, or the other components were inert under the test conditions). | |
| Medium<br>(score = 2) | The test substance source was not reported<br>**AND/OR**<br>the test substance purity was low or not reported (e.g., lack of information on hydration state of a compound introduces uncertainty into concentration calculations); however, the omissions or identified impurities were not likely to have a substantial impact on the study results. | |
| Low<br>(score = 3) | The source and purity of the test substance were not reported or verified by analytical means<br>**OR**<br>The test substance was synthesized or extracted and its identity was not verified by analytical means (i.e., chemical analysis, etc.)<br>**OR**<br>identified impurities were likely to have a substantial impact on study results. | |
| Unacceptable<br>(score = 4) | The nature and quantity of reported impurities were such that study results were unduly influenced by one or more of the impurities. These are serious flaws that make the study unusable. | |
| Not rated/ applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 2. Test** Design | | |
| **Metric 3: Study controls**<br>Was a concurrent negative control or blank group included? Were positive and toxicity controls included? If a vehicle was used, was the control group exposed to the vehicle? Is the selected vehicle unlikely to influence the study results, stability, bioavailability or/toxicity of the test substance? | | |
| High<br>(score = 1) | A concurrent negative control, or blank group, toxicity control, and positive control were included (where applicable)<br>**AND**<br>results from controls were within the ranges specified for test validity (or validity criteria for equivalent or similar tests, if not a guideline test)<br>**AND**<br>a concurrent blank with vehicle (e.g., oil or carrier solvent) was included and the vehicle was not likely to influence the study results (where applicable). | |
| Medium<br>(score = 2) | Some concurrent control group details were not included; however, the lack of data was not likely to have a substantial impact on study results<br>**AND**<br>the vehicle was not likely to influence the study results (where applicable). | |
| Low<br>(score = 3) | Reported results from control group(s) were outside the ranges specified for test validity (or validity criteria for equivalent or similar tests, if not a guideline test)<br>**OR**<br>the vehicle was likely to have a substantial impact on study results. | |
| Unacceptable<br>(score = 4) | The study did not include or report crucial control groups that consequently made the study unusable (e.g., no positive control for a biodegradation study reporting 0% removal)<br>**OR**<br>the vehicle used in the study was likely to unduly influence the study results. These are serious flaws that make the study unusable. | |
| Not rated/ applicable | The study did not require concurrent control groups. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 4: Test substance stability**<br>Did the study characterize and accommodate the test substance stability, homogeneity, preparation, and storage conditions? Were the frequency of preparation and storage conditions appropriate to the test substance stability? | | |
| High<br>(score = 1) | The test substance stability, homogeneity, preparation, and storage conditions were reported (e.g., mixing temperature, stock concentration, stirring methods, centrifugation or filtration), and were appropriate for the study (e.g., a test substance known to degrade in light was stored in dark or amber bottles). | |
| Medium<br>(score = 2) | The test substance stability, homogeneity, preparation or storage conditions were not reported; however, these factors were not likely to influence the test substance or were not likely to have a substantial impact on study results. | |
| Low<br>(score = 3) | The test substance stability, homogeneity, preparation, and storage conditions were not reported and these factors likely influenced the test substance or are likely to have a substantial impact on the study results. | |
| Unacceptable<br>(score = 4) | There were problems with test substance stability, homogeneity, preparation, or storage conditions that had an impact on concentration or dose estimates and interfered with interpretation of study results. These are serious flaws that make the study unusable. | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| Not rated/ applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 3. Test Conditions** | | |
| **Metric 5: Test method suitability**<br>Was the test method reported and suitable for the test material? Was the target chemical tested at concentrations below its aqueous solubility? | | |
| High (score = 1) | The test method was suitable for the test substance<br>**AND**<br>the target chemical was tested at concentrations below its aqueous solubility (when applicable). | |
| Medium (score = 2) | The test method was suitable for the test substance with minor deviations<br>**AND/OR**<br>nominal estimates of media concentrations were provided, but, the levels were not measured or suitable to the study type or outcome(s) of interest<br>**AND**<br>these deviations or omissions were not likely to have a substantial impact on study results. | |
| Low (score = 3) | Applied target chemical concentrations were greater than the aqueous solubility<br>**AND**<br>the deviations were likely to have a substantial impact on the results. | |
| Unacceptable (score = 4) | The test method was not reported or not suitable for the test substance. These deviations or lack of information resulted in serious flaws that make the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 6: Testing conditions**<br>Were the test conditions monitored, reported, and appropriate for the study method (e.g., the temperature range reported, dissolved organic matter, aeration, total organic matter, pH or water hardness reported and maintained throughout the test)? | | |
| High (score = 1) | Testing conditions were monitored, reported, and appropriate for the method. For example, depending on the study, the following conditions were reported:<br>• aerobic/anaerobic conditions reported<br>• dissolved oxygen (DO) measured<br>• redox/electron activity (pE) parameters listed and/or anaerobic conditions otherwise identified (e.g., sulfate reducing, methanogenic, etc.)<br>• pH buffer for studies on the fate of a substance that may exist in ionized form(s) in the pH range of environmental relevance<br>• For studies in aquatic environments, conditions reported separately for both the water and sediment column<br>• For studies in soil, soil type (location if available), moisture level, soil particle size distribution, background SOM (soil organic matter) or OC (organic carbon) content, CEC (cation exchange capacity) or soil pH, soil name (e.g., USDA series) | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| Medium (score = 2) | There were reported deviations or omissions in testing conditions (e.g., temperature was not constant or was not in a standard range for the test but, results can be extrapolated to approximate appropriate temperatures); however, sufficient data were reported to determine that the deviations and omissions were not likely to have a substantial impact on study results. | |
| Low (score = 3) | Inappropriate test conditions for the study method (e.g., temperature fluctuations) and the deviations were likely to have a substantial impact on the results. | |
| Unacceptable (score = 4) | Testing conditions were not reported and data provided were insufficient to interpret results<br>**OR**<br>testing conditions were not appropriate for the method (e.g., a biodegradation study at temperatures that inhibit the microorganisms) resulting in serious flaws that make the study unusable. | |
| Not rated/ applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 7: Testing consistency**<br>Were test conditions established to be consistent across samples or study groups? Were multiple exposures evaluated, where applicable? | | |
| High (score = 1) | Test conditions were consistent across samples or study groups (i.e., same exposure method and timing, comparable particle size characteristics). The conditions of the exposure were documented. | |
| Medium (score = 2) | There were minor inconsistencies in test conditions across samples or study groups<br>**OR**<br>some test conditions across samples or study groups were not reported, but these discrepancies were not likely to have a substantial impact on study results. | |
| Low (score = 3) | There were inconsistencies in test conditions across samples or study groups that are likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | Critical exposure details across samples or study groups were not reported and these omissions resulted in serious flaws that had a substantial impact on the overall confidence, consequently making the study unusable. | |
| Not rated/ applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 8: System type and design***<br>Was equilibrium established? Were the system type and design capable of appropriately maintaining substance concentrations for experimental studies?<br>* For studies of partitioning | | |
| High (score = 1) | Equilibrium was established. The system type and design (i.e., static, semi-static, and flow-through; sealed, open) were capable of appropriately maintaining substance concentrations. | |
| Medium (score = 2) | Equilibrium was not established or reported but this was not likely to have a substantial impact on study results<br>**OR** | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | the system type and design (i.e., static, semi-static, and flow-through; sealed, open) were not capable of appropriately maintaining substance concentrations or not described but the deviation was not likely to have a substantial impact on study results. | |
| Low (score = 3) | -- | |
| Unacceptable (score = 4) | Equilibrium was not established or reported preventing meaningful interpretation of study results<br>**OR**<br>the system type and design (i.e., static, semi-static, and flow-through; sealed, open) were not capable of appropriately maintaining substance concentrations preventing meaningful interpretation of study results. These are serious flaws that make the study unusable. | |
| Not rated/ applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 4. Test Organisms (does not apply to all fate studies)** | | |
| **Metric 9: Test organism – degradation**<br>Was information about the test organism, species or inoculum reported? Were inoculum source, concentration or number of microorganisms, and any pre-conditioning or pre-adaptation procedures reported? Are the test organism, species or inoculum source routinely used for similar study types or outcome(s)* of interest? Were the chosen organisms or inoculum appropriate for the study method or route?<br>* For studies of degradation | | |
| High (score = 1) | The test organism information or inoculum source were reported<br>**AND**<br>the test organism, species, or inoculum are routinely used for similar study types and appropriate (e.g., aerobic microorganisms used for anaerobic biodegradation study) for the study method or route. | |
| Medium (score = 2) | The test organism, species, or inoculum source were reported, but are not routinely used for similar study types; however, the deviation was not likely to have a substantial impact on study results. | |
| Low (score = 3) | The test organism, species, or inoculum source are not routinely used for similar study types or were not appropriate for the evaluation of the specific outcome(s) of interest or route (e.g., genetically modified strains uniquely susceptible or resistant to one or more outcome of interest). In practice, this manifests as using an inappropriate inoculum for the study method (e.g., polyseed capsules instead of activated sludge from a publicly owned treatment works (POTW) for a ready biodegradability test). **OR**<br>an inoculum that was pre-adapted to the test substance was used for a biodegradation rate study<br>**AND**<br>no justification for selection of the test organism was provided. The deviation was likely to have a substantial impact on study results. | |
| Unacceptable (score = 4) | The test organism, species, or inoculum source were not reported. | |
| Not rated/ | | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 10: Test organism – partitioning**<br>Was information about the test organism reported? Was the test organism source known? Is the test organism or species routinely used for similar study types or outcome(s)* of interest?<br>* For studies of partitioning | | |
| High (score = 1) | Test organism information was reported, including species or sex, age, and starting body weight (where applicable)<br>**OR**<br>the test organism was obtained from a reliable or commercial source<br>**AND**<br>the test organism or species is routinely used for similar study types. | |
| Medium (score = 2) | The test organism was obtained from a reliable or commercial source<br>**OR**<br>the test organism or species is routinely used for similar study types; however, one or more additional characteristics of the organisms were not reported (i.e., sex, health status, age, or starting body weight), but these omissions were not likely to have a substantial impact on study results. | |
| Low (score = 3) | The test organism was not obtained from a reliable or commercial source<br>**OR**<br>the test organism or species is not routinely used for similar study types or was not appropriate (i.e., species, life-stage) for the evaluation of the specific outcome(s) of interest (e.g., genetically modified organisms, strain was uniquely susceptible or resistant to one or more outcome of interest)<br>**AND**<br>no justification for selection of the test organism was provided. The deviations were likely to have a substantial impact on study results. | |
| Unacceptable (score = 4) | The test organism information was not reported**.** | |
| Not rated/ applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 5. Outcome Assessment** | | |
| **Metric 11: Outcome* assessment methodology**<br>Did the outcome* assessment methodology address and report the outcome(s)* of interest?<br>* For all fate studies (i.e., degradation, partitioning, etc.) | | |
| High (score = 1) | The outcome assessment methodology addressed or reported the intended outcome(s) of interest. | |
| Medium (score = 2) | There were minor differences between the assessment methodology and the intended outcome assessment (i.e. biodegradation rate not reported; however, degradation products and a degradation pathway were determined)<br>**OR**<br>there was incomplete reporting of outcome assessment methods; however, such differences or absence of details were not likely to be severe or have a substantial impact on the study results. | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| Low (score = 3) | Deficiencies in the outcome assessment methodology of the assessment or reporting were likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | The assessment methodology did not address or report the outcome(s) of interest. This is a serious flaw that makes the study unusable. | |
| Not rated/ applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 12: Sampling adequacy**<br>Were the sampling methods, including timing and frequency, adequate, for the outcome(s)* of interest?<br>* For all fate studies (i.e., degradation, partitioning, etc.) | | |
| High (score = 1) | The study reported the use of sampling methods that address the outcome(s) of interest, and used widely accepted methods/approaches for the chemical and media being analyzed (e.g., sampling equipment, sample storage conditions)<br>**AND**<br>no notable uncertainties or limitations were expected to influence results. | |
| Medium (score = 2) | Minor limitations were identified in sampling methods of the outcome(s) of interest were reported (i.e., the sampling intervals were such that a half-life or other rate could be determined and/or pathways could be defined); however, the limitations were not likely to have a substantial impact on results. | |
| Low (score = 3) | Details regarding sampling methods of the outcome(s) were not fully reported, and the omissions were likely to have a substantial impact on study results<br>**AND/OR**<br>an accepted method/approach for the chemical and media being analyzed was not used (e.g., inappropriate sampling equipment, improper storage conditions). | |
| Unacceptable (score = 4) | Serious uncertainties or limitations were identified in sampling methods of the outcome(s) of interest and these were likely to have a substantial impact on the results, resulting in serious flaws which make the study unusable. | |
| Not rated/ applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 6. Confounding/Variable Control** | | |
| **Metric 13: Confounding variables**<br>Were sources of variability or uncertainty noted in the study? Did confounding differences among the study groups influence the outcome* assessment?<br>* For all fate studies (i.e., degradation, partitioning, etc.) | | |
| High (score = 1) | Sources of variability and uncertainty in the measurements, and statistical techniques and between study groups (if applicable) were considered and accounted for in data evaluation<br>**AND**<br>all reported variability or uncertainty was not likely to influence the outcome assessment. | |
| Medium (score = 2) | Sources of variability and uncertainty in the measurements and statistical techniques and between study groups (if applicable) were reported in the study<br>**AND** | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | the differences in the measurements and statistical techniques and between study groups were considered or accounted for in data evaluation with minor deviations or omissions<br>**AND**<br>the minor deviations or omissions were not likely to have a substantial impact on study results. | |
| Low (score = 3) | Sources of variability and uncertainty in the measurements and statistical techniques and between study groups (if applicable) were not considered or accounted for in data evaluation resulting in some uncertainty<br>**AND**<br>there is concern that variability or uncertainty was likely to have a substantial impact on the results. | |
| Unacceptable (score = 4) | There were sources of variability and uncertainty in the measurements and statistical techniques or between study groups resulting in serious flaws that make the study unusable. | |
| Not rated/ applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 14: Outcomes unrelated to exposure**<br>Were there differences among the study groups in organism attrition or health outcomes unrelated to exposure to the test substance that influenced the outcome* assessment?<br>* For studies of partitioning in organisms | | |
| High (score = 1) | There were multiple study groups, and there were no differences among the study groups in organism attrition or health outcomes (i.e., unexplained mortality) that influenced the outcome assessment. | |
| Medium (score = 2) | Attrition or health outcomes were not reported; however, this omission was not likely to have a substantial impact on study results. | |
| Low (score = 3) | -- | |
| Unacceptable (score = 4) | Attrition or health outcomes were not reported and this omission was likely to have a substantial impact on study results<br>**OR**<br>one or more study groups experienced disproportionate organism attrition or health outcomes that influenced the outcome assessment (e.g., pH drastically decreased for one treatment and resulted in pH effects versus effects from the chemical being tested). This is a serious flaw that makes the study unusable. | |
| Not rated/ applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 7. Data Presentation and Analysis** | | |
| **Metric 15: Data reporting**<br>Were the target chemical and transformation product(s) concentrations reported? Was the extraction efficiency, percent recovery, and/or mass balance reported? Was the analytical method used suitable for detection and capable of identifying or quantifying the parent and transformation products? Was sufficient evidence presented to confirm that the disappearance of the parent compound was not due to some other process (e.g., sorption)? | | |
| High (score = 1) | The target chemical and transformation product(s) concentrations (if required), extraction efficiency, percent recovery, or mass balance were reported<br>**AND**<br>analytical methods used were suitable for detection and quantification of the target chemical and transformation product(s) (if required)<br>**AND**<br>for degradation studies, sufficient evidence was presented to confirm that parent compound disappearance was not likely due to some other process<br>**AND**<br>the lipid content or the lipid-normalized bioconcentration factor (BCF) was reported for BCF studies<br>**AND**<br>detection limits were sensitive enough to follow decline of parent and formation of the metabolites; structures of metabolites were given. Volatile products were trapped and identified. | |
| Medium (score = 2) | The target chemical and transformation product(s) concentrations, extraction efficiency, percent recovery, or mass balance were not reported; however, these omissions were not likely to have a substantial impact on study results<br>**OR**<br>the lipid content or lipid normalized BCF was not reported for BCF studies, but these deficiencies or omissions were not likely to have a substantial impact on study results. | |
| Low (score = 3) | There was insufficient evidence presented to confirm that parent compound disappearance was not likely due to some other process<br>**OR**<br>concentrations of the target chemical or transformation product(s), extraction efficiency, percent recovery, or mass balance were not measured or reported, preventing meaningful interpretation of study results<br>**OR**<br>lipid normalized BCF and lipid content were not measured or reported, preventing meaningful interpretation of study results<br>**AND**<br>these omissions were likely to have a substantial impact on study results. | |
| Unacceptable (score = 4) | The analytical method used was not suitable for detection of the test substance. | |
| Not rated/ applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Metric 16. Statistical methods & kinetic calculations**<br>Were statistical methods or kinetic calculations clearly described and consistent? | | |
| High (score = 1) | Statistical methods or kinetic calculations were clearly described and address the dataset(s). | |
| Medium (score = 2) | Statistical analysis used an outdated, unusual, or non-robust method; however, the study results were likely to be similar to those obtained using a current/ more robust method<br>**OR**<br>kinetic calculations were not clearly described<br>**AND**<br>these differences were not likely to have a substantial impact on study results.<br>**OR**<br>No statistical analyses were conducted; however, sufficient data were provided to conduct an independent statistical analysis. | |
| Low (score = 3) | Statistical analysis or kinetic calculations were not conducted or were not described clearly<br>**AND**<br>the lack of information was likely to have a substantial impact on study results. | |
| Unacceptable (score = 4) | Statistical methods or kinetic calculations used were likely to provide biased results. These are serious flaws that make the study unusable. | |
| Not rated/ applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 8. Other** | | |
| **Metric 17.** Verification or Plausibility of Results<br>Were the study results reasonable? Was anything not covered in the evaluation questions? | | |
| High (score = 1) | Reported values were within expected range as defined by reference substance(s)<br>**OR**<br>reported values were consistent with related physical chemical properties (e.g., considering $K_{OW}$, pKa, vapor pressure, etc.). | |
| Medium (score = 2) | The study results were reasonable<br>**AND**<br>the reported value was outside expected range, as defined by reference substance(s) or in relation to related physical chemical properties (e.g., considering $K_{OW}$, vapor pressure, etc.); however, no serious study deficiencies were identified, and the value was plausible. | |
| Low (score = 3) | Due to limited information, evaluation of the reasonableness of the study results was not possible (i.e., reference substance(s) not used or physical-chemical properties unknown and unable to be estimated). | |
| Unacceptable (score = 4) | Reported value was completely inconsistent with reference substance data, related physical chemical properties, analog data, or otherwise implausible, suggesting that an unidentified serious study deficiency exists. These are serious flaws that make the study unusable. | |
| Not rated/ applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | *relevance]* | |
| **Metric 18. QSAR Models**<br>Did the QSAR model have a defined, unambiguous endpoint and appropriate measures of goodness-of-fit, robustness and predictivity, defined by $r^2 > 0.7$, $q^2 > 0.5$ and SE < 0.3, where $r^2$ is the correlation coefficient, $q^2$ is the cross-validated correlation coefficient and SE is the standard error (ECHA, 2016)? | | |
| High (score = 1) | The QSAR model had a defined, unambiguous endpoint<br>**AND**<br>the model performance was known and $r^2 > 0.7$, $q^2 > 0.5$, and SE < 0.3 (ECHA, 2016). | |
| Medium (score = 2) | Model endpoint is broad (i.e., overall persistence)<br>**AND/OR**<br>non-transparent and difficult to reproduce methods were used to build the (Q)SAR model (e.g. artificial neural networks using many structural descriptors). | |
| Low (score = 3) | Algorithm is not publicly available to verify or reproduce the predictions<br>**AND/OR**<br>statistics on the external validation set are unavailable. | |
| Unacceptable (score = 4) | The model performance was either not known or $r^2 < 0.7$, $q^2 < 0.5$ or SE > 0.3 (ECHA, 2016). These are serious flaws that make the study unusable. | |
| Not rated/ applicable | A QSAR model was not reported. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

## C.6 References


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2. ECHA. (2016). Practical guide. How to use and report (Q)SARs. Version 3.1. July 2016. https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/4262860.
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# APPENDIX D: DATA QUALITY CRITERIA FOR OCCUPATIONAL EXPOSURE AND RELEASE DATA

## D.1 Types of Environmental Release and Occupational Exposure Data Sources

Environmental release and occupational exposure data and information may be found in a variety of sources, and most are not found in controlled studies. The evaluation of this data and information requires approaches that differ from evaluation of controlled studies. These differences are inherently covered by the tables for the different sources (e.g., all tables in section D.7). In these tables, some metrics are shown *as not applicable* and will not be scored. Other metrics may have criteria that reflect differences in the documentation of background information about the data or information, especially if the data or information are not collected from a controlled study that is fully documented.

The data quality will be evaluated for five different types of data sources that contain environmental release and occupational exposure data: (1) monitoring data from various sources (e.g., journal articles, government reports, public databases); (2) release data from various sources; (3) published models for exposures or releases; (4) completed exposure or risk assessments; (5) and reports for data or information other than exposure or release data. Definitions for these data types are shown below in Table D-1; note that these data types do not include epidemiology sources that lack occupational exposure data.

**Table D-1. Types of Occupational Exposure and Environmental Release Data Sources**

| Type of Data Source | Definition |
|---|---|
| Monitoring Data | Measured occupational exposures, which include, but not limited to, personal inhalation exposure monitoring, area/stationary airborne concentration monitoring, and surface wipe sampling. |
| Environmental Release Data | Measured or calculated quantities of chemical or chemical substance released across a facility fence line into an environmental media or waste management/disposal method. |
| Published Models for Exposures or Releases | Published models used to calculate occupational exposures or environmental releases. |
| Completed Exposure or Risk Assessments | Completed exposure or risk assessments containing a broad range of data types (i.e., exposure concentrations, doses, estimated values, exposure factors). Examples: ATSDR assessments, risk assessments completed by other countries. |
| Reports for Data or Information Other than Exposure or Release Data | Data sources used for data or information other than exposure or release data, such as process description information. Example: Kirk-Othmer Encyclopedia of Chemical Technology |

Note:
ATSDR = Agency for Toxic Substances and Disease Registry

## D.2 Data Quality Evaluation Domains

The data sources will be evaluated against the following four data quality evaluation domains: (1) reliability; (2) representativeness; (3) accessibility/clarity; (4) and variability and uncertainty. These domains, as defined in Table D-2, address elements of TSCA Science Standards 26(h)(1) through 26(h)(5).

**Table D-2. Data Evaluation Domains and Definitions**

| Evaluation Domain | Definition |
|---|---|
| Reliability | The inherent property of a study or data, which includes the use of well-founded scientific approaches, the avoidance of bias within the study or data collection design and faithful study or data collection conduct and documentation (ECHA, 2011b). |
| Representativeness | The data reported address exposure scenarios (e.g., sources, pathways, routes, receptors) that are relevant to the assessment. |
| Accessibility/Clarity | The data and supporting information are accessible and clearly documented. |
| Variability and Uncertainty | The data describe variability and uncertainty (quantitative and qualitative) or the procedures, measures, methods, or models are evaluated and characterized. |

## D.3 Data Quality Evaluation Metrics

Table D-3 provides a summary of the quality metrics for each data type. EPA may adjust these quality metrics as more experience is acquired with the evaluation tools to support fit-for-purpose TSCA risk evaluations. If this happens, EPA will document the changes to the evaluation tool.

**Table D-3. Summary of Quality Metrics for the Five Types of Data Sources**

| Type of Data Source | Overall Number of Metrics | Metric Names |
|---|---|---|
| Monitoring Data | 7 | Sampling and analytical methodology; Geographic Scope; Applicability; Temporal representativeness; Sample size; Metadata completeness informing the Accessibility and Clarity domain; Metadata completeness informing the Variability and Uncertainty domain |
| Environmental Release Data | 7 | Methodology; Geographic Scope; Applicability; Temporal representativeness; Sample size; Metadata completeness informing the Accessibility and Clarity domain; Metadata completeness informing the Variability and Uncertainty domain |
| Published Models for Exposures or Releases | Up to 6 | Methodology; Geographic Scope; Applicability; Temporal representativeness; Metadata completeness informing the Accessibility and Clarity domain; Metadata completeness informing the Variability and Uncertainty domain |
| Completed Exposure or Risk Assessments | Up to 7 | Methodology; Geographic Scope; Applicability; Temporal representativeness; Sample Size; Metadata completeness informing the Accessibility and Clarity domain; Metadata completeness informing the Variability and Uncertainty domain |
| Reports for Data or Information Other than Exposure or Release Data | Up to 7 | Methodology; Geographic Scope; Applicability; Temporal representativeness; Sample size; Metadata completeness informing the Accessibility and Clarity domain; Metadata completeness informing the Variability and Uncertainty domain |

Notes:

- *Number of Metrics Overall* indicates the number of metrics across evaluation domains.
- Metadata are data that provide descriptive information about other data. Examples include the date of the data, the author and author's affiliation of a report or study, and the type of exposure monitoring sample (e.g., personal breathing zone sample).

## D.4 Scoring Method and Determination of Overall Data Quality Level

Appendix A provides information about the evaluation method that will be applied across the various data/information sources being assessed to support TSCA risk evaluations. This section provides details about the scoring system that will be applied to occupational exposure and release data/information, including the weighting factors assigned to each metric score of each domain.

Some metrics may be given greater weights than others, if they are regarded as key or critical metrics, based on expert judgment (Moermond et al., 2016a). Thus, EPA will use a weighting approach to reflect that some metrics are more important that others when assessing the overall quality of the data.

### D.4.1 Weighting Factors

EPA developed the weighting factors by beginning with an even weight for each metric. In other words, there are seven metrics for many data types; thus, each weighting factor began with a value of 1. Then, EPA used expert judgement to determine the importance of a particular metric relative to others. Following the prioritization of criteria, each metric was assigned a weighting factor of 1 or 2, with the higher weighting factor (2) given to metrics deemed critical for the evaluation.

EPA judged applicability and temporal representativeness to be the most important towards overall confidence, and these two metrics were determined to be twice as important as other metrics (weighting factors assigned a value of 2).

- Applicability is one of the most important metrics for occupational data because occupational settings have a diverse set of determinants of exposure and release. Therefore, when evaluating occupational data, it is important for EPA's purposes that those data capture as many of the determinants of exposure and release that apply to the condition of use of interest as possible.

- Representativeness of current workplace practices is the other most important metric for occupational data because industry and business practices are expected to change with time. Therefore, when evaluating occupational data, it is important for EPA's purposes that those data represent current day practices.

Table D-4 summarizes the weighting factor for each metric, the range of possible scores for each metric, and the range of resulting weighted scores, which are the products of the weighting factor and the metric score, if all of the metrics are scored for a particular data type.

**Table D-4. Metric Weighting Factors and Range of Weighted Metric Scores for Scoring the Quality of Environmental Release and Occupational Data**

| Domain | Metric | Metric Weighting Factor | Metric Score (range of possible values) | Weighted Metric Score (range of possible values) |
|---|---|---|---|---|
| Reliability | Methodology | 1 | 1 to 3 | 1 to 3 |
| Representativeness | Applicability | 2 | 1 to 3 | 2 to 6 |
| | Geographic Scope | 1 | 1 to 3 | 1 to 3 |
| | Temporal representativeness | 2 | 1 to 3 | 2 to 6 |
| | Sample Size | 1 | 1 to 3 | 1 to 3 |
| Accessibility / Clarity | Metadata Completeness | 1 | 1 to 3 | 1 to 3 |
| Variability and Uncertainty | Metadata Completeness | 1 | 1 to 3 | 1 to 3 |
| Sum (if all metrics scored) [a] | | 9 | -- | 9 to 27 |
| Range of Overall Scores, where Overall Score = ∑(Metric Score x Metric Weighting Factor)/∑(Metric Weighting Factors) | | | | 9/9=1; 27/9=3 |

| High | Medium | Low |
|---|---|---|
| ≥1 and <1.7 | ≥1.7 and <2.3 | ≥2.3 and ≤3 |

Range of overall score = 1 to 3

Note:
[a] The sum of weighting factors and the sum of the weighted scores will differ if some metrics are not scored (not applicable).

### D.4.2 Calculation of Overall Study Score

To determine the overall study score, the first step is to multiply the score for each metric (1, 2, or 3 for high, medium, or low confidence, respectively) by the appropriate weighting factor, as shown in Table C-4, to obtain a weighted metric score. The weighted metric scores are then summed and divided by the sum of the weighting factors (for all metrics that are scored) to obtain an overall study score between 1 and 3. The equation for calculating the overall score is shown below:

$$\textit{Overall Score (range of 1 to 3)} = \sum (\textit{Metric Score} \times \textit{Weighting Factor}) / \sum (\textit{Weighting Factors})$$

EPA/OPPT plans to use data with an overall confidence rating of *High*, *Medium*, or *Low* to quantitatively or qualitatively support the risk evaluations, but does not plan to use data rated *Unacceptable*. If any single metric for a data source has a score of *Unacceptable*, then the overall confidence of the data is automatically rated with an overall confidence score of 4. An *Unacceptable* score means that serious flaws are noted in the domain metric that consequently make the data unusable (or invalid). There is no need to calculate weighted scores for metrics that score less than four when serious flaws are identified in one of the metrics, which receives a score of four. Therefore, Table D-4 does not include metric scores of four.

If any metric is not applicable to a data set, that metric is not rated. In that case, the metric is not included in the scoring. In the case that the source type contains more than one data set or information element, the reviewer provides an overall confidence score for each data set or information element that is found in the source. Therefore, it is possible that a source may have more than one overall quality/ confidence score.

Table D-5 provides an example of scoring when a particular metric is not rated. In this example, the sample size metric under the representativeness domain is not applicable for published models.

Detailed tables showing quality criteria for the metrics are provided in Tables D-10 through D-19 for each data type, including separate tables which summarize the serious flaws which would make the data unacceptable for use in the environmental release and occupational exposure assessment.

**Table D-5. Scoring Example for Published Models where Sample Size is Not Applicable**

| Domain | Metric | Metric Score | Metric Weighting Factor | Weighted Metric Score |
|---|---|---|---|---|
| Reliability | Methodology | 2 | 1 | 2 |
| Representativeness | Applicability | 1 | 2 | 2 |
| | Geographic Scope | 2 | 1 | 2 |
| | Temporal representativeness | 1 | 2 | 2 |
| | Sample Size | NR | N/A | N/A |
| Accessibility / Clarity | Metadata Completeness | 2 | 1 | 2 |
| Variability and Uncertainty | Metadata Completeness | 3 | 1 | 3 |
| | | | Sum= 8 | Sum= 13 |
| Range of Overall Scores, where Overall Score = ∑(Metric Score x Metric Weighting Factor)/∑(Metric Weighting Factors)<br>High: ≥1 and <1.7 \| Medium: ≥1.7 and <2.3 \| Low: ≥2.3 and ≤3 | | | | 13/8=1.6<br>1.6 (High) |

Notes:
N/A: Not applicable
NR: Not rated

## D.5 Data Sources Frequently Used in Occupational Exposure and Release Assessments

A key component in many of the metric criteria is if the methodology is sound and widely accepted (i.e., from a source generally using sound methods and/or approaches). Table D-7 provides examples of data sources that EPA frequently uses to support the data needs of occupational exposure and release assessments. EPA notes that some data sources may use or include data or information that are not of high quality but are still acceptable (e.g., medium or low quality) for use in risk evaluation. The methodologies in the individual studies under review will still be assessed in relation to chemical- and scenario- specific considerations. Thus, the data source may still receive quality scores ranging from *Unacceptable* to *High* even though the

data source used a methodology from a source commonly known to use sound methods and/or approaches. EPA may determine standard quality ratings for some of these sources as more experience is acquired with TSCA risk evaluations.

**Table D-6. Examples of Data Sources Frequently Used in Occupational Exposure and Release Data**

| Data Source | |
|---|---|
| U.S. EPA | Chemical Data Reporting (CDR) |
| | High Production Volume (HPV) Challenge Submissions |
| | Extra HPV Program Submissions |
| | EPA Existing Chemicals Engineering Files |
| | EPA Generic Scenarios |
| | Toxics Release Inventory (TRI) |
| | National Emissions Inventory (NEI) |
| | Office of Water |
| | Office of Air |
| | Office of Enforcement and Compliance Assistance Sector Notebooks |
| | AP-42 |
| | Other EPA Programs (e.g., Design for Environment) |
| Occupational Safety and Health Administration (OSHA) | |
| National Institute of Occupational Safety and Health (NIOSH) | |
| American Conference of Governmental Industrial Hygienists (ACGIH) | |
| Agency for Toxic Substances and Disease Registry (ATSDR) | |
| Other federal agencies (e.g., Department of Defense, Department of Energy) | |
| Organisation for Economic Co-operation and Development (OECD) | Screening Information Dataset (SIDS) |
| | Emission Scenario Documents (ESDs) |
| | Other Programs |
| Environment Canada | Canadian Pollution Prevention Information Clearinghouse |
| | Other Programs |
| U.S. Census Bureau | North American Industry Classification System (NAICS) Definitions |
| | County Business Patterns |
| | Annual Survey of Manufacturers |
| | Current Industrial Reports |
| | Economic Census |
| Bureau of Labor Statistics (BLS) | |
| States (e.g., North Carolina Division of Pollution Prevention and Environmental Assistance) | |
| Kirk-Othmer Encyclopedia of Chemical Technology | |
| Hazardous Substances Data Bank (HSDB) | |
| National Library of Medicine's HazMap | |

Note: The list in this table is not intended to be comprehensive but to show examples used by EPA/OPPT in the past.

## D.6 Data Extraction Templates to Assist the Data Quality Evaluation

The reviewer will extract the data or information element from the source into the data extraction table. Tables D-7, D-8, and D-9 are examples of data extraction and evaluation templates. The tables consist of the key data needs elements for occupational exposures and environmental releases, which accompany the inclusion criteria for full text screening as shown in the TSCA problem formulation documents, and also the evaluation elements described above.

For each data quality evaluation metric, the reviewer will document relevant metadata in the metadata column and then provide a score, or a notation of not rated or not applicable, in the scoring column based on the quality criteria of the metrics provided in Tables D-11 through D-20. Metadata are data or information that describe the collected data and include, but are not limited to, the following:

- Number of samples collected by authors in a monitoring study;
- Number of sites or workers included in a survey;
- Full bibliographic information of the data source;
- Date of the data source; and
- Date of the data within the data source (for example, an article published in 2015 may cite data from 2000).

After scorings are complete, the reviewer calculates the overall confidence score and provides the corresponding bin (*High, Medium, Low*, or *Unacceptable*). If the source contains more than one data or information element, the reviewer provides an overall confidence rating for each data or information element that is found in the source. Therefore, it is possible that a source may have more than one data or information set or type and associated overall confidence scores.

**Table D-7. Data Extraction and Evaluation Template for General Life Cycle and Facility Data**

| | | |
|---|---|---|
| **Data Source (HERO ID)** | | |
| **General Life Cycle and Facility Data (note: these apply to both occupational exposures and environmental releases)** | **Life Cycle Stage** | |
| | **Life Cycle Description (Subcategory of Use)** | |
| | **Process Description** | |
| | **Total Annual U.S. Volume (and % of PV)** | |
| | **Number of Sites** | |
| | **Batch Size** | |
| | **Operating Days per Year and Batches per Day** | |
| | **Site Daily Throughput** | |
| | **Possible Physical Form** | |
| | **Chemical Concentration** | |
| **Data Quality Evaluation** | **Domain 1: Reliability** | |
| | Methodology | Score |
| | | Associated Meta Data and Rationale for Score |
| | **Domain 2: Representativeness** | |
| | Geographic Scope | Score |
| | | Associated Meta Data and Rationale for Score |
| | Applicability | Score |
| | | Associated Meta Data and Rationale for Score |
| | Temporal representativeness | Score |
| | | Associated Meta Data and Rationale for Score |
| | Sample Size | Score |
| | | Associated Meta Data and Rationale for Score |
| | **Domain 3. Accessibility / Clarity** | |
| | Metadata Completeness | Score |
| | | Associated Meta Data and Rationale for Score |
| | **Domain 4. Variability and Uncertainty** | |
| | Metadata Completeness | Score |
| | | Associated Meta Data and Rationale for Score |
| | **Overall Confidence Score** | |

## Table D-8. Data Extraction and Evaluation Template for Occupational Exposure Data

| | | |
|---|---|---|
| **Data Source (HERO ID)** | | |
| **Occupational Exposure Data** | Life Cycle Stage | |
| | Physical Form | |
| | Route of Exposure | |
| | Exposure Concentration (Unit) | |
| | Number of Samples | |
| | Number of Sites | |
| | Type of Measurement (e.g., TWA, STEL) or Method (e.g., modeling) | |
| | Worker Activity (or source of exposure if stationary sampling) or Job Description | |
| | Number of Workers | |
| | Type of Sampling (e.g., personal - pump/ passive, stationary) | |
| | Sampling Location/ Key Environmental Factors (e.g., temperature, humidity) | |
| | Exposure Duration | |
| | Exposure Frequency | |
| | Bulk and Dust Particle Size Distribution | |
| | Engineering Control & % Exposure Reduction | |
| | Personal Protective Equipment (PPE) | |
| | Analytic Method | |
| **Data Quality Evaluation** | **Domain 1: Reliability** | |
| | Methodology | Score |
| | | Associated Meta Data and Rationale for Score |
| | **Domain 2: Representativeness** | |
| | Geographic Scope | Score |
| | | Associated Meta Data and Rationale for Score |
| | Applicability | Score |
| | | Associated Meta Data and Rationale for Score |
| | Temporal representativeness | Score |
| | | Associated Meta Data and Rationale for Score |
| | Sample Size | Score |
| | | Associated Meta Data and Rationale for Score |
| | **Domain 3. Accessibility / Clarity** | |
| | Metadata Completeness | Score |
| | | Associated Meta Data and Rationale for Score |
| | **Domain 4. Variability and Uncertainty** | |
| | Metadata Completeness | Score |
| | | Associated Meta Data and Rationale for Score |
| | **Overall Confidence Score** | |

## Table D-9. Data Extraction and Evaluation Template for Environmental Release Data

| | | |
|---|---|---|
| **Data Source (HERO ID)** | | |
| **Environmental Release Data** | Life Cycle Stage | |
| | Release Source (at the process- or unit-level with the type of waste) | |
| | Disposal / Treatment Method | |
| | Environmental Media | |
| | Release or Emission Factor | |
| | Release Estimation Method | |
| | Daily and Annual Release Quantity | (kg/day) |
| | | (kg/yr) |
| | Release Days per Year | |
| | Number of Sites | |
| | Waste Treatment Method | |
| | Pollution Prevention / Control & %Efficiency | |
| **Data Quality Evaluation** | **Domain 1: Reliability** | |
| | Methodology | Score |
| | | Associated Meta Data and Rationale for Score |
| | **Domain 2: Representativeness** | |
| | Geographic Scope | Score |
| | | Associated Meta Data and Rationale for Score |
| | Applicability | Score |
| | | Associated Meta Data and Rationale for Score |
| | Temporal representativeness | Score |
| | | Associated Meta Data and Rationale for Score |
| | Sample Size | Score |
| | | Associated Meta Data and Rationale for Score |
| | **Domain 3. Accessibility / Clarity** | |
| | Metadata Completeness | Score |
| | | Associated Meta Data and Rationale for Score |
| | **Domain 4. Variability and Uncertainty** | |
| | Metadata Completeness | Score |
| | | Associated Meta Data and Rationale for Score |
| | **Overall Confidence Score** | |

## D.7 Data Quality Criteria

This section presents tables showing quality criteria for the metrics for each data type, including separate tables which summarize the serious flaws which would make the data unacceptable for use in the environmental release and occupational exposure assessment. The overall data confidence level is automatically rated as *Unacceptable* if any single metric for a data set has a score of 4, or serious flaws that would make the data unusable (or invalid) for the environmental release and occupational exposure assessment. If the source type contains more than one data set or information element, the review provides an overall confidence score for each data set or information element that is found in the source. Therefore, it is possible that a source may have more than one overall quality/ confidence score.

### D.7.1 Monitoring Data

The general approach for setting the criteria for an unacceptable rating is to only assign an unacceptable rating when EPA can confirm that the data or information is unacceptable. If the data source lacks documentation of needed metadata, EPA will not rate the metric as unacceptable but will rate it as low. The reason for this approach is to avoid omitting potentially valid data or information since occupational exposure and release data are often sparse. EPA will not use data/information that exhibit serious flaws as described in Table D-10.

**Table D-10. Serious Flaws that Would Make Monitoring Data Unacceptable for Use in the Environmental Release and Occupational Exposure Assessment**

Optimization of the list of serious flaws may occur after pilot calibration exercises.

| Domain | Metric | Description of Serious Flaw(s) in Data |
|---|---|---|
| Reliability | Sampling and Analytical Methodology | Sampling or analytical methodology is specified and EPA has information that indicates the methodology is unacceptable. |
| Representativeness | Geographic Scope | This metric does not have an unacceptable criterion since no geographic location is known to have unacceptable data. |
| | Applicability | The data are from an occupational or non-occupational scenario that does not apply to any occupational scenario within the scope of the risk evaluation. |
| | Temporal representativeness | Known factors (e.g., new and completely different process or equipment) are so different as to make outdated information unacceptable. |
| | Sample Size | This metric does not have an unacceptable criterion. |
| Accessibility / Clarity | Metadata Completeness | Monitoring data do not include any needed metadata to understand what the data represent and are not usable in the risk evaluation. |
| Variability and Uncertainty | Metadata Completeness | This metric does not have an unacceptable criterion. |

**Table D-11. Evaluation Criteria for Monitoring Data**

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 1. Reliability** | | |
| **Metric 1. Sampling and Analytical Methodology** | | |
| High (score = 1) | Sampling or analytical methodology is an approved OSHA or NIOSH method or is well described and found to be equivalent to approved OSHA or NIOSH methods. | |
| Medium (score = 2) | Sampling or analytical methodology is not equivalent to an approved OSHA or NIOSH method and EPA review of information indicates the methodology is acceptable. Differences in methods are not expected to lead to lower quality data. | |
| Low (score = 3) | Sampling or analytical methodology is not specified. | |
| Unacceptable (score = 4) | Sampling or analytical methodology is specified and EPA has information that indicates the methodology is unacceptable. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 2. Representative** | | |
| **Metric 2. Geographic Scope** | | |
| High (score = 1) | The data are from the United States and are representative of the industry being evaluated. | |
| Medium (score = 2) | The data are from an OECD country. other than the U.S., and locality-specific factors (e.g., potential differences in regulatory occupational exposure limits, industry/ process technologies) may impact exposures relative to the U.S. | |
| Low (score = 3) | The data are from a non-OECD country, and locality-specific factors (e.g., potentially greater differences in regulatory occupational exposure limits, industry/ process technologies) may impact exposures relative to the U.S., or the country of origin is not specified. | |
| Unacceptable (score = 4) | This metric does not have an unacceptable criterion since no geographic location is known to have unacceptable data. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 3. Applicability** | | |
| High (score = 1) | The data are for an occupational scenario within the scope of the risk evaluation. | |
| Medium (score = 2) | The data are for an occupational scenario that is similar to an occupational scenario within the scope of the risk evaluation, in terms of the type of industry, operations, and work activities. | |
| Low (score = 3) | The data are for a non-occupational scenario that is similar to an occupational scenario within the scope of the risk evaluation, such as a consumer DIY scenario that is similar to a worker scenario. | |
| Unacceptable (score = 4) | The data are from an occupational or non-occupational scenario that does not apply to any occupational scenario within the scope of the risk evaluation. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Metric 4. Temporal representativeness** | | |
| High (score = 1) | The operations, equipment, and worker activities associated with the data are expected to be representative of current operations, equipment, and activities. The monitoring data were collected after the most recent permissible exposure limit (PEL) establishment or update or are generally, no more than 10 years old, whichever is shorter. If no PEL is established, the data are no more than 10 years old. Metadata on the operations, equipment, and worker activities associated with the data show that the data should be representative of current operations, equipment, and activities. | |
| Medium (score = 2) | Operations, equipment, and worker activities are expected to be reasonably representative of current conditions. The monitoring data were collected after the most recent PEL establishment or update but are generally more than 10 years old. If no PEL is established, the data are more than 10 years but generally, no more than 20 years old. | |
| Low (score = 3) | Metadata on the operations, equipment, and worker activities associated with the data show that the data agree representative of outdated operations, equipment, and activities rather than current operations, equipment, and worker activities. The data were collected before the most recent PEL establishment or update or are more than 20 years old if no PEL is established. | |
| Unacceptable (score = 4) | Known factors (e.g., new and completely different process or equipment) are so different as to make outdated information unacceptable. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 5. Sample Size** | | |
| High (score = 1) | Statistical distribution of samples is fully characterized. | |
| Medium (score = 2) | Distribution of samples is characterized by a range with uncertain statistics. | |
| Low (score = 3) | Distribution of samples is qualitative or characterized by no statistics. | |
| Unacceptable (score = 4) | This metric does not have an unacceptable criterion. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 3. Accessibility / Clarity** | | |
| **Metric 6. Metadata Completeness** | | |
| High (score = 1) | Monitoring data include all associated metadata, including sample types, exposure types, sample durations, exposure durations worker activities, and exposure frequency. | |
| Medium (score = 2) | Monitoring data include most critical metadata, such as sample type and exposure type, but lacks additional metadata, such as sample durations, exposure durations, exposure frequency, and/or worker activities. | |
| Low (score = 3) | Monitoring data include sample type (e.g., personal breathing zone) but no other metadata. | |
| Unacceptable (score = 4) | Monitoring data do not include any needed metadata to understand what the data represent and are not usable in the risk evaluation. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 4. Variability and Uncertainty** | | |
| **Metric 7. Variability and Uncertainty** | | |
| High (score = 1) | The monitoring study addresses variability in the determinants of exposure for the sampled site or sector. The monitoring study addresses uncertainty in the exposure estimates or uncertainty can be determined from the sampling and analytical method. | |
| Medium (score = 2) | The monitoring study provides only limited discussion of the variability in the determinants of exposure for the sampled site or sector. The monitoring study provides only limited discussion of the uncertainty in the exposure estimates. | |
| Low (score = 3) | The monitoring study does not address variability or uncertainty. | |
| Unacceptable (score = 4) | This metric does not have an unacceptable criterion. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

Notes:
OSHA = Occupational Safety and Health Administration
NIOSH = National Institute for Occupational Safety and Health
OECD = Organisation for Economic Co-operation and Development
PEL = Permissible exposure limit

### D.7.2 Environmental Release Data

The general approach for setting the criteria for an unacceptable rating is to only assign an unacceptable rating when EPA can confirm that the data or information is unacceptable. If the data source lacks documentation of needed metadata, EPA will not rate the metric as unacceptable but will rate it as low. The reason for this approach is to avoid omitting potentially valid data or information since occupational exposure and release data are often sparse. EPA will not use data/information from data sources that exhibit serious flaws as described in Table D-12.

**Table D-12. Serious Flaws that Would Make Environmental Release Data Unacceptable for Use in the Environmental Release Assessment**

Optimization of the list of serious flaws may occur after calibrating evaluation tool during pilot exercise.

| Domain | Metric | Description of Serious Flaw(s) in Data Source |
|---|---|---|
| Reliability | Methodology | The release data methodology is specified and EPA has information that indicates the methodology is unacceptable. |
| Representativeness | Geographic Scope | This metric does not have an unacceptable criterion since no geographic location is known to have unacceptable data. |
| | Applicability | The release data are from an occupational or non-occupational scenario that does not apply to any occupational scenario within the scope of the risk evaluation. |
| | Temporal representativeness | Known factors (e.g., new and completely different process or equipment) are so different as to make outdated information unacceptable. |
| | Sample Size | EPA has information that indicates the samples are not expected to represent the assessed release. |
| Accessibility / Clarity | Metadata Completeness | Release data do not include any needed metadata to understand what the data represent and are not usable in the risk evaluation. |
| Variability and Uncertainty | Metadata Completeness | This metric does not have an unacceptable criterion. |

**Table D-13. Evaluation Criteria for Environmental Release Data**

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 1. Reliability** | | |
| **Metric 1. Methodology** | | |
| High (score = 1) | The release data methodology is known or expected (see section D.5 and Table D-6) to be accurate and is known to cover all release sources at the site. | |
| Medium (score = 2) | The release data methodology is known or expected to be accurate (e.g., see section D.5 and Table D-6) but may not cover all release sources at the site. | |
| Low (score = 3) | The release data methodology is not specified. | |
| Unacceptable (score = 4) | The release data methodology is specified and EPA has information that indicates the methodology is unacceptable. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 2. Representative** | | |
| **Metric 2. Geographic Scope** | | |
| High (score = 1) | The data are from the United States and are representative of the industry being evaluated. | |
| Medium (score = 2) | The data are from an OECD country other than the U.S., and locality-specific factors (e.g., potential differences in regulatory emission limits, industry/ process technologies) may impact releases relative to the U.S. | |
| Low (score = 3) | The data are from a non-OECD country, and locality-specific factors may impact (e.g., potentially greater differences in regulatory emission limits, industry/ process technologies) releases relative to the U.S., or the country of origin is not specified. | |
| Unacceptable (score = 4) | This metric does not have an unacceptable criterion since no geographic location is known to have unacceptable data. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 3. Applicability** | | |
| High (score = 1) | The release data are for an occupational scenario within the scope of the risk evaluation. | |
| Medium (score = 2) | The release data are for an occupational scenario that is similar to an occupational scenario within the scope of the risk evaluation, in terms of the type of industry, operations, and work activities. | |
| Low (score = 3) | The release data are for a non-occupational scenario that is similar to an occupational scenario within the scope of the risk evaluation, such as a consumer DIY scenario that is similar to a worker scenario. | |
| Unacceptable (score = 4) | The release data are from an occupational or non-occupational scenario that does not apply to any occupational scenario within the scope of the risk evaluation. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 4. Temporal representativeness** | | |
| High (score = 1) | The operations, equipment, and worker activities associated with the data indicate that the data should to be representative of current operations, equipment, and activities. The release data were collected after the most recent federal regulatory action (e.g., NESHAP for air release or effluent limit guideline (ELG) for water release) | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | or update or are no more than 10 years old, whichever is shorter. If no federal regulation is established, the data are generally no more than 10 years old. | |
| Medium (score = 2) | The release data were collected after the most recent federal regulatory action or update but are generally, more than 10 years old. If no federal regulation is established, the data are more than 10 years but no more than 20 years old. However, operations, equipment, and worker activities are expected to be reasonably representative of current conditions. | |
| Low (score = 3) | The data were collected before the most recent federal regulatory action or update or are more than 20 years old if no federal regulation is established. The operations, equipment, and worker activities are not available or indicate that the associated data are expected to be outdated. | |
| Unacceptable (score = 4) | Known factors (e.g., new and completely different process or equipment) are so different as to make outdated information unacceptable. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 5. Sample Size** | | |
| High (score = 1) | Statistical distribution of samples is fully characterized. Sample size is sufficiently representative. | |
| Medium (score = 2) | Distribution of samples is characterized by a range with uncertain statistics. It is unclear if analysis is representative. | |
| Low (score = 3) | Distribution of samples is qualitative or characterized by no statistics. | |
| Unacceptable (score = 4) | EPA has information that indicates the samples are not expected to represent the assessed release. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 3. Accessibility / Clarity** | | |
| **Metric 6. Metadata Completeness** | | |
| High (score = 1) | Release data include all associated metadata, including release media; process, unit operation, or activity that is the source of the release; and release frequency. | |
| Medium (score = 2) | Release data include most critical metadata, including release media and release frequency, but lacks additional metadata, such as process, unit operation, and/or activity that is the source of the release. | |
| Low (score = 3) | Release data include release media but no other metadata. | |
| Unacceptable (score = 4) | Release data do not include any needed metadata to understand what the data represent and are not usable in the risk evaluation. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 4. Variability and Uncertainty** | | |
| **Metric 7. Variability and Uncertainty** | | |
| High (score = 1) | The release data study addresses variability in the determinants of release. The release data study addresses uncertainty in the release results. | |
| Medium (score = 2) | The release data study provides only limited discussion of the variability in the determinants of release. The release data study provides only limited discussion of the uncertainty in the release results. | |
| Low (score = 3) | The release data study does not address variability or uncertainty. | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| Unacceptable (score = 4) | This metric does not have an unacceptable criterion. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

Notes:
DIY = Do it yourself
ELG = Effluent limit guideline
NESHAP = National Emissions Standards for Hazardous Air Pollutants
OECD = Organisation for Economic Co-operation and Development

### D.7.3 Published Models for Environmental Releases or Occupational Exposures

The general approach for setting the criteria for an unacceptable rating is to only assign an unacceptable rating when EPA can confirm that the data or information is unacceptable. If the data source lacks documentation of needed metadata, EPA will not rate the metric as unacceptable but will rate it as low. The reason for this approach is to avoid omitting potentially valid data or information since occupational exposure and release data are often sparse. EPA will not use data/information from data sources that exhibit serious flaws as described in Table D-14.

**Table D-14. Serious Flaws that Would Make Published Models Unacceptable for Use in the Environmental Release and Occupational Exposure Assessment**

Optimization of the list of serious flaws may occur after pilot calibration exercises.

| Domain | Metric | Description of Serious Flaw(s) in Data Source |
|---|---|---|
| Reliability | Methodology | Mathematical equations of the model have significant errors, parameters use erroneous values, or the model is based on flawed logic. |
| Representativeness | Geographic Scope | This metric does not have an unacceptable criterion since no geographic location is known to have unacceptable data. |
| | Applicability | The model is not applicable and cannot be adapted to any occupational scenario within the scope of the risk evaluation. |
| | Temporal representativeness | Known factors (e.g., new and completely different process or equipment) are so different as to make outdated information unacceptable. |
| Accessibility / Clarity | Metadata Completeness | The model is a “black box” and provides no documentation or clarity of its approaches, equations, and parameter values. |
| Variability and Uncertainty | Metadata Completeness | This metric does not have an unacceptable criterion. |

**Table D-15. Evaluation Criteria for Published Models**

EPA will consult with the *Guidance on the Development, Evaluation, and Application of Environmental Models* (U.S. EPA, 2009) when evaluating models and modeling data types.

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 1. Reliability** | | |
| **Metric 1. Methodology** | | |
| High (score = 1) | The model is free of mathematical errors and is based on scientifically sound approaches or methods. Equations and choice of parameter values are appropriate for the model's application (note: peer review may address appropriate application). | |
| Medium (score = 2) | The model is free of mathematical errors and is based on scientifically sound approaches or methods. However, equations and choice of parameter values are not fully described and some equations and/or parameter values may not be appropriate for the model's application. | |
| Low (score = 3) | The model is free of mathematical errors. However, the model makes assumptions or uses parameter values that lead to significant uncertainties. | |
| Unacceptable (score = 4) | Mathematical equations of the model have significant errors, parameters use erroneous values, or the model is based on flawed logic. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 2. Representative** | | |
| **Metric 2. Geographic Scope** | | |
| High (score = 1) | The data are from the United States and are representative of the industry being evaluated. | |
| Medium (score = 2) | The data are from an OECD country other than the U.S., and locality-specific factors (e.g., potential differences in regulatory occupational exposure or emission limits, industry/ process technologies) may impact exposures or releases relative to the U.S. | |
| Low (score = 3) | The data are from a non-OECD country, and locality-specific factors (e.g., potentially greater differences in regulatory occupational exposure or emission limits, industry/ process technologies) may impact exposures or releases relative to the U.S., or the country of origin is not specified. | |
| Unacceptable (score = 4) | This metric does not have an unacceptable criterion since no geographic location is known to have unacceptable data. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 3. Applicability** | | |
| High (score = 1) | The model can be appropriately applied to an occupational scenario within the scope of the risk evaluation. | |
| Medium (score = 2) | Not applicable: this domain is dichotomous: applicable or not applicable. | |
| Low (score = 3) | Not applicable: this domain is dichotomous: applicable or not applicable.<br>Can a poor fit model be used? | |
| Unacceptable (score = 4) | The model is not applicable and cannot be adapted to any occupational scenario within the scope of the risk evaluation. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Metric 4. Temporal representativeness** | | |
| High (score = 1) | The model is based on operations, equipment, and worker activities expected to be representative of current conditions. The model is based on data that are generally no more than 10 years old. | |
| Medium (score = 2) | The model is based on data that are generally more than 10 years but no more than 20 years old. However, the model is based on operations, equipment, and worker activities are expected to be reasonably representative of current conditions. | |
| Low (score = 3) | The model is based on data that are more than 20 years old. The model is based on operations, equipment, and worker activities that are expected to be outdated. | |
| Unacceptable (score = 4) | Known factors (e.g., new and completely different process or equipment) are so different as to make outdated information unacceptable. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 3. Accessibility / Clarity** | | |
| **Metric 6. Metadata Completeness** | | |
| High (score = 1) | Model approach, equations, and choice of parameter values are transparent and clear and can be evaluated. Rationale for selection of approach, equations, and parameter values is provided. | |
| Medium (score = 2) | Model approach, equations, and choice of parameter values are transparent. However, rationale for selection of approach, equations, and parameter values is not provided. | |
| Low (score = 3) | The model documentation describes the approach and parameters, but the equations and/or selection of parameter values are not provided. Rationale for modeling approach and parameter value selection is not provided. | |
| Unacceptable (score = 4) | The model is a "black box" and provides no documentation or clarity of its approaches, equations, and parameter values. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 4. Variability and Uncertainty** | | |
| **Metric 7. Variability and Uncertainty** | | |
| High (score = 1) | The model characterizes variability and uncertainty in the results. | |
| Medium (score = 2) | The model has limited characterization of the variability of parameter values. The model has limited characterization of the uncertainty in the results. | |
| Low (score = 3) | The model does not characterize variability or uncertainty. | |
| Unacceptable (score = 4) | This metric does not have an unacceptable criterion. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

Note:
OECD = Organisation for Economic Co-operation and Development

### D.7.4 Data/Information from Completed Exposure or Risk Assessments

The general approach for setting the criteria for an unacceptable rating is to only assign an unacceptable rating when EPA can confirm that the data or information is unacceptable. If the data source lacks documentation of needed metadata, EPA will not rate the metric as unacceptable but will rate it as low. The reason for this approach is to avoid omitting potentially valid data or information since occupational exposure and release data are often sparse. EPA will not use data/information from data sources that exhibit serious flaws as described in Table D-16.

**Table D-16. Serious Flaws that Would Make Data/Information from Completed Exposure or Risk Assessments Unacceptable for Use in the Environmental Release and Occupational Exposure Assessment**

Optimization of the list of serious flaws may occur after pilot calibration exercises.

| Domain | Metric | Description of Serious Flaw(s) in Data Source |
|---|---|---|
| Reliability | Methodology | The assessment or report uses data or techniques or methods that are not consistent with the best available science. Assumptions, extrapolations, measurements, and models are not appropriate. There appears to be mathematical errors or errors in logic. |
| Representativeness | Geographic Scope | This metric does not have an unacceptable criterion since no geographic location is known to have unacceptable data. |
| | Applicability | The assessment is from an occupational or non-occupational scenario that does not apply to any occupational scenario within the scope of the risk evaluation. |
| | Temporal representativeness | Known factors (e.g., new and completely different process or equipment) are so different as to make outdated information unacceptable. |
| | Sample Size | This metric does not have an unacceptable criterion. |
| Accessibility / Clarity | Metadata Completeness | Assessment or report does not document its data sources, assessment methods, and assumptions. |
| Variability and Uncertainty | Metadata Completeness | This metric does not have an unacceptable criterion. |

**Table D-17. Evaluation Criteria for Data/Information from Completed Exposure or Risk Assessments**

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 1. Reliability** | | |
| **Metric 1. Methodology** | | |
| High (score = 1) | The assessment or report uses high quality data and/or techniques or sound methods that are from a frequently used source (e.g., European Union or OECD reports, NIOSH HHEs, journal articles, Kirk-Othmer; see section D.5 and Table D-6) and are generally accepted by the scientific community, and associated information does not indicate flaws or quality issues. | |
| Medium (score = 2) | The assessment or report uses high quality data and/or techniques or sound methods that are not from a frequently used source, and associated information does not indicate flaws or quality issues. | |
| Low (score = 3) | The data, data sources, and/or techniques or methods used in the assessment or report are not specified. | |
| Unacceptable (score = 4) | The assessment or report uses data or techniques or methods that are not consistent with the best available science. Assumptions, extrapolations, measurements, and models are not appropriate. There appears to be mathematical errors or errors in logic. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 2. Representative** | | |
| **Metric 2. Geographic Scope** | | |
| High (score = 1) | The data are from the United States and are representative of the industry being evaluated. | |
| Medium (score = 2) | The data are from an OECD country other than the U.S., and locality-specific factors (e.g., potential differences in regulatory occupational exposure or emission limits, industry/ process technologies) may impact exposures or releases relative to the U.S. | |
| Low (score = 3) | The data are from a non-OECD country, and locality-specific factors (e.g., potentially greater differences in regulatory occupational exposure or emission limits, industry/ process technologies) may impact exposures or releases relative to the U.S. or the country of origin is not specified. | |
| Unacceptable (score = 4) | This metric does not have an unacceptable criterion since no geographic location is known to have unacceptable data. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 3. Applicability** | | |
| High (score = 1) | The assessment is for an occupational scenario within the scope of the risk evaluation. | |
| Medium (score = 2) | The assessment is for an occupational scenario that is similar to an occupational scenario within the scope of the risk evaluation, in terms of the type of industry, operations, and work activities. | |
| Low (score = 3) | The assessment is for a non-occupational scenario that is similar to an occupational scenario within the scope of the risk evaluation, such as a consumer DIY scenario that is similar to a worker scenario. | |
| Unacceptable (score = 4) | The assessment is from an occupational or non-occupational scenario that does not apply to any occupational scenario within the scope of the risk evaluation. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 4. Temporal representativeness** | | |
| High (score = 1) | The assessment captures operations, equipment, and worker activities expected to be representative of current conditions. EPA has no reason to believe exposures have changed. The completed exposure or risk assessment is generally no more than 10 years old. | |
| Medium (score = 2) | The assessment captures operations, equipment, and worker activities that are expected to be reasonably representative of current conditions. The completed exposure or risk assessment is generally, more than 10 years but no more than 20 | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | years old. | |
| Low (score = 3) | The completed exposure or risk assessment is more than 20 years old. The assessment captures operations, equipment, and worker activities that are expected to be outdated. | |
| Unacceptable (score = 4) | Known factors (e.g., new and completely different process or equipment) are so different as to make outdated information unacceptable. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 5. Sample Size** | | |
| High (score = 1) | Statistical distribution of samples is fully characterized. Sample size is sufficiently representative. | |
| Medium (score = 2) | Distribution of samples is characterized by a range with uncertain statistics. It is unclear if analysis is representative. | |
| Low (score = 3) | Distribution of samples is qualitative or characterized by no statistics. | |
| Unacceptable (score = 4) | This metric does not have an unacceptable criterion. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 3. Accessibility / Clarity** | | |
| **Metric 6. Metadata Completeness** | | |
| High (score = 1) | Assessment or report clearly documents its data sources, assessment methods, results, and assumptions. | |
| Medium (score = 2) | Assessment or report clearly documents results, methods, and assumptions. Data sources are generally described but not fully transparent. | |
| Low (score = 3) | Assessment or report provides results, but the underlying methods, data sources, and assumptions are not fully transparent. | |
| Unacceptable (score = 4) | Assessment or report does not document its data sources, assessment methods, and assumptions. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 4. Variability and Uncertainty** | | |
| **Metric 7. Variability and Uncertainty** | | |
| High (score = 1) | The assessment addresses variability and uncertainty in the results. Uncertainty is well characterized. | |
| Medium (score = 2) | The assessment provides only limited discussion of the variability and uncertainty in the results. | |
| Low (score = 3) | The assessment does not address variability or uncertainty. | |
| Unacceptable (score = 4) | This metric does not have an unacceptable criterion. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

Notes:
HHE = Health Hazard Evaluations
NIOSH = National Institute for Occupational Safety and Health
OECD = Organisation for Economic Co-operation and Development

### D.7.5 Data/Information from Reports Containing Other than Exposure or Release Data

The general approach for setting the criteria for an unacceptable rating is to only assign an unacceptable rating when EPA can confirm that the data or information is unacceptable. If the data source lacks documentation of needed metadata, EPA will not rate the metric as unacceptable but will rate it as low. The reason for this approach is to avoid omitting potentially valid data or information since occupational exposure and release data are often sparse. EPA will not use data/information from data sources that exhibit serious flaws as described in Table D-18.

**Table D-18. Serious Flaws that Would Make Data / Information from Reports Containing Other than Exposure or Release Data Unacceptable for Use in the Environmental Release and Occupational Exposure Assessment**

Optimization of the list of serious flaws may occur after pilot calibration exercises.

| Domain | Metric | Description of Serious Flaw(s) in Data Source |
|---|---|---|
| Reliability | Methodology | The assessment or report uses data or techniques or methods that are not consistent with the best available science. Assumptions, extrapolations, measurements, and models are not appropriate. There appears to be mathematical errors or errors in logic. |
| Representativeness | Geographic Scope | This metric does not have an unacceptable criterion since no geographic location is known to have unacceptable data. |
| | Applicability | The report is from an occupational or non-occupational scenario that does not apply to any occupational scenario within the scope of the risk evaluation |
| | Temporal representativeness | Known factors (e.g., new and completely different process or equipment) are so different as to make outdated information unacceptable. |
| | Sample Size | This metric does not have an unacceptable criterion. |
| Accessibility / Clarity | Metadata Completeness | Assessment or report does not document its data sources, assessment methods, and assumptions. |
| Variability and Uncertainty | Metadata Completeness | This metric does not have an unacceptable criterion. |

**Table D-19. Evaluation Criteria for Data /Information Reports Containing Other than Exposure or Release Data**

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 1. Reliability** | | |
| **Metric 1. Methodology** | | |
| High (score = 1) | The assessment or report uses high quality data and/or techniques or sound methods that are from frequently used sources (e.g., European Union or OECD reports, NIOSH HHEs, journal articles, Kirk-Othmer; see section D.5 and Table D-6) and are generally accepted by the scientific community, and associated information does not indicate flaws or quality issues. | |
| Medium (score = 2) | The assessment or report uses high quality data and/or techniques or sound methods that are not from a frequently used source and associated information does not indicate flaws or quality issues. | |
| Low (score = 3) | The data, data sources, and/or techniques or methods used in the assessment or report are not specified. | |
| Unacceptable (score = 4) | The assessment or report uses data or techniques or methods that are not high quality or not consistent with the best available science. Assumptions, extrapolations, measurements, and models are not appropriate. There appears to be mathematical errors or errors in logic. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 2. Representative** | | |
| **Metric 2. Geographic Scope** | | |
| High (score = 1) | The data are from the United States and are representative of the industry being evaluated. | |
| Medium (score = 2) | The data are from an OECD country other than the U.S., and locality-specific factors (e.g., potential differences in regulatory occupational exposure or emission limits, industry/ process technologies) may impact exposures or releases relative to the U.S. | |
| Low (score = 3) | The data are from a non-OECD country, and locality-specific factors (e.g., potentially greater differences in regulatory occupational exposure or emission limits, industry/ process technologies) may impact exposures or releases relative to the U.S., or the country of origin is not specified. | |
| Unacceptable (score = 4) | This metric does not have an unacceptable criterion since no geographic location is known to have unacceptable data. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 3. Applicability** | | |
| High (score = 1) | The report is for an occupational scenario within the scope of the risk evaluation. | |
| Medium (score = 2) | The report is for an occupational scenario that is similar to an occupational scenario within the scope of the risk evaluation, in terms of the type of industry, operations, and work activities. | |
| Low (score = 3) | The report is for a non-occupational scenario that is similar to an occupational scenario within the scope of the risk evaluation, such as a consumer DIY scenario that is similar to a worker scenario. | |
| Unacceptable (score = 4) | The report is from an occupational or non-occupational scenario that does not apply to any occupational scenario within the scope of the risk evaluation. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 4. Temporal representativeness** | | |
| High (score = 1) | The report captures operations, equipment, and worker activities expected to be representative of current conditions. The report is generally no more than 10 years old. | |
| Medium | The report captures operations, equipment, and worker activities that are expected to | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| (score = 2) | be reasonably representative of current conditions. The report is generally more than 10 years but no more than 20 years old. | |
| Low (score = 3) | The report is more than 20 years old. The report captures operations, equipment, and worker activities that are expected to be outdated. | |
| Unacceptable (score = 4) | Known factors (e.g., new and completely different process or equipment) are so different as to make outdated information unacceptable. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 5. Sample Size** | | |
| High (score = 1) | Statistical distribution of samples is fully characterized. Sample size is sufficiently representative. | |
| Medium (score = 2) | Distribution of samples is characterized by a range with uncertain statistics. It is unclear if analysis is representative. | |
| Low (score = 3) | Distribution of samples is qualitative or characterized by no statistics. | |
| Unacceptable (score = 4) | This metric does not have an unacceptable criterion. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 3. Accessibility / Clarity** | | |
| **Metric 6. Metadata Completeness** | | |
| High (score = 1) | Assessment or report clearly documents its data sources, assessment methods, results, and assumptions. | |
| Medium (score = 2) | Assessment or report clearly documents results, methods, and assumptions. Data sources are generally described but not fully transparent. | |
| Low (score = 3) | Assessment or report provides results, but the underlying methods, data sources, and assumptions are not fully transparent. | |
| Unacceptable (score = 4) | Assessment or report does not document its data sources, assessment methods, and assumptions. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 4. Variability and Uncertainty** | | |
| **Metric 7. Variability and Uncertainty** | | |
| High (score = 1) | The report addresses variability and uncertainty in the results. Uncertainty is well characterized. | |
| Medium (score = 2) | The report provides only limited discussion of the variability and uncertainty in the results. | |
| Low (score = 3) | The report does not address variability or uncertainty. | |
| Unacceptable (score = 4) | This metric does not have an unacceptable criterion. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

Notes:
HHE = Health Hazard Evaluation
NIOSH = National Institute for Occupational Safety and Health
OECD = Organisation for Economic Co-operation and Development

## D.8 References


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2. Moermond, CB, A. Breton, R. Junghans, M. Laskowski, R. Solomon, K. Zahner, H. (2016). Assessing the reliability of ecotoxicological studies: An overview of current needs and approaches. Integr Environ Assess Manag. 13: 1-12. http://dx.doi.org/10.1002/ieam.1870; http://onlinelibrary.wiley.com/store/10.1002/ieam.1870/asset/ieam1870.pdf?v=1&t=jerdoypz&s=ee96db9e589f470deb10651cdb1460d9ada93486.
3. U.S. EPA. (2009). Guidance on the Development, Evaluation, and Application of Environmental Models. (EPA/100/K-09/003). Washington, DC: Office of the Science Advisor. https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/4262976.

# APPENDIX E: DATA QUALITY CRITERIA FOR STUDIES ON CONSUMER, GENERAL POPULATION AND ENVIRONMENTAL EXPOSURE

## E.1 Types of Consumer, General Population and Environmental Exposure Data Sources

The data quality of consumer, general population, and environmental exposure data sources will be evaluated for seven different types of data sources: monitoring data, modeling data, survey-based data, epidemiological based data, experimental data, completed exposure assessments and risk characterizations, and database sources not unique to a chemical. Definitions for these data types are shown below in Table E-1.

**Table E-1. Types of Exposure Data Sources**

| Type of Data Source | Definition |
|---|---|
| Monitoring Data | Measured chemical concentration(s) obtained from sampling of environmental media (e.g., air, water, soil, and biota) to observe and study conditions of the environment. Monitoring data also include measured concentrations of chemicals or their metabolites in biological matrices (i.e., blood, urine, breastmilk, breath, hair, and organs) that provide direct evidence about exposure of environmental contaminants in humans and wildlife, as well as measured chemical concentrations obtained from personal exposure monitoring (i.e., breathing zone, skin patch samples). |
| Modeling Data | Calculated values derived from computational models for estimation of environmental concentrations (i.e., indoor, outdoor, microenvironments) and uptakes (e.g., ADD, LADD, Cmax, or AUC) associated with relevant exposure scenarios and routes (i.e., inhalation, oral, dermal). |
| Survey-based Data | Data collected from survey questionnaires about activity and use patterns (e.g., habits, practices, food intake) to evaluate exposure to an individual, a population segment or a population. |
| Epidemiological Data | Exposure data obtained from epidemiological studies collected as part of the examination of the association between chemical exposure and the occurrence and causes of health effects in human populations. The data may also come from case study reports which characterize exposures to one person. |
| Experimental Data | Data obtained from experimental studies conducted in a controlled environment with pre-defined testing conditions. Examples include data from laboratory/chamber tests such as those conducted for product testing, source characterization, emissions testing, and migration testing. Experimental data may also include chemical concentrations from personal exposure or biomonitoring studies conducted in laboratory/chamber test settings. |
| Completed Exposure Assessments and Risk Characterizations | Data reported in completed exposure assessments and risk characterizations containing a broad range of exposure data types (e.g., media concentrations, doses, estimated values, exposure factors). Examples: ATSDR assessments, risk assessments completed by other countries. |
| Database Sources Not Unique to a Chemical | Data obtained from large databases which collate information for a wide variety of chemicals using methods that are reasonable and consistent with sound scientific theory and/or accepted approaches, and are from sources generally using sound methods and/or approaches (e.g., state or federal governments, academia). Example databases: NHANES, STORET. |

**Notes:**

ADD = Average daily dose
ATSDR = Agency for Toxic Substances and Disease Registry
AUC = Area under the curve
$C_{max}$ = maximum concentration in plasma
LADD = Lifetime average daily dose
NHANES = National Health and Nutrition Examination Survey
STORET = Storage and Retrieval for Water Quality Data database

In general, the studies will inform the following basic data needs for exposures assessment (NRC, 1991):

- measures or estimates of the chemical
- the source of the chemical exposure
- environmental media of exposure
- specific populations exposed, including potentially exposed or susceptible subpopulations
- intensity and frequency of contact
- spatial and temporal concentration patterns

Some data sources identified as *on-topic*[26] for consumer, general population, and environmental exposure will also be identified as *on-topic* for the other disciplines (Engineering, Fate, Human Health Hazard, Environmental Health Hazard) supporting the development of the TSCA risk evaluations. In these cases, each discipline will consider different aspects of the same study. This is the case for epidemiological studies which examine disease patterns among populations during a specific duration of time. While the human health assessors are primarily interested in the hazards and effects that exposure to pollutants have on key biological, chemical, and physical processes affecting human health, exposure assessors are primarily interested in estimating exposure via direct measurements (e.g., media concentrations coupled with uptake rates, biomonitoring concentrations) or modeling. EPA anticipates that many epidemiological studies will need to be assessed by both the exposure and the human health assessors.

## E.2 Data Quality Evaluation Domains

The data sources will be evaluated against the following four data quality evaluation domains: reliability, representativeness, accessibility/clarity, and variability and uncertainty. These domains, as defined in Table E-2, address elements of TSCA Science Standards 26(h)(1) through 26(h)(5).

**Table E-2. Data Evaluation Domains and Definitions**

| Evaluation Domain | Definition |
|---|---|
| Reliability | The inherent property of a study, which includes the use of well-founded scientific approaches, the avoidance of bias within the study design and faithful study conduct and documentation (ECHA, 2011a). |
| Representativeness | The data reported address exposure scenarios (e.g., sources, pathways, routes, receptors) that are relevant to the assessment. |
| Accessibility/Clarity | The data and supporting information are accessible and clearly documented. |
| Variability and Uncertainty | The data describe variability and uncertainty (quantitative and qualitative) or the procedures, measures, methods, or models are evaluated and characterized. |

26 For the scoping phase, EPA/OPPT developed specific criteria to determine which references should be tagged as "on-topic" (inclusion criteria) and "off-topic" (exclusion criteria). Refer to the literature search strategies and bibliographies developed for each of the 10 existing chemicals under evaluation. https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/risk-evaluations-existing-chemicals-under-tsca

## E.3 Data Quality Evaluation Metrics

The data quality evaluation domains will be evaluated by assessing unique metrics that have been developed for each data type. A summary of the number of metrics and metric name for each data type is provided in Table E-3.

EPA may adjust these metrics as more experience is acquired with the evaluation tools to support fit-for-purpose TSCA risk evaluations. If this happens, EPA will document the changes to the evaluation tool.

**Table E-3. Summary of Metrics for the Seven Data Types**

| Type of Data Source | Overall Number of Metrics[a] | Metric Types |
|---|---|---|
| Monitoring Data | 10 | Sampling Methodology; Analytical Methodology; Selection of Biomarker of Exposure; Geographic Area; Temporality; Spatial and Temporal Variability; Exposure Scenario; Reporting of Results; Quality Assurance; Variability and Uncertainty |
| Modeling Data | 6 | Mathematical Equations; Model Evaluation; Exposure Scenario; Model and Model Documentation Availability; Model Inputs and Defaults; Variability and Uncertainty |
| Survey-based Data | 8 | Data Collection Methodology; Data Analysis Methodology, Geographic Area; Sampling/Sampling Size; Response Rate; Reporting of Results; Quality Assurance; Variability and Uncertainty |
| Epidemiological Data | 18 | Measurement or Exposure Characterization; Reporting Bias; Exposure Variability and Misclassification; Sample Contamination; Method Requirements; Matrix Adjustment; Method Sensitivity; Stability; Use of Biomarker of Exposure; Relevance; Population; Participant Selection; Comparison Group; Attrition; Documentation; QA/QC; Variability; Uncertainties |
| Experimental Data | 9 | Sampling Methodology and Conditions; Analytical Methodology; Selection of Biomarker of Exposure; Testing Scenario, Sample Size and Variability; Temporality; Reporting of Results; Quality Assurance; Variability and Uncertainty |
| Completed Exposure Assessments and Characterizations | 4 | Methodology; Exposure Scenario; Documentation of References; Variability and Uncertainty |
| Database Sources Not Unique to a Chemical | 8 | Sampling Methodology; Analytical Methodology; Geographic Area; Temporal; Exposure Scenario; Availability of Database and Supporting Documents; Reporting of Results; Variability and Uncertainty |

Note:
[a] Number of metrics across evaluation domains.

## E.4 Scoring Method and Determination of Overall Data Quality Level

A scoring system will be used to assign the overall quality of the data source, as discussed in Appendix A.

### E.4.1 Weighting Factors

EPA/OPPT is not applying weighting factors to the general population, consumer, and environmental exposure data types. In practice, it is equivalent to assigning a weighting factor of 1, which statistically assumes that each metric carries an equal amount of weight. This approach was adopted because of the wide range of objectives exhibited by the data sources across and within each data type and variations in their protocols, making it difficult to fairly apply a standard weighting scheme to all studies. Additionally, it is expected that weighting inherently occurs for most data types because more metrics are assigned to the reliability and representativeness domains (when combined) than the accessibility/clarity and variability/uncertainty domains. This is consistent with the logic that the reliability and representativeness domains are considered more important than other domains since these domains are considered fundamental aspects of the study.

### E.4.2 Calculation of Overall Study Score

To determine the overall study score, the first step is to multiply the score for each metric (1, 2, or 3 for high, medium, or low confidence, respectively) by the appropriate weighting factor, as shown in Table E-4, to obtain a weighted metric score. The weighted metric scores are then summed and divided by the sum of the weighting factors (for all metrics that are scored) to obtain an overall study score between 1 and 3. The equation for calculating the overall score is shown below. Although weighting factors are not used, the equation is showing the term for *Weighting Factor* (equivalent to 1) to be transparent about the calculation and to provide a consistent equation among the disciplines:

$$\textit{Overall Score (range of 1 to 3)} = \sum (\textit{Metric Score} \times \textit{Weighting Factor}) / \sum (\textit{Weighting Factors})$$

Table E-4 provides an example scoring for monitoring data.

Studies with any single metric scored as 4 will be automatically assigned an overall quality score of *Unacceptable* and further evaluation of the remaining metrics is not necessary. An *Unacceptable* score means that serious flaws are noted in the domain metric that consequently make the data unusable (or invalid). EPA/OPPT plans to use data with an overall quality level of *High*, *Medium*, or *Low* to quantitatively or qualitatively support the risk evaluations, but does not plan to use data rated as *Unacceptable*.

Any metrics that are *Not rated/not applicable* to the study under evaluation will not be considered in the calculation of the study's overall quality score. These metrics will not be included in the nominator or denominator of the *overall score* equation. The overall score will be calculated using only those metrics that receive a numerical score. In addition, if a publication reports more than one study or endpoint, each study and, as needed, each endpoint will be evaluated separately.

Detailed tables showing quality criteria for the metrics are provided in Tables E-6 through E-18, including a table that summarizes the serious flaws that would make the data unacceptable for use in the exposure assessment.

**Table E-4.Scoring Example for Monitoring Data**

| Metric | Selected Metric Score | Metric Weighting Factor | Weighted Metric Score |
|---|---|---|---|
| Metric 1: Sampling Methodology | 1 | 1 | 1 |
| Metric 2: Analytical Methodology | 2 | 1 | 2 |
| Metric 3: Selection of Biomarker of Exposure | 2 | 1 | 2 |
| Metric 4: Geographic Area | 1 | 1 | 1 |
| Metric 5: Temporality | 1 | 1 | 1 |
| Metric 6: Spatial and Temporal Variability | 1 | 1 | 1 |
| Metric 7: Exposure Scenario | 3 | 1 | 3 |
| Metric 8: Reporting of Results | 1 | 1 | 1 |
| Metric 9: Quality Assurance | 2 | 1 | 2 |
| Metric 10: Variability and Uncertainty | 2 | 1 | 2 |
| | | Sum = 10 | Sum = 16 |
| **∑(Metric Score × Metric Weighting Factor)/∑(Metric Weighting Factors)** | | | =16/10=1.6 |
| High: ≥1 and <1.7 / Medium: ≥1.7 and <2.3 / Low: ≥2.3 and ≤3 | | | |
| | | **Overall Score:** | 1.6 (High) |

## E.5 Data Sources Frequently Used in Consumer, General Population and Environmental Exposure Assessments

Many of the metric criteria definitions for the confidence levels (i.e.,high, medium, low, and unacceptable) examine if the methodology used was sound and widely accepted. Table E-5 provides examples of data sources that EPA frequently uses to support the data needs of consumer, general population and environmental exposure assessments. EPA notes that some data sources in Table E-5 may use or include data or information that are not of high quality but are still acceptable (e.g., medium or low quality) for use in risk evaluation. The methodologies in the individual studies under review will still be assessed in relation to chemical- and scenario-

specific considerations, thus the study may still receive study quality scores ranging from unacceptable to high even though the study used a methodology from a source commonly known to use sound methods and/or approaches. EPA may determine standard quality ratings for some of these sources as more experience is acquired with TSCA risk evaluations.

**Table E-5. Examples of Data Sources Frequently Used for Consumer, General Population and Environmental Exposure Assessments**

| Source | |
|---|---|
| U.S. EPA | Chemical Data Reporting (CDR) |
| | High Production Volume (HPV) Challenge Submissions |
| | Extra HPV Program Submissions |
| | EPA Existing Chemicals Engineering Files |
| | EPA Generic Scenarios |
| | Toxics Release Inventory (TRI) |
| | National Emissions Inventory (NEI) |
| | Office of Water |
| | Office of Air |
| | Office of Enforcement and Compliance Assistance Sector Notebooks |
| | AP-42 |
| | Other EPA Programs (e.g., Design for Environment) |
| Occupational Safety and Health Administration (OSHA) | |
| National Institute of Occupational Safety and Health (NIOSH) | |
| American Conference of Governmental Industrial Hygienists (ACGIH) | |
| Agency for Toxic Substances and Disease Registry (ATSDR) | |
| Organisation for Economic Co-operation and Development (OECD) | Screening Information Dataset (SIDS) |
| | Emission Scenario Documents (ESDs) |
| | Other Programs |
| Environment Canada | Canadian Pollution Prevention Information Clearinghouse |
| | Other Programs |
| U.S. Census Bureau | North American Industry Classification System (NAICS) Definitions |
| | County Business Patterns |
| | Annual Survey of Manufacturers |
| | Current Industrial Reports |
| | Economic Census |
| Bureau of Labor Statistics (BLS) | |
| North Carolina Division of Pollution Prevention and Environmental Assistance | |
| Kirk-Othmer Encyclopedia of Chemical Technology | |
| Hazardous Substances Data Bank (HSDB) | |
| National Library of Medicine's HazMap | |

# E.6 Data Quality Criteria

## E.6.1 Monitoring Data

**Table E-6. Serious Flaws that Would Make Sources of Monitoring Data Unacceptable for Use in the Exposure Assessment**

Optimization of the list of serious flaws may occur after pilot calibration exercises.

| Domain | Metric | Description of Serious Flaw(s) in Data Source |
|---|---|---|
| Reliability | Sampling Methodology | The sampling methodology is not discussed in the data source or companion source. |
| | | Sampling methodology is not scientifically sound or is not consistent with widely accepted methods/approaches for the chemical and media being analyzed (e.g., inappropriate sampling equipment, improper storage conditions). |
| | | There are numerous inconsistencies in the reporting of sampling information, resulting in high uncertainty in the sampling methods used. |
| | Analytical Methodology | Analytical methodology is not described, including analytical instrumentation (i.e., HPLC, GC). |
| | | Analytical methodology is not scientifically appropriate for the chemical and media being analyzed (e.g., method not sensitive enough, not specific to the chemical, out of date). |
| | | There are numerous inconsistencies in the reporting of analytical information, resulting in high uncertainty in the analytical methods used. |
| | Selection of Biomarker of Exposure | This metric does not have an unacceptable criterion. |
| Representative | Geographic Area | Geographic location is not reported, discussed, or referenced. |
| | Currency | Timing of sample collection for monitoring data is not reported, discussed, or referenced. |
| | Spatial and Temporal Variability | Sample size is not reported. |
| | | Single sample collected per data set. |
| | | For biomonitoring studies, the timing of sample collected is not appropriate based on chemical properties (e.g., half-life), the pharmacokinetics of the chemical (e.g., rate of uptake and elimination), and when the exposure event occurred. |
| | Exposure Scenario | If reported, the exposure scenario discussed in the monitored study does not represent the exposure scenario of interest for the chemical. |
| Accessibility / Clarity | Reporting of Results | There are numerous inconsistencies or errors in the calculation and/or reporting of results, resulting in highly uncertain reported results. |
| | Quality Assurance | QA/QC issues have been identified which significantly interfere with the overall reliability of the study. |
| Variability and Uncertainty | Variability and Uncertainty | Estimates are highly uncertain based on characterization of variability and uncertainty. |

Notes:
GC = Gas chromatography
HPLC = High pressure liquid chromatography
QA/QC = Quality assurance/quality control

## Table E-7. Evaluation Criteria for Sources of Monitoring Data

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 1. Reliability** | | |
| **Metric 1. Sampling Methodology** | | |
| High (score = 1) | • Samples were collected according to publicly available SOPs that are scientifically sound and widely accepted (i.e., from a source generally using sound methods and/or approaches) for the chemical and media of interest. Example SOPs include USGS's "National Field Manual for the Collection of Water-Quality Data", EPA's "Ambient Air Sampling" (SESDPROC-303-R5), etc.<br>**OR**<br>• The sampling protocol used was not a publicly available SOP from a from a source generally using sound methods and/or approaches, but the sampling methodology is clear, appropriate (i.e., scientifically sound), and similar to widely accepted protocols for the chemical and media of interest. All pertinent sampling information is provided in the data source or companion source. Examples include:<br>➢ sampling equipment<br>➢ sampling procedures/regime<br>➢ sample storage conditions/duration<br>➢ performance/calibration of sampler<br>➢ study site characteristics<br>➢ matrix characteristics | |
| Medium (score = 2) | • Sampling methodology is discussed in the data source or companion source and is generally appropriate (i.e., scientifically sound) for the chemical and media of interest, however, **one or more pieces of sampling information is not described.** The missing information is unlikely to have a substantial impact on results.<br>**OR**<br>• Standards, methods, protocols, or test guidelines may not be widely accepted, but a successful validation study for the new/unconventional procedure was conducted prior to the sampling event and is consistent with sound scientific theory and/or accepted approaches. Or a review of information indicates the methodology is acceptable and differences in methods are not expected to lead to lower quality data. | |
| Low (score = 3) | • Sampling methodology is only briefly discussed; therefore, **most sampling information is missing** and likely to have a substantial impact on results.<br>**AND/OR**<br>• The sampling methodology d**oes not represent best sampling methods, protocols, or guidelines** for the chemical and media of interest (e.g., outdated (but still valid) sampling equipment or procedures, long storage durations).<br>**AND/OR**<br>• There are **some inconsistencies** in the reporting of sampling information (e.g., differences between text and tables in data source, differences between standard method and actual procedures reported to have been used, etc.) which lead to a low confidence in the sampling methodology used. | |
| Unacceptable (score = 4) | • The sampling methodology is not discussed in the data source or companion source.<br>**AND/OR**<br>• Sampling methodology is not scientifically sound or is not consistent with widely accepted methods/approaches for the chemical and media being analyzed (e.g., inappropriate sampling equipment, improper storage conditions). | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | **AND/OR**<br>• There are **numerous inconsistencies** in the reporting of sampling information, resulting in high uncertainty in the sampling methods used. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 2. Analytical Methodology** | | |
| High<br>(score = 1) | • Samples were analyzed according to publically available analytical methods that are scientifically sound and widely accepted (i.e., from a source generally using sound methods and/or approaches) and are appropriate for the chemical and media of interest. Examples include EPA SW-846 Methods, NIOSH Manual of Analytical Methods 5th Edition, etc.<br>**OR**<br>• The analytical method used was not a publically available method from a source generally known to use sound methods and/or approaches, but the methodology is clear and appropriate (i.e., scientifically sound) and similar to widely accepted protocols for the chemical and media of interest. All pertinent sampling information is provided in the data source or companion source. Examples include:<br>➢ extraction method<br>➢ analytical instrumentation (required)<br>➢ instrument calibration<br>➢ LOQ, LOD, detection limits, and/or reporting limits<br>➢ recovery samples<br>➢ biomarker used (if applicable)<br>➢ matrix-adjustment method (i.e., creatinine, lipid, moisture) | |
| Medium<br>(score = 2) | • Analytical methodology is discussed in detail and is clear and appropriate (i.e., scientifically sound) for the chemical and media of interest; however, **one or more pieces of analytical information is not described**. The missing information is unlikely to have a substantial impact on results.<br>**AND/OR**<br>• The analytical **method may not be standard/widely accepted, but a method validation study was conducted** prior to sample analysis and is expected to be consistent with sound scientific theory and/or accepted approaches.<br>**AND/OR**<br>• Samples were collected at a site and immediately analyzed using an on-site mobile laboratory, rather than shipped to a stationary laboratory. | |
| Low<br>(score = 3) | • Analytical methodology is only briefly discussed. Analytical instrumentation is provided and consistent with accepted analytical instrumentation/methods. However, **most analytical information is missing** and likely to have a substantial impact on results.<br>**AND/OR**<br>• Analytical method **is not s**tandard/widely accepted, and method validation is limited or not available.<br>**AND/OR**<br>• Samples were analyzed using field screening techniques.<br>**AND/OR**<br>• LOQ, LOD, detection limits, and/or reporting limits not reported. | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | **AND/OR**<br>• There are **some inconsistencies or possible errors** in the reporting of analytical information (e.g., differences between text and tables in data source, differences between standard method and actual procedures reported to have been used, etc.) which leads to a lower confidence in the method used. | |
| Unacceptable (score = 4) | • Analytical methodology is not described, **including analytical instrumentation** (i.e., HPLC, GC).<br>**AND/OR**<br>• Analytical methodology is not scientifically appropriate for the chemical and media being analyzed (e.g., method not sensitive enough, not specific to the chemical, out of date).<br>**AND/OR**<br>• There are numerous inconsistencies in the reporting of analytical information, resulting in high uncertainty in the analytical methods used. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 3. Selection of Biomarker of Exposure** | | |
| High (score = 1) | • Biomarker in a specified matrix is known to have an accurate and precise quantitative relationship with external exposure, internal dose, or target dose (e.g., previous studies (or the current study) have indicated the biomarker of interest reflects external exposures).<br>**AND**<br>• Biomarker (parent chemical or metabolite) is derived from exposure to the chemical of interest. | |
| Medium (score = 2) | • Biomarker in a specified matrix has accurate and precise quantitative relationship with external exposure, internal dose, or target dose.<br>**AND**<br>• Biomarker is derived from multiple parent chemicals, not only the chemical of interest, **but** there is a stated method to apportion the estimate to only the chemical of interest | |
| Low (score = 3) | • Biomarker in a specified matrix has accurate and precise quantitative relationship with external exposure, internal dose, or target dose.<br>**AND**<br>• Biomarker is derived from multiple parent chemicals, not only the chemical of interest, **and** there is NOT an accurate method to apportion the estimate to only the chemical of interest.<br>**OR**<br>• Biomarker in a specified matrix is a poor surrogate (low accuracy and precision) for exposure/dose. | |
| Unacceptable (score = 4) | • Not applicable. A study will not be deemed unacceptable based on the use of biomarker of exposure. | |
| Not rated/applicable | • Metric is not applicable to the data source. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 2. Representative** | | |
| **Metric 4. Geographic Area** | | |
| High (score = 1) | • Geographic location(s) **is reported, discussed, or referenced.** | |
| Medium (score = 2) | • Not applicable. This metric is dichotomous (i.e., high versus unacceptable). | |
| Low (score = 3) | • Not applicable. This metric is dichotomous (i.e., high versus unacceptable). | |
| Unacceptable (score = 4) | • Geographic location is **not reported, discussed, or referenced.** | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 5. Temporality** | | |
| High (score = 1) | • Timing of sample collection for monitoring data is consistent with current or recent exposures **(within 5 years)** may be expected. | |
| Medium (score = 2) | • Timing of sample collection for monitoring data **is less consistent** with current or recent exposures **(>5 to 15 years)** may be expected. | |
| Low (score = 3) | • Timing of sample collection for monitoring data is not consistent with when current exposures **(>15 years old)** may be expected and likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | • Timing of sample collection for monitoring data is **not reported, discussed, or referenced.** | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 6. Spatial and Temporal Variability** | | |
| High (score = 1) | • Sampling approach accurately captures variability of environmental contamination in population/scenario/media of interest based on the heterogeneity/homogeneity and dynamic/static state of the environmental system. For example:<br>➢ **Large sample size** (i.e., ≥ 10 samples for a single scenario).<br>➢ Use of replicate samples.<br>➢ Use of systematic or continuous monitoring methods.<br>➢ Sampling over a sufficient period of time to characterize trends.<br>➢ For urine, 24-hr samples are collected (vs first morning voids or spot).<br>➢ For biomonitoring studies, the timing of sample collected is appropriate based on chemical properties (e.g., half-life), the pharmacokinetics of the chemical (e.g., rate of uptake and elimination), and when the exposure event occurred. | |
| Medium (score = 2) | • Sampling approach likely captures variability of environmental contamination in population/scenario/media of interest based on the heterogeneity/homogeneity and dynamic/static state of the environmental system. Some uncertainty may exist, but it is unlikely to have a substantial impact on results. For example:<br>➢ **Moderate sample size** (i.e., 5-10 samples for a single scenario), or<br>➢ Use of judgmental (non-statistical) sampling approach, or<br>➢ No replicate samples. | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | ➢ For urine, first morning voids or pooled spot samples. | |
| Low (score = 3) | • Sampling approach poorly captures variability of environmental contamination in population/scenario/media of interest. For example:<br>➢ **Small sample size** (i.e., <5 samples), or<br>➢ Use of haphazard sampling approach, or<br>➢ No replicate samples, or<br>➢ Grab or spot samples in single space or time, or<br>➢ Random sampling that doesn't include all periods of time or locations, or<br>➢ For urine, un-pooled spot samples. | |
| Unacceptable (score = 4) | • Sample **size is not reported**.<br>• **Single sample** collected per data set.<br>• For biomonitoring studies, the timing of sample collected is not appropriate based on chemical properties (e.g., half-life), the pharmacokinetics of the chemical (e.g., rate of uptake and elimination), and when the exposure event occurred. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 7. Exposure Scenario** | | |
| High (score = 1) | • The data **closely represent relevant exposure scenario (i.e., the population/scenario/media** of interest). Examples include:<br>➢ amount and type of chemical / product used<br>➢ source of exposure<br>➢ method of application or by-stander exposure<br>➢ use of exposure controls<br>➢ microenvironment (location, time, climate) | |
| Medium (score = 2) | • The data likely represent the relevant exposure scenario (i.e., population/scenario/media of interest). **One or more key pieces of information may not be described** but the deficiencies are unlikely to have a substantial impact on the characterization of the exposure scenario.<br>**AND/OR**<br>• If surrogate data, activities seem similar to the activities within scope. | |
| Low (score = 3) | • The data lack multiple key pieces of information and the deficiencies are likely to have a substantial impact on the characterization of the exposure scenario.<br>**AND/OR**<br>• There are **some inconsistencies or possible errors** in the reporting of scenario information (e.g., differences between text and tables in data source, differences between standard method and actual procedures reported to have been used, etc.) which leads to a lower confidence in the scenario assessed.<br>**AND/OR**<br>• If surrogate data, activities have lesser similarity but are still potentially applicable to the activities within scope. | |
| Unacceptable (score = 4) | • If reported, the exposure scenario discussed in the monitored study does not represent the exposure scenario of interest for the chemical. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 3. Accessibility / Clarity** | | |
| **Metric 8. Reporting of Results** | | |
| High (score = 1) | • Supplementary or raw data (i.e., individual data points) are reported, allowing summary statistics to be calculated or reproduced.<br>**AND**<br>• Summary statistics are detailed and complete. Example parameters include:<br>➢ Description of data set summarized (i.e., location, population, dates, etc.)<br>➢ Range of concentrations or percentiles<br>➢ Number of samples in data set<br>➢ Frequency of detection<br>➢ Measure of variation (CV, standard deviation)<br>➢ Measure of central tendency (mean, geometric mean, median)<br>➢ Test for outliers (if applicable)<br>**AND**<br>• Both adjusted and unadjusted results are provided (i.e., correction for void completeness in urine biomonitoring, whole-volume or lipid adjusted for blood biomonitoring, wet or dry weight for ecological tissue samples or soil samples) [only if applicable]. | |
| Medium (score = 2) | • Supplementary or raw data (i.e., individual data points) are not reported, and therefore summary statistics cannot be reproduced.<br>**AND/OR**<br>• Summary statistics are reported but are missing one or more parameters (see description for high).<br>**AND/OR**<br>• Only adjusted or unadjusted results are provided, but not both [only if applicable]. | |
| Low (score = 3) | • Supplementary data are not provided, and summary statistics are missing most parameters (see description for high).<br>**AND/OR**<br>• There are some inconsistencies or errors in the results reported, resulting in low confidence in the results reported (e.g., differences between text and tables in data source, less appropriate statistical methods). | |
| Unacceptable (score = 4) | • There are numerous inconsistencies or errors in the calculation and/or reporting of results, resulting in highly uncertain reported results. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 9. Quality Assurance** | | |
| High (score = 1) | • The study applied quality assurance/quality control measures and all pertinent quality assurance information is provided in the data source or companion source. Examples include:<br>➢ Field, laboratory, and/or storage recoveries.<br>➢ Field and laboratory control samples.<br>➢ Baseline (pre-exposure) samples.<br>➢ Biomarker stability<br>➢ Completeness of sample (i.e., creatinine, specific gravity, osmolality for urine samples)<br>**AND**<br>• No quality control issues were identified or any identified issues were minor and adequately addressed (i.e., correction for low recoveries, correction for | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | completeness). | |
| Medium (score = 2) | • The study applied and documented quality assurance/quality control measures; however, **one or more pieces of QA/QC information is not described.** Missing information is unlikely to have a substantial impact on results.<br>**AND**<br>• No quality control issues were identified or any identified issues were minor and addressed (i.e., correction for low recoveries, correction for completeness). | |
| Low (score = 3) | • Quality assurance/quality control techniques and results were not directly discussed, but can be implied through the study's use of standard field and laboratory protocols.<br>**AND/OR**<br>• Deficiencies were noted in quality assurance/quality control measures that are likely to have a substantial impact on results.<br>**AND/OR**<br>• There are some inconsistencies in the quality assurance measures reported, resulting in low confidence in the quality assurance/control measures taken and results (e.g., differences between text and tables in data source). | |
| Unacceptable (score = 4) | • QA/QC issues have been identified which significantly interfere with the overall reliability of the study. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 4. Variability and Uncertainty** | | |
| **Metric 10. Variability and Uncertainty** | | |
| High (score = 1) | • The study characterizes variability in the population/media studied.<br>**AND**<br>• Key uncertainties, limitations, and data gaps have been identified.<br>**AND**<br>• The uncertainties are minimal and have been characterized. | |
| Medium (score = 2) | • The study has limited characterization of variability in the population/media studied.<br>**AND/OR**<br>• The study has limited discussion of key uncertainties, limitations, and data gaps.<br>**AND/OR**<br>• Multiple uncertainties have been identified, but are unlikely to have a substantial impact on results. | |
| Low (score = 3) | • The characterization of variability is absent.<br>**AND/OR**<br>• Key uncertainties, limitations, and data gaps are not discussed.<br>**AND/OR**<br>• Uncertainties identified may have a substantial impact on the exposure the exposure assessment | |
| Unacceptable (score = 4) | • Estimates are highly uncertain based on characterization of variability and uncertainty. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|

**Notes:**

ADME = Absorption, distribution, metabolism, and elimination
CV = Coefficient of variation
GC = Gas chromatography
HPLC = High pressure liquid chromatography
LOD = Limit of detection
LOQ = Limit of quantitation
NIOSH = National Institute for Occupational Safety and Health
QA/QC = Quality assurance/quality control
SOPs = Standard operating procedures
USGS = U.S. Geological Survey

### E.6.2 Modeling Data[27]

**Table E-8. Serious Flaws that Would Make Sources of Modeling Data Unacceptable for Use in the Exposure Assessment**

Optimization of the list of serious flaws may occur after pilot calibration exercises.

| Domain | *Metric* | Description of Serious Flaw(s) in Data Source |
|---|---|---|
| Reliability | *Mathematical Equations* | For widely accepted models from a source generally known to use sound methods and/or approaches, the module used is not germane to the scenario being assessed**.** |
| | | For other (non-public/non-authoritative) models, key mathematical equations and/or theory are not provided in the data source or in a companion reference. |
| | | Key mathematical equations are not based on scientifically sound approaches. |
| | | Key mathematical equations are incorrect. |
| | *Model Evaluation* | The model used in the data source has not undergone evaluation. |
| | | It is unknown whether the model has undergone evaluation. |
| | | Evaluation efforts indicate that the model results do not correctly estimate concentrations or uptakes. |
| | | Model has no acceptance among the scientific or regulatory community. |
| Representative | *Exposure Scenario* | Model inputs do not reflect relevant conditions for the scenario of interest, or insufficient information is provided to make a determination. |
| Accessibility / Clarity | *Model and Model Documentation Availability* | This metric does not have an unacceptable criterion. |
| | *Model Inputs and Defaults* | There is at most a very limited description of model inputs/defaults and their associated data sources. |
| Variability and Uncertainty | *Variability and Uncertainty* | Estimates are highly uncertain based **on** characterization of uncertainty. |

[27] Evaluation of models and modeling data types will largely follow guidance from (U.S. EPA, 2009).

**Table E-9. Evaluation Criteria for Sources of Modeling Data**

EPA will consult with the *Guidance on the Development, Evaluation, and Application of Environmental Models* (U.S. EPA, 2009) when evaluating models and modeling data types.

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 1. Reliability** | | |
| **Metric 1. Mathematical Equations/Theory** | | |
| High (score = 1) | • The model is scientifically sound and widely accepted (i.e., from a source generally using sound methods and/or approaches) for the scenario being assessed.<br>**OR**<br>• For other (non-public/non-authoritative) models, key mathematical equations to calculate concentrations or uptakes are provided in the data source or in a companion reference. Equations are described in detail and correctness can be assessed. | |
| Medium (score = 2) | • For other (non-public/authoritative) models, key mathematical equations to calculate concentrations or uptakes are not available in the data source, but the scientific and mathematical theory (i.e., conceptual model) is described in detail. | |
| Low (score = 3) | • For other (non-public/authoritative) models, key mathematical equations or theory to calculate concentrations or uptakes are unclear or not detailed enough to thoroughly assess. | |
| Unacceptable (score = 4) | • For widely accepted models from a source generally known to use sound methods and/or approaches, the module used is not germane to the scenario being assessed.<br>**AND/OR**<br>• For other (non-public/non-authoritative) models, key mathematical equations and/or theory are not provided in the data source or in a companion reference.<br>**AND/OR**<br>• Key mathematical equations are not based on scientifically sound approaches.<br>**AND/OR**<br>• Key mathematical equations are incorrect. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 2. Model Evaluation** | | |
| High (score = 1) | • The model used in the data source has undergone extensive evaluation. The evaluation methodology and results are either discussed in the data source or provided in a companion source. Example evaluation methods include:<br>- formal peer review<br>- quantitative corroboration of model results with monitoring data directly relevant for the scenario of interest<br>- benchmarking against other models<br>- quality assurance checks during model development. | |
| Medium (score = 2) | • The model used in the data source has undergone only targeted/limited evaluation. For example:<br>- informal peer review<br>- at most limited evaluation with monitoring data<br>- qualitative corroboration of model results through expert elicitation | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | - evaluation via other model predictions<br>- quality assurance checks during model development.<br>**AND/OR**<br>• There is only limited discussion on the evaluation methodology and results in either the data source or other references.<br>**AND/OR**<br>• Model has wide acceptance among the scientific and regulatory community but has not have been validated for the scenario of interest, peer reviewed or well documented. | |
| Low (score = 3) | • Model evaluation was conducted according to the author; however, there is no information provided regarding model peer review, corroboration, or quality assurance checks.<br>**AND/OR**<br>• Model has only limited acceptance among the scientific and regulatory community. | |
| Unacceptable (score = 4) | • The model used in the data source has not undergone evaluation.<br>**AND/OR**<br>• It is unknown whether the model has undergone evaluation.<br>**AND/OR**<br>• Evaluation efforts indicate that the model results do not correctly estimate concentrations or uptakes.<br>**AND/OR**<br>• Model has no acceptance among the scientific and regulatory community. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 2. Representative** | | |
| **Metric 3. Exposure Scenario** | | |
| High (score = 1) | • The modeled scenario closely represents current exposures (within 5 years) and/or relevant conditions (e.g., environmental conditions, consumer products, exposure factors, geographical location). | |
| Medium (score = 2) | • The modeled scenario is less representative of current exposures (>5 to 15 years) and/or relevant conditions for the scenario of interest (e.g., environmental conditions, consumer products, exposure factors, geographical location). | |
| Low (score = 3) | • The modeled scenario is not consistent with when current exposures are expected (>15 years) and/or with relevant conditions (e.g., environmental conditions, consumer products, exposure factors, geographical location); inconsistencies are likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | • Model inputs do not reflect relevant conditions for the scenario of interest, or insufficient information is provided to make a determination. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 3. Accessibility / Clarity** | | |
| **Metric 4. Model and Model Documentation Availability** | | |
| High (score = 1) | • The model and documentation (user guide, documentation manual) are publicly available or there is sufficient documentation in the data source or in a companion reference. | |
| Medium (score = 2) | • Not applicable. This metric is dichotomous (i.e., high versus low). | |
| Low (score = 3) | • The model and documentation (user guide, documentation manual) are not available, or there is insufficient documentation in the data source or in a companion reference. | |
| Unacceptable (score = 4) | • Not applicable. This metric is dichotomous (i.e., high versus low). | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 5. Model Inputs and Defaults** | | |
| High (score = 1) | • Key model inputs (e.g., chemical mass released, release pattern over time, receptor uptake rates and locations over time) and defaults are identified, referenced and clearly described.<br>**AND**<br>• Model inputs meet data quality acceptance criteria specified by the authors or are standard or commonly accepted inputs (e.g., from Exposure Factors Handbook). | |
| Medium (score = 2) | • Key model inputs and defaults and associated data sources are generally identified, referenced and clearly described, but the descriptions are not detailed.<br>**AND/OR**<br>• Data quality acceptance criteria specified by the author are not discussed, but inputs appear appropriate. | |
| Low (score = 3) | • Numerous key model inputs and defaults and associated data sources are not identified, referenced or clearly described;<br>**AND/OR**<br>• There are some inconsistencies in the reporting of inputs and defaults and their associated data sources (e.g., differences between text and tables in data source, differences between standard method and actual procedures reported to have been used) that lead to a low confidence in the inputs and defaults used.<br>**AND/OR**<br>• Data quality acceptance criteria specified by the author are not discussed and some inputs appear inappropriate. | |
| Unacceptable (score = 4) | • There is at most a very limited description of model inputs/defaults and their associated data sources. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 4. Variability and Uncertainty** | | |
| **Metric 6. Variability and Uncertainty** | | |
| High (score = 1) | • The study characterizes variability in the population/media studied.<br>**AND**<br>• Key uncertainties, limitations, and data gaps have been identified.<br>**AND**<br>• The uncertainties are minimal and have been characterized. | |
| Medium (score = 2) | • The study has limited characterization of variability in the population/media studied.<br>**AND/OR**<br>• The study has limited discussion of key uncertainties, limitations, and data gaps.<br>**AND/OR**<br>• Multiple uncertainties have been identified, but are unlikely to have a substantial impact on results. | |
| Low (score = 3) | • The characterization of variability is absent.<br>**AND/OR**<br>• Key uncertainties, limitations, and data gaps are not discussed.<br>**AND/OR**<br>• Uncertainties identified may have a substantial impact on the exposure the exposure assessment | |
| Unacceptable (score = 4) | • Estimates are highly uncertain based on characterization of variability and uncertainty. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

### E.6.3 Survey Data

**Table E-10. Serious Flaws that Would Make Sources of Survey Data Unacceptable for Use in the Exposure Assessment**

Optimization of the list of serious flaws may occur after pilot calibration exercises.

| Domain | Metric | Description of Serious Flaw(s) in Data Source |
|---|---|---|
| Reliability | Data Collection Methodology | Data collection methods are not described. |
| | | Data collection methods used are not appropriate (i.e., scientifically sound) for the target population, the intended purpose, data requirements of the survey, or the target response rate. |
| | | There are numerous inconsistencies in the reporting of data collection information resulting in high uncertainty in the data collection methods used. |
| | Data Analysis Methodology | Data analysis methodology is not described. |
| | | Data analysis methodology is not appropriate (i.e., scientifically sound) for the intended purpose of the survey and the data/information collected. |
| | | There are numerous inconsistencies in the reporting of analytical information resulting in high uncertainty in the data analysis methods used. |
| Representative | Geographic Area | Geographic location is not reported, discussed, or referenced. |
| | Sampling/ Sampling Size | Sampling procedures (e.g., stratified sampling, cluster sampling, multi-stage sampling, non-probability sampling, etc.) are not documented in the data source or companion source. |
| | | Sample size is not reported. |
| | Response Rate | This metric does not have an unacceptable criterion.. |
| Accessibility / Clarity | Reporting of Results | There are numerous inconsistencies or errors in the calculation and/or reporting of results, resulting in highly uncertain reported results. |
| | Quality Assurance | QA/QC issues have been identified which significantly interfere with the overall reliability of the survey results. |
| Variability and Uncertainty | Variability and Uncertainty | Estimates are highly uncertain based on characterization of variability and uncertainty. |

Note:
QA/QC = Quality assurance/quality control

## Table E-11. Evaluation Criteria for Source of Survey Data

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 1. Reliability** | | |
| **Metric 1. Data Collection Methodology** | | |
| High (score = 1) | • Survey data were collected using a standard or validated data collection methods (e.g., mail, phone, personal interview, online surveys, etc.) that are appropriate (i.e., scientifically sound) given the characteristics of the target population, the intended purpose, data requirements of the survey, and the target response rate.<br>**AND**<br>• All pertinent information regarding data collection methodology is provided in the data source or companion source. Examples include:<br>➢ data collection instrument (e.g., questionnaire, diaries, etc.)<br>➢ data collection protocols for field personnel<br>➢ date of data collection<br>➢ description of target population | |
| Medium (score = 2) | • Survey data were collected using standard or validated data collection methods appropriate given the characteristics of the target population, the intended purpose and data requirements of the survey, and the target response rate. However, one or more pieces of pertinent information regarding data collection is not described. The missing information is unlikely to have a substantial impact on results. | |
| Low (score = 3) | • Data collection methods are only briefly discussed, therefore most data collection information is missing and likely to have a substantial impact on results.<br>**AND/OR**<br>• There are some inconsistencies in the reporting of data collection information (e.g., differences between text and tables in data source) which lead to a low confidence in the data collection methodology used. | |
| Unacceptable (score = 4) | • Data collection methods are not described.<br>**AND/OR**<br>• Data collection methods used are not appropriate (i.e., scientifically sound) for the target population, the intended purpose, data requirements of the survey, or the target response rate.<br>**AND/OR**<br>• There are numerous inconsistencies in the reporting of data collection information resulting in high uncertainty in the data collection methods used. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 2. Data Analysis Methodology** | | |
| High (score = 1) | • Data analysis methodology is discussed in detail and is clear and appropriate (i.e., scientifically sound) for the intended purpose of the survey and the data/information collected. Methods employed are standard/widely accepted.<br>**AND**<br>• All pertinent analytical methodology information is provided in the data source or companion source. Examples include:<br>➢ information on statistical and weighting methods (if applicable)<br>➢ discussion regarding treatment of missing data | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | ➢ Identification of sources of error, including coverage error, nonresponse error, measurement error, and data processing error (e.g., keying, coding, editing, and imputation error)<br>➢ Methods for measuring sampling and nonsampling errors | |
| Medium (score = 2) | • Data analysis methodology is discussed and is clear and appropriate for the intended purpose of the survey and the data/information collected. Methods employed are standard/widely accepted; however, one or more pieces of analytical information is not described. The missing information is unlikely to have a substantial impact on results. | |
| Low (score = 3) | • Data analysis methodology is only briefly discussed in the data source or companion source, therefore most analytical information is missing and likely to have a substantial impact on results.<br>**AND/OR**<br>• Methods for data analysis are not standard/widely accepted.<br>**AND/OR**<br>• There are some inconsistencies in the reporting of analytical information which lead to a low confidence in the data analysis methodology used. | |
| Unacceptable (score = 4) | • Data analysis methodology is not described in the data source or companion source.<br>**OR**<br>• Data analysis methodology is not appropriate (i.e., scientifically sound) for the intended purpose of the survey and the data/information collected.<br>**OR**<br>• There are numerous inconsistencies in the reporting of analytical information resulting in high uncertainty in the data analysis methods used. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 2. Representative** | | |
| **Metric 3. Geographic Area** | | |
| High (score = 1) | • Geographic location(s) is reported, discussed, or referenced. | |
| Medium (score = 2) | • Not applicable. This metric is dichotomous (i.e., high versus unacceptable). | |
| Low (score = 3) | • Not applicable. This metric is dichotomous (i.e., high versus unacceptable). | |
| Unacceptable (score = 4) | • Geographic location is not reported, discussed, or referenced. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 4. Sampling/Sampling Size** | | |
| High (score = 1) | • Sampling procedures are documented (e.g., stratified sampling, cluster sampling, multi-stage sampling, non-probability sampling, etc.).<br>**AND** | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | • Sample size and method of calculation is reported.<br>**AND**<br>• Sample size is large enough to be reasonably assured that the samples represent the population of interest. For example, sample size has a margin of error of <10% and a confidence level of >90%. | |
| Medium (score = 2) | • Sampling procedures are documented (e.g., stratified sampling, cluster sampling, multi-stage sampling, non-probability sampling, etc.).<br>**AND**<br>• Sample size is reported, but the sample size calculation method is not reported.<br>**AND/OR**<br>• Sample size is small, indicating that the survey results are less likely to represent the target population. For example, sample size has a margin of error of >10% and a confidence level of <90%. | |
| Low (score = 3) | • Sampling procedures are documented (e.g., stratified sampling, cluster sampling, multi-stage sampling, non-probability sampling, etc.).<br>**AND**<br>• Sample size is reported, but the sample size calculation method is not reported.<br>**AND/OR**<br>• Adequacy of sample size is not discussed or cannot be determined from information in the study. | |
| Unacceptable (score = 4) | • Sampling procedures (e.g., stratified sampling, cluster sampling, multi-stage sampling, non-probability sampling, etc.) are not documented in the data source or companion source.<br>**AND/OR**<br>• Sample size is not reported. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 5. Response Rate** | | |
| High (score = 1) | • The survey response rate is documented and is high enough (i.e., >70%) to reasonably ensure that the survey results are representative of the target population. | |
| Medium (score = 2) | • The survey response rate is documented and the response rate is >40-70%, indicating that the survey results will likely represent the target population. | |
| Low (score = 3) | • The survey response rate is documented and the response rate is <40%, indicating that the survey results are less likely to represent the target population.<br>**OR**<br>• The survey response rate is not documented in the data source or companion source. | |
| Unacceptable (score = 4) | • This metric does not have an unacceptable criterion. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 3. Accessibility / Clarity** | | |
| **Metric 6. Reporting of Results** | | |
| High (score = 1) | • Supplementary or raw data (i.e., individual data points) are reported, allowing summary statistics to be calculated or reproduced.<br>**AND**<br>• Summary statistics are detailed and complete. Example parameters include:<br>➢ Description of data set summarized<br>➢ Number of samples in data set<br>➢ Range or percentiles<br>➢ Measure of variation (coefficient of variation (CV), standard deviation)<br>➢ Measure of central tendency (mean, geometric mean, median)<br>➢ Test for outliers (if applicable) | |
| Medium (score = 2) | • Supplementary or raw data (i.e., individual data points) are not reported, and therefore summary statistics cannot be reproduced.<br>**AND/OR**<br>• Summary statistics are reported but are missing one or more parameters (see description for high). | |
| Low (score = 3) | • Supplementary data are not provided, and summary statistics are missing most parameters (see description for high).<br>**AND/OR**<br>• There are some inconsistencies or errors in the results reported, resulting in low confidence in the results reported (e.g., differences between text and tables in data source, less appropriate statistical methods). | |
| Unacceptable (score = 4) | • There are numerous inconsistencies or errors in the calculation and/or reporting of results, resulting in highly uncertain reported results. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 7. Quality Assurance** | | |
| High (score = 1) | • Survey quality assurance/control measures were employed during each phase of the survey and are documented. Examples may include:<br>➢ training staff in protocols<br>➢ monitoring interviewers<br>➢ conducting response analysis surveys<br>➢ contingencies to modify the survey procedures<br>➢ monitoring of data collection activities<br>**AND**<br>• No quality control issues were identified or any identified issues were minor and were addressed. | |
| Medium (score = 2) | • The study applied and documented quality assurance/quality control measures; however, one or more pieces of QA/QC information is not described. Missing information is unlikely to have a substantial impact on results.<br>**AND**<br>• No quality control issues were identified or any identified issues were minor and addressed. | |
| Low (score = 3) | • Quality assurance/quality control techniques and results were not directly discussed, but can be implied through the study's use of standard survey | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | protocols.<br>**AND/OR**<br>• Deficiencies were noted in quality assurance/quality control measures that are likely to have a substantial impact on results.<br>**AND/OR**<br>• There are some inconsistencies in the quality assurance measures reported, resulting in low confidence in the quality assurance/control measures taken and results (e.g., differences between text and tables in data source). | |
| Unacceptable (score = 4) | • QA/QC issues have been identified which significantly interfere with the overall reliability of the survey results. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 4. Variability and Uncertainty** | | |
| **Metric 8. Variability and Uncertainty** | | |
| High (score = 1) | • The variability in the population and data collected in the survey is characterized (e.g., sampling and non-sampling errors).<br>**AND**<br>• Key uncertainties, limitations, and data gaps have been identified.<br>**AND**<br>• The uncertainties are minimal and have been characterized. | |
| Medium (score = 2) | • The study has limited characterization of variability in the population studied and data collected in the survey.<br>**AND/OR**<br>• The study has limited discussion of key uncertainties, limitations, and data gaps.<br>**AND/OR**<br>• Multiple uncertainties have been identified, but are unlikely to have a substantial impact on results. | |
| Low (score = 3) | • The characterization of variability is absent.<br>**AND/OR**<br>• Key uncertainties, limitations, and data gaps are not discussed.<br>**AND/OR**<br>• Uncertainties identified may have a substantial impact on the exposure the exposure assessment | |
| Unacceptable (score = 4) | • Estimates are highly uncertain based on characterization of variability and uncertainty. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

Note:
QA/QC = Quality assurance/quality control

### E.6.4 Epidemiology Data to Support Exposure Assessment

**Table E-12. Serious Flaws that Would Make Sources of Epidemiology Data Unacceptable for Use in the Exposure Assessment**

EPA will not use data/information from data sources that exhibit serious flaws as described in Table E-12. Optimization of the list of serious flaws may occur after pilot calibration exercises.

| Domain | Metric | Description of Serious Flaw(s) in Data Source |
|---|---|---|
| Reliability (All Study Types) | Measurement or Exposure Characterization | Exposure misclassification (e.g., differential recall of self-reported exposure) is present, but no attempt is made to address it. |
| | Reporting Bias | This metric does not have an unacceptable criterion. |
| Reliability (Applicable to Study Types with Direct Exposure Measurements Only) | Exposure Variability and Misclassification | Exposure based on a single sample and error is known to be so large that the results are too uncertain to be useful. |
| | Sample Contamination | There are known contamination issues and the issues were not addressed. |
| | Method Requirements | The method used is known to produce unreliable or invalid results. |
| | Matrix Adjustment | This metric does not have an unacceptable criterion. |
| | Method Sensitivity | This metric does not have an unacceptable criterion. |
| | Stability | This metric does not have an unacceptable criterion. |
| Reliability (Applicable to Study Types with Biomarker Measurements Only) | Use of Biomarker of Exposure | This metric does not have an unacceptable criterion. |
| Representativeness | Relevance | This metric does not have an unacceptable criterion. |
| | Geographic Area | Geographic location is not reported, discussed, or referenced. |
| | Participant Selection | This metric does not have an unacceptable criterion. |
| | Attrition | ***For cohort studies:*** The loss of subjects (i.e., incomplete exposure data) was both large and unacceptably handled (as described in the low confidence category).<br>***For case-control and cross-sectional studies:*** The exclusion of subjects from analyses was both large and unacceptably handled (as described in the low confidence category). |
| | Comparison Group | Subjects in all groups were not similar, recruited within very different time frames, or had very different participation/ response rates. |
| Accessibility/ Clarity | Documentation | There are numerous inconsistencies or errors in the calculation and/or reporting of information and results, resulting in highly |

| Domain | Metric | Description of Serious Flaw(s) in Data Source |
|---|---|---|
| | | uncertain reported results. |
| | QA/QC | QA/QC issues have been identified which significantly interfere with the overall reliability of the study, and are not addressed. |
| Variability and Uncertainty | Variability | This metric does not have an unacceptable criterion. |
| | Uncertainties | This metric does not have an unacceptable criterion. |

## Table E-13. Evaluation Criteria for Sources of Epidemiology Data to Support the Exposure Assessment

| Confidence Level (Score) | Metric Description | Selected Score |
|---|---|---|
| **Domain 1. Reliability** | | |
| **Metrics 1-2 = Applicable to All Study Types** | | |
| **Metric 1. Measurement or Exposure Characterization** | | |
| High (score = 1) | • Exposure was consistently assessed (i.e., under the same method and time-frame across cases, controls or the entire cohort) using well-established methods that directly measure exposure (e.g., measurement of the chemical in air or measurement of the chemical in blood, plasma, urine, etc.).<br>**OR**<br>• Exposure was consistently assessed using less-established methods that directly measure exposure and are validated against well-established methods. | |
| Medium (score = 2) | • Exposure was assessed using indirect measures (e.g., questionnaire or occupational exposure assessment by a certified industrial hygienist) that have been validated or empirically shown to be consistent with methods that directly measure exposure (i.e., inter-methods validation: one method vs. another) | |
| Low (score = 3) | • Exposure was assessed using direct or indirect measures that have not been validated or have poor validity.<br>**OR**<br>• If using indirect methods, they have not empirically shown to be consistent with methods that directly measure exposure (e.g., a job-exposure matrix or self-report without validation).<br>**OR**<br>• There is insufficient information provided about the exposure assessment, including validity and reliability, but no evidence for concern about the method used. | |
| Unacceptable (score = 4) | • Exposure misclassification (e.g., differential recall of self-reported exposure) is present and likely to impact results, but no attempt is made to address it. | |
| Not rated/applicable | | |
| **Reviewer's Comments:**<br>*[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | | |
| **Metric 2. Reporting Bias** | | |
| High (score = 1) | • All of the study's measured exposures outlined in the protocol, methods, abstract, and/or introduction (that are relevant for the evaluation) are reported. | |
| Medium (score = 2) | • Not applicable. This metric is dichotomous (i.e., high versus low) | |
| Low | • All of the study's measured exposures outlined in the protocol, methods, | |

| Confidence Level (Score) | Metric Description | Selected Score |
|---|---|---|
| (score = 3) | abstract, and/or introduction (that are relevant for the evaluation) have not been reported. | |
| Unacceptable (score = 4) | • Not applicable. This metric is dichotomous (i.e., high versus low). | |
| Not rated/applicable | | |
| **Reviewer's Comments:** *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | | |
| **Metrics 3-8 = Applicable Only to Study Types with Direct Exposure Measurements (i.e., Measurement of Chemical in Specific Media or Biomarker Measurement)** | | |
| **Metric 3. Exposure Variability and Misclassification** | | |
| High (score = 1) | • There are a sufficient number of samples per individual to estimate exposure over the appropriate duration, or through the use of adequate long-term sampling data. A "sufficient" number is dependent upon the chemical and the research question.<br>**AND**<br>• Error is considered by calculating measures of accuracy (e.g., sensitivity and specificity) and reliability (e.g., intra-class correlation coefficient (ICC)). | |
| Medium (score = 2) | • One sample is used per individual, **and** there is stated evidence that errors from a single measurement are negligible. | |
| Low (score = 3) | • More than one sample collected per individual, **but** without evaluation of error.<br>**OR**<br>• Exposure based on a single sample without consideration or recognition of error | |
| Unacceptable (score = 4) | • Exposure based on a single sample and error is known to be so large that the results are too uncertain to be useful. | |
| Not rated/applicable | | |
| **Reviewer's Comments:** *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | | |
| **Metric 4. Sample Contamination** | | |
| High (score = 1) | • Samples are contamination-free from the time of collection to the time of measurement (e.g., by use of certified analyte free collection supplies and reference materials, and appropriate use of blanks both in the field and lab).<br>**AND**<br>• Documentation of the steps taken to provide the necessary assurance that the study data are reliable is included. | |
| Medium (score = 2) | • Samples are stated to be contamination-free from the time of collection to the time of measurement.<br>**AND**<br>• There is incomplete documentation of the steps taken to provide the necessary assurance that the study data are reliable. | |
| Low (score = 3) | • Samples are known to have contamination issues, but steps have been taken to address and correct contamination issues.<br>**OR**<br>• Samples are stated to be contamination-free from the time of collection to the time of measurement, but there is no use or documentation of the steps taken to provide the necessary assurance that the study data are reliable. | |

| Confidence Level (Score) | Metric Description | Selected Score |
|---|---|---|
| Unacceptable (score = 4) | • There are known contamination issues and the issues were not addressed. | |
| Not rated/applicable | | |
| **Reviewer's Comments:**<br>*[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | | |
| **Metric 5. Method Requirements** | | |
| High (score = 1) | • Study uses instrumentation that provides *unambiguous* identification and quantitation of the biomarker or chemical in media at the required sensitivity (e.g., gas chromatography-high-resolution mass spectrometry (GC-HRMS), gas chromatography-tandem mass spectrometry (GC-MS/MS), liquid chromatography-tandem mass spectrometry (LC-MS/MS)). | |
| Medium (score = 2) | • Study uses instrumentation that allows for identification of the biomarker or chemical in media with confidence and the required sensitivity (e.g., gas chromatography-mass spectrometry (GC-MS), gas chromatography-electron capture detector (GC-ECD)). | |
| Low (score = 3) | • Study uses instrumentation that only allows for possible quantification of the biomarker or chemical in media but the method has known interferants (e.g., gas chromatography-flame ionization detector (GC-FID)).<br>**OR**<br>• Study uses a semi-quantitative method to assess the biomarker or chemical in media (e.g., fluorescence). | |
| Unacceptable (score = 4) | • The method used is known to produce unreliable or invalid results. | |
| Not rated/applicable | | |
| **Reviewer's Comments:**<br>*[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | | |
| **Metric 6. Matrix Adjustment** | | |
| High (score = 1) | • If applicable for the biomarker under consideration, study provides results, either in the main publication or as a supplement, for adjusted and unadjusted matrix concentrations (e.g., creatinine-adjusted or SG-adjusted and non-adjusted urine concentrations) and reasons are given for adjustment approach. | |
| Medium (score = 2) | • If adjustments are needed, study only provides results using one method (matrix adjusted or not). | |
| Low (score = 3) | • If applicable for the biomarker under consideration, no established method for matrix adjustment was conducted. | |
| Unacceptable (score = 4) | • Not applicable. A study will not be deemed unacceptable based on matrix adjustment. | |
| Not rated/applicable | | |
| **Reviewer's Comments:**<br>*[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | | |

| Confidence Level (Score) | Metric Description | Selected Score |
|---|---|---|
| **Metric 7. Method Sensitivity** | | |
| High (score = 1) | • Limits of detection/quantification are reported and low enough to detect chemicals in a sufficient percentage of the samples to address the research questions (e.g., 50-60% detectable values if the research hypothesis requires estimates of both central tendencies and upper tails of the population concentrations).<br>**OR**<br>• All samples are above the LOD/LOQ. | |
| Medium (score = 2) | • Not applicable. This metric is dichotomous (i.e., high versus low). | |
| Low (score = 3) | • Frequency of detection too low to address the research question<br>**OR**<br>• There are samples below the LOD/LOQ, and LOD/LOQ are not stated. | |
| Unacceptable (score = 4) | • Not applicable. This metric is dichotomous (i.e., high versus low). | |
| Not rated/applicable | | |
| **Reviewer's Comments:**<br>*[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | | |
| **Metric 8. Stability** | | |
| High (score = 1) | • Samples with a known history and documented stability data or those using real-time measurements. | |
| Medium (score = 2) | • Samples have known losses during storage but the difference between low and high exposures can be qualitatively assessed. | |
| Low (score = 3) | • Samples with either unknown history and/or no stability data for analytes of interest. | |
| Unacceptable (score = 4) | • Not applicable. A study will not be deemed unacceptable based on stability. | |
| Not rated/applicable | | |
| **Reviewer's Comments:**<br>*[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | | |
| **Metric 9 = Only Applicable to Studies with Biomarker Measurements** | | |
| **Metric 9. Use of Biomarker of Exposure** | | |
| High (score = 1) | • Biomarker in a specified matrix is known to have an accurate and precise quantitative relationship with external exposure, internal dose, or target dose (e.g., previous studies (or the current study) have indicated the biomarker of interest reflects external exposures).<br>**AND**<br>• Biomarker (parent chemical or metabolite) is derived from exposure to the chemical of interest. | |
| Medium (score = 2) | • Biomarker in a specified matrix has accurate and precise quantitative relationship with external exposure, internal dose, or target dose.<br>**AND**<br>• Biomarker is derived from multiple parent chemicals, not only the chemical of interest, **but** there is a stated method to apportion the estimate to only the chemical of interest. | |

| Confidence Level (Score) | Metric Description | Selected Score |
|---|---|---|
| Low (score = 3) | • Biomarker in a specified matrix has accurate and precise quantitative relationship with external exposure, internal dose, or target dose.<br>**AND**<br>• Biomarker is derived from multiple parent chemicals, not only the chemical of interest, **and** there is NOT an accurate method to apportion the estimate to only the chemical of interest.<br>**OR**<br>• Biomarker in a specified matrix is a poor surrogate (low accuracy and precision) for exposure/dose. | |
| Unacceptable (score = 4) | • Not applicable. A study will not be deemed unacceptable based on the use of biomarker of exposure. | |
| Not rated/applicable | | |
| **Reviewer's Comments:**<br>*[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | | |
| **Domain 2. Representativeness** | | |
| **Metric 10. Relevance** | | |
| High (score = 1) | • The study represents current exposures (within 5 years) and relevant conditions (e.g., environmental conditions, consumer products, exposure factors, geographical location). | |
| Medium (score = 2) | • The study is less representative of current exposures (>5 to 15 years) and/or relevant conditions for the scenario of interest (e.g., environmental conditions, consumer products, exposure factors, geographical location). | |
| Low (score = 3) | • The study is not consistent with current exposures (>15 years) and/or with relevant conditions (e.g., environmental conditions, consumer products, exposure factors, geographical location); inconsistencies are likely to have a substantial impact on results.<br>**OR**<br>• Insufficient information is provided to determine whether the study represents current relevant conditions for the scenario of interest. | |
| Unacceptable (score = 4) | • Not applicable. A study will not be deemed unacceptable based on relevance. | |
| Not rated/applicable | | |
| **Reviewer's Comments:**<br>*[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | | |
| **Metric 11. Geographic Area** | | |
| High (score = 1) | • Geographic location(s) is reported, discussed, or referenced. | |
| Medium (score = 2) | • Not applicable. This metric is dichotomous (i.e., high versus unacceptable). | |
| Low (score = 3) | • Not applicable. This metric is dichotomous (i.e., high versus unacceptable). | |
| Unacceptable (score = 4) | • Geographic location is not reported, discussed, or referenced. | |
| Not rated/applicable | | |

| Confidence Level (Score) | Metric Description | Selected Score |
|---|---|---|
| **Reviewer's Comments:**<br>*[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | | |
| **Metric 12. Participant Selection** | | |
| High<br>(score = 1) | • The participants selected are representative of the larger population from which they were sampled.<br>**OR**<br>• Approaches (e.g., survey weights, inverse probability weighting) were applied to ensure representativeness. | |
| Medium<br>(score = 2) | • Not applicable. This metric is dichotomous (i.e., high versus low). | |
| Low<br>(score = 3) | • The participants selected do not appear to be representative of the larger population from which they were sampled.<br>**OR**<br>• There is insufficient information to determine whether participants selected are representative of the population from which they were sampled. | |
| Unacceptable<br>(score = 4) | • Not applicable. This metric is dichotomous (i.e., high versus low). | |
| Not rated/applicable | | |
| **Reviewer's Comments:**<br>*[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | | |
| **Metric 13. Attrition** | | |
| High<br>(score = 1) | • ***For cohort studies:*** There was minimal subject attrition during the study (or exclusion from the analysis sample) and exposure data were largely complete.<br>**OR**<br>• Any loss of subjects (i.e., incomplete exposure data) was adequately* addressed (as described above) and reasons were documented when human subjects were removed from a study.<br>**OR**<br>• Missing data have been imputed using appropriate methods (e.g., random regression imputation), and characteristics of subjects lost to follow up or with unavailable records are described in identical way and are not significantly different from those of the study participants.<br>• ***For case-control studies and cross-sectional studies:*** There was minimal subject withdrawal from the study (or exclusion from the analysis sample) and exposure data were largely complete.<br>**OR**<br>• Any exclusion of subjects from analyses was adequately* addressed (as described above), and reasons were documented when subjects were removed from the study or excluded from analyses.<br><br>***NOTE for all study types:*** Adequate handling of subject attrition includes: very little missing exposure data; missing exposure data balanced in numbers across study groups, with similar reasons for missing data across groups. | |

| Confidence Level (Score) | Metric Description | Selected Score |
|---|---|---|
| Medium (score = 2) | • ***For cohort studies:*** There was moderate subject attrition during the study (or exclusion from the analysis sample).<br>**AND**<br>• Any loss or exclusion of subjects was adequately addressed (as described in the acceptable handling of subject attrition in the high confidence category) and reasons were documented when human subjects were removed from a study.<br>• ***For case-control studies and cross-sectional studies:*** There was moderate subject withdrawal from the study (or exclusion from the analysis sample), but exposure data were largely complete.<br>**AND**<br>• Any exclusion of subjects from analyses was adequately addressed (as described above), and reasons were documented when subjects were removed from the study or excluded from analyses. | |
| Low (score = 3) | • ***For cohort studies:*** There was large subject attrition during the study (or exclusion from the analysis sample), but it was adequately addressed (i.e., missing exposure data was balanced in numbers across groups and reasons for missing data were similar across groups).<br>**OR**<br>• Subject attrition was not large but it was inadequately addressed. Inadequate handling of subject attrition: reason for missing exposure data likely to be related to true exposure, with either imbalance in numbers or reasons for missing data across study groups; or potentially inappropriate application of imputation.<br>**OR**<br>• Numbers of individuals were not reported at each stage of study (e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study or analysis sample, completing follow-up, and analyzed). Reasons were not provided for non-participation at each stage.<br>• ***For case-control and cross-sectional studies:*** There was large subject withdrawal from the study (or exclusion from the analysis sample), but it was adequately addressed (i.e., missing exposure data was balanced in numbers across groups and reasons for missing data were similar across groups).<br>**OR**<br>• Subject attrition was not large but it was inadequately addressed. Inadequate handling of subject attrition: reason for missing exposure data likely to be related to true exposure, with either imbalance in numbers or reasons for missing data across study groups; or potentially inappropriate application of imputation.<br>**OR**<br>Numbers of individuals were not reported at each stage of study (e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study or analysis sample, and analyzed). Reasons were not provided for non-participation at each stage. | |
| Unacceptable (score = 4) | • ***For cohort studies:*** The loss of subjects (i.e., incomplete exposure data) was both large and unacceptably handled (as described above in the low confidence category).<br>• ***For case-control and cross-sectional studies:*** The exclusion of subjects from analyses was both large and unacceptably handled (as described above in the low confidence category). | |
| Not rated/applicable | | |

| Confidence Level (Score) | Metric Description | Selected Score |
|---|---|---|
| **Reviewer's Comments:**<br>*[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | | |
| **Metric 14 = Only Applicable to Studies that Compare Exposure in Different Groups** | | |
| **Metric 14. Comparison Group** | | |
| High (1) | • Key elements of the study design are reported (i.e., setting, inclusion and exclusion criteria, and methods of participant selection), and indicate that subjects (in all groups) were similar (e.g., recruited with the same method of ascertainment and within the same time frame using the same inclusion and exclusion criteria, and were of similar age and health status)<br>**OR**<br>• Baseline characteristics of groups differed ***but*** these differences were considered as potential confounding or stratification variables, and were thereby controlled by statistical analysis. | |
| Medium (2) | • There is indirect evidence (i.e., stated by the authors without providing a description of methods) that subjects (in all groups) were similar (as described above for the high confidence rating).<br>**AND**<br>• Baseline characteristics for subjects (in all groups) reported in the study were similar. | |
| Low (3) | • There is indirect evidence (i.e., stated by the authors without providing a description of methods) that subjects (in all groups) were similar (as described above for the high confidence rating).<br>**AND**<br>• Baseline characteristics for subjects (in all groups) were not reported. | |
| Unacceptable (4) | • Subjects in all groups were not similar, recruited within very different time frames, or had very different participation/ response rates. | |
| Not rated/applicable | | |
| **Reviewer's Comments:**<br>*[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | | |
| **Domain 3. Accessibility / Clarity** | | |
| **Metric 15. Documentation** | | |
| High (score = 1) | • Study clearly states aims, methods, assumptions and limitations.<br>**AND**<br>• Study clearly states the time frame over which exposures were estimated and what the exposure level represents (e.g., spot measurement, peak, or average over a specified time frame).<br>**AND**<br>• Discussion of sample collection requirements, relevant participant characteristics, and matrix treatment is provided.<br>**AND**<br>• Supplementary data is included, allowing summary statistics to be reproduced. | |
| Medium (score = 2) | • Study clearly states aims, methods, assumptions and limitations.<br>**AND**<br>• Study clearly states the time frame over which exposures were estimated and what the exposure level represents (e.g., spot measurement, peak, or average over a specified time frame). | |

| Confidence Level (Score) | Metric Description | Selected Score |
|---|---|---|
| | **AND**<br>• Discussion of sample collection requirements, relevant participant characteristics, and matrix treatment is provided.<br>**AND**<br>• Supplementary data is not included; summary statistics cannot be reproduced. | |
| Low (score = 3) | • Aims, methods, assumptions and limitations are not clear or not completely reported.<br>**OR**<br>• The time frame over which exposures were estimated and/or what the exposure level represents (e.g., peak, average over a specified time frame) are not clear (e.g., spot measurement, peak, average over a specified time frame).<br>**OR**<br>• Discussion of sample collection requirements, relevant participant characteristics, and matrix treatment is not provided. | |
| Unacceptable (score = 4) | • There are numerous inconsistencies or errors in the calculation and/or reporting of information and results, resulting in highly uncertain reported results. | |
| Not rated/applicable | | |
| **Reviewer's Comments:**<br>*[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | | |
| **Metric 16. Quality Assurance/Quality Control** | | |
| High (score = 1) | • The study applied quality assurance/quality control measures and all pertinent quality assurance information is provided in the data source or companion source. Examples include:<br>➢ Field, laboratory, and/or storage recoveries<br>➢ Field and laboratory control samples<br>➢ Baseline (pre-exposure) samples<br>➢ Biomarker stability<br>➢ Completeness of sample (i.e., creatinine, specific gravity, osmolality for urine samples)<br>**AND**<br>• No quality control issues were identified or, if they were identified, were appropriately addressed (i.e., correction for low recoveries, correction for completeness). | |
| Medium (score = 2) | • It is stated that quality assurance/quality control measures were used, but no details were provided.<br>**AND**<br>• No quality control issues were identified or any identified issues were minor and addressed (i.e., correction for low recoveries, correction for completeness). | |
| Low (score = 3) | • Information on quality assurance/quality control was absent.<br>**OR**<br>• Quality assurance/quality control measures were applied and documented; however, minor quality control issues have been identified but not addressed, or there may be some reporting inconsistencies. | |
| Unacceptable (score = 4) | • QA/QC issues have been identified which significantly interfere with the overall reliability of the study, and are not addressed. | |
| Not rated/applicable | | |

| Confidence Level (Score) | Metric Description | Selected Score |
|---|---|---|
| **Reviewer's Comments:**<br>*[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | | |
| **Domain 4. Variability and Uncertainty** | | |
| **Metric 17. Variability** | | |
| High (score = 1) | • Study summarizes mean and variation in exposure levels for one or more groups.<br>**AND**<br>• Study presents discussion of sources of variability. | |
| Medium (score = 2) | • Not applicable. This metric is dichotomous (i.e., high versus low). | |
| Low (score = 3) | • Study does not summarize mean and variation in exposure levels for any groups.<br>**AND/OR**<br>• Study does not present discussion of sources of variability. | |
| Unacceptable (score = 4) | • Not applicable. This metric is dichotomous (i.e., high versus low). | |
| Not rated/applicable | | |
| **Reviewer's Comments:**<br>*[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | | |
| **Metric 18. Uncertainties** | | |
| High (score = 1) | • Key uncertainties, limitations, and data gaps are recognized and discussed (e.g., those related to inherent variability in environmental and exposure-related parameters or possible measurement errors).<br>**AND**<br>• The uncertainties are minimal. | |
| Medium (score = 2) | • Not applicable. This metric is dichotomous (i.e., high versus low). | |
| Low (score = 3) | • Key uncertainties, limitations, or data gaps are not recognized or discussed.<br>**AND/OR**<br>• Estimates are highly uncertain. | |
| Unacceptable (score = 4) | • Not applicable. This metric is dichotomous (i.e., high versus low). | |
| Not rated/applicable | | |
| **Reviewer's Comments:**<br>*[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | | |

### E.6.5 Experimental Data

**Table E-14. Serious Flaws that Would Make Sources of Experimental Data Unacceptable for Use in the Exposure Assessment**

Optimization of the list of serious flaws may occur after pilot calibration exercises.

| Domain | Metric | Description of Serious Flaw(s) in Data Source |
|---|---|---|
| Reliability | Sampling Methodology and Conditions | The sampling methodology is not discussed in the data source or companion source. |
| | | Sampling methodology is not scientifically sound or is not consistent with widely accepted methods/approaches for the chemical and media being analyzed (e.g., inappropriate sampling equipment, improper storage conditions). |
| | | There are numerous inconsistencies in the reporting of sampling information, resulting in high uncertainty in the sampling methods used. |
| | Analytical Methodology | Analytical methodology is not described, including analytical instrumentation (i.e., HPLC, GC). |
| | | Analytical methodology is not scientifically appropriate for the chemical and media being analyzed (e.g., method not sensitive enough, not specific to the chemical, out of date). |
| | | There are numerous inconsistencies in the reporting of analytical information, resulting in high uncertainty in the analytical methods used. |
| | Selection of Biomarker of Exposure | Biomarker in a specified matrix is a poor surrogate (low accuracy and precision) for exposure/dose. |
| Representative | Testing Scenario | Testing conditions are not relevant to the exposure scenario of interest for the chemical. |
| | Sample Size and Variability | Sample size is not reported. |
| | | Single sample collected per data set. |
| | | For biomonitoring studies, the timing of sample collected is not appropriate based on chemical properties (e.g., half-life), the pharmacokinetics of the chemical (e.g., rate of uptake and elimination), and when the exposure event occurred. |
| | Temporality | Temporality of tested items is not reported, discussed, or referenced. |
| Accessibility / Clarity | Reporting of Results | There are numerous inconsistencies or errors in the calculation and/or reporting of results, resulting in highly uncertain reported results. |
| | Quality Assurance | QA/QC issues have been identified which significantly interfere with the overall reliability of the study. |
| Variability and Uncertainty | Variability and Uncertainty | Estimates are highly uncertain based on characterization of variability and uncertainty. |

Notes:
GC = Gas chromatography
HPLC = High pressure liquid chromatography
QA/QC = Quality assurance/quality control

## Table E-15. Evaluation Criteria for Sources of Experimental Data

| Confidence Level (Score) | Metric Description | Selected Score |
|---|---|---|
| **Domain 1. Reliability** | | |
| **Metric 1. Sampling Methodology and Conditions** | | |
| High (score = 1) | • Samples were collected according to publicly available SOPs, methods, protocols, or test guidelines that are scientifically sound and widely accepted from a source generally known to use sound methods and/or approaches such as EPA, NIST, ASTM, ISO, and ACGIH.<br>**OR**<br>• The sampling protocol used was not a publicly available SOP from a source generally known to use sound methods and/or approaches, but the sampling methodology is clear, appropriate (i.e., scientifically sound), and similar to widely accepted protocols for the chemical and media of interest. All pertinent sampling information is provided in the data source or companion source. Examples include:<br>➢ sampling conditions (e.g., temperature, humidity)<br>➢ sampling equipment and procedures<br>➢ sample storage conditions/duration<br>➢ performance/calibration of sampler | |
| Medium (score = 2) | • Sampling methodology is discussed in the data source or companion source and is generally appropriate (i.e., scientifically sound) for the chemical and media of interest, however, one or more pieces of sampling information is not described. The missing information is unlikely to have a substantial impact on results.<br>**OR**<br>• Standards, methods, protocols, or test guidelines may not be widely accepted, but a successful validation study for the new/unconventional procedure was conducted prior to the sampling event and is consistent with sound scientific theory and/or accepted approaches. | |
| Low (score = 3) | • Sampling methodology is only briefly discussed, therefore, most sampling information is missing and likely to have a substantial impact on results.<br>**AND/OR**<br>• The sampling methodology does not represent best sampling methods, protocols, or guidelines for the chemical and media of interest (e.g., outdated (but still valid) sampling equipment or procedures, long storage durations).<br>**AND/OR**<br>• There are some inconsistencies in the reporting of sampling information (e.g., differences between text and tables in data source, differences between standard method and actual procedures reported to have been used, etc.) which lead to a low confidence in the sampling methodology used. | |
| Unacceptable (score = 4) | • The sampling methodology is not discussed in the data source or companion source.<br>**AND/OR**<br>• Sampling methodology is not scientifically sound or is not consistent with widely accepted methods/approaches for the chemical and media being analyzed (e.g., inappropriate sampling equipment, improper storage conditions).<br>**AND/OR**<br>There are numerous inconsistencies in the reporting of sampling information, resulting in high uncertainty in the sampling methods used. | |
| Not rated/applicable | | |

| Confidence Level (Score) | Metric Description | Selected Score |
|---|---|---|
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 2. Analytical Methodology** | | |
| High (score = 1) | • Samples were analyzed according to publically available analytical methods that are scientifically sound and widely accepted (i.e.,from a source generally using sound methods and/or approaches) and are appropriate for the chemical and media of interest. Examples include EPA SW-846 Methods, NIOSH Manual of Analytical Methods 5th Edition, etc.<br>**OR**<br>• The analytical method used was not a publically available method from a source generally known to use sound methods and/or approaches, but the methodology is clear and appropriate (i.e., scientifically sound) and similar to widely accepted protocols for the chemical and media of interest. All pertinent sampling information is provided in the data source or companion source. Examples include:<br>➢ extraction method<br>➢ analytical instrumentation (required)<br>➢ instrument calibration<br>➢ LOQ, LOD, detection limits, and/or reporting limits<br>➢ recovery samples<br>➢ biomarker used (if applicable)<br>➢ matrix-adjustment method (i.e., creatinine, lipid, moisture) | |
| Medium (score = 2) | • Analytical methodology is discussed in detail and is clear and appropriate (i.e., scientifically sound) for the chemical and media of interest; however, one or more pieces of analytical information is not described. The missing information is unlikely to have a substantial impact on results.<br>**AND/OR**<br>• The analytical method may not be standard/widely accepted, but a method validation study was conducted prior to sample analysis and is expected to be consistent with sound scientific theory and/or accepted approaches.<br>**AND/OR**<br>• Samples were collected at a site and immediately analyzed using an on-site mobile laboratory, rather than shipped to a stationary laboratory. | |
| Low (score = 3) | • Analytical methodology is only briefly discussed. Analytical instrumentation is provided and consistent with accepted analytical instrumentation/methods. However, most analytical information is missing and likely to have a substantial impact on results.<br>**AND/OR**<br>• Analytical method is not standard/widely accepted, and method validation is limited or not available.<br>**AND/OR**<br>• Samples were analyzed using field screening techniques.<br>**AND/OR**<br>• LOQ, LOD, detection limits, and/or reporting limits not reported.<br>**AND/OR**<br>• There are some inconsistencies or possible errors in the reporting of analytical information (e.g., differences between text and tables in data source, differences between standard method and actual procedures reported to have | |

| Confidence Level (Score) | Metric Description | Selected Score |
|---|---|---|
| | been used, etc.) which leads to a lower confidence in the method used. | |
| Unacceptable (score = 4) | • Analytical methodology is not described, including analytical instrumentation (i.e., HPLC, GC).<br>**AND/OR**<br>• Analytical methodology is not scientifically appropriate for the chemical and media being analyzed (e.g., method not sensitive enough, not specific to the chemical, out of date).<br>**AND/OR**<br>• There are numerous inconsistencies in the reporting of analytical information, resulting in high uncertainty in the analytical methods used. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 3. Selection of Biomarker of Exposure** | | |
| High (score = 1) | • Biomarker in a specified matrix is known to have an accurate and precise quantitative relationship with external exposure, internal dose, or target dose (e.g., previous studies (or the current study) have indicated the biomarker of interest reflects external exposures).<br>**AND**<br>• Biomarker (parent chemical or metabolite) is derived from exposure to the chemical of interest. | |
| Medium (score = 2) | • Biomarker in a specified matrix has accurate and precise quantitative relationship with external exposure, internal dose, or target dose.<br>**AND**<br>• Biomarker is derived from multiple parent chemicals, not only the chemical of interest, **but** there is a stated method to apportion the estimate to only the chemical of interest | |
| Low (score = 3) | • Biomarker in a specified matrix has accurate and precise quantitative relationship with external exposure, internal dose, or target dose.<br>**AND**<br>• Biomarker is derived from multiple parent chemicals, not only the chemical of interest, **and** there is NOT a stated method to apportion the estimate to only the chemical of interest. | |
| Unacceptable (score = 4) | • Biomarker in a specified matrix is a poor surrogate (low accuracy and precision) for exposure/dose. | |
| Not rated/applicable | • Metric is not applicable to the data source. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 2. Representative** | | |
| **Metric 4. Testing Scenario** | | |
| High (score = 1) | • Testing conditions closely represent relevant exposure scenarios (i.e., population/scenario/media of interest). Examples include:<br>➢ amount and type of chemical / product used<br>➢ source of exposure/test substance | |

| Confidence Level (Score) | Metric Description | Selected Score |
|---|---|---|
| | ➢ method of application or by-stander exposure<br>➢ use of exposure controls<br>➢ microenvironment (location, time, climate, temperature, humidity, pressure, airflow)<br>**AND**<br>• Testing conducted under a broad range of conditions for factors such as temperature, humidity, pressure, airflow, and chemical mass / weight fraction (if appropriate). | |
| Medium (score = 2) | • The data likely represent the relevant exposure scenario (i.e., population/scenario/media of interest). One or more key pieces of information may not be described but the deficiencies are unlikely to have a substantial impact on the characterization of the exposure scenario.<br>**AND/OR**<br>• If surrogate data, activities seem similar to the activities within scope. | |
| Low (score = 3) | • The data lack multiple key pieces of information and the deficiencies are likely to have a substantial impact on the characterization of the exposure scenario.<br>**AND/OR**<br>• There are some inconsistencies or possible errors in the reporting of scenario information (e.g., differences between text and tables in data source, differences between standard method and actual procedures reported to have been used, etc.) which leads to a lower confidence in the scenario assessed.<br>**AND/OR**<br>• If surrogate data, activities have lesser similarity but are still potentially applicable to the activities within scope.<br>**AND/OR**<br>• Testing conducted under a single set of conditions. | |
| Unacceptable (score = 4) | • Testing conditions are not relevant to the exposure scenario of interest for the chemical. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 5. Sample Size and Variability** | | |
| High (score = 1) | • Sample size is reported and large enough (i.e., ≥ 10 samples) to be reasonably assured that the samples represent the scenario of interest.<br>**AND**<br>• Replicate tests performed and variability across tests is characterized (if appropriate). | |
| Medium (score = 2) | • Sample size is moderate (i.e., 5 to 10 samples), thus the data are likely to represent the scenario of interest.<br>**AND**<br>• Replicate tests performed and variability across tests is characterized (if appropriate). | |
| Low (score = 3) | • Sample size is small (i.e., <5 samples), thus the data are likely to poorly represent the scenario of interest.<br>**AND/OR**<br>• Replicate tests were not performed. | |
| Unacceptable | • Sample size is not reported. | |

| Confidence Level (Score) | Metric Description | Selected Score |
|---|---|---|
| (score = 4) | **AND/OR**<br>• Single sample collected per data set.<br>**AND/OR**<br>• For biomonitoring studies, the timing of sample collected is not appropriate based on chemical properties (e.g., half-life), the pharmacokinetics of the chemical (e.g., rate of uptake and elimination), and when the exposure event occurred. | |
| Not rated/applicable | • | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 6. Temporality** | | |
| High (score = 1) | • Source(s) of tested items appears to be current (within 5 years). | |
| Medium (score = 2) | • Source(s) of tested items is less consistent with when current or recent exposures (>5 to 15 years) are expected. | |
| Low (score = 3) | • Source(s) of tested items is not consistent with when current or recent exposures (>15 years) are expected or is not identified. | |
| Unacceptable (score = 4) | • Temporality of tested items is not reported, discussed, or referenced. | |
| Not rated/applicable | • | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 3. Accessibility / Clarity** | | |
| **Metric 7. Reporting of Results** | | |
| High (score = 1) | • Supplementary or raw data (i.e., individual data points) are reported, allowing summary statistics to be calculated or reproduced.<br>**AND**<br>• Summary statistics are detailed and complete. Example parameters include:<br>➢ Description of data set summarized (i.e., location, population, dates, etc.)<br>➢ Range of concentrations or percentiles<br>➢ Number of samples in data set<br>➢ Frequency of detection<br>➢ Measure of variation (CV, standard deviation)<br>➢ Measure of central tendency (mean, geometric mean, median)<br>➢ Test for outliers (if applicable)<br>**AND**<br>• Both adjusted and unadjusted results are provided (i.e., correction for void completeness in urine biomonitoring, whole-volume or lipid adjusted for blood biomonitoring) [only if applicable]. | |
| Medium (score = 2) | • Supplementary or raw data (i.e., individual data points) are not reported, and therefore summary statistics cannot be reproduced.<br>**AND/OR**<br>• Summary statistics are reported but are missing one or more parameters (see description for high). | |

| Confidence Level (Score) | Metric Description | Selected Score |
|---|---|---|
| | **AND/OR**<br>• Only adjusted or unadjusted results are provided, but not both [only if applicable]. | |
| Low (score = 3) | • Supplementary data are not provided, and summary statistics are missing most parameters (see description for high).<br>**AND/OR**<br>• There are some inconsistencies or errors in the results reported, resulting in low confidence in the results reported (e.g., differences between text and tables in data source, less appropriate statistical methods). | |
| Unacceptable (score = 4) | There are numerous inconsistencies or errors in the calculation and/or reporting of results, resulting in highly uncertain reported results. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 8. Quality Assurance** | | |
| High (score = 1) | • The study applied quality assurance/quality control measures and all pertinent quality assurance information is provided in the data source or companion source. Examples include:<br>➢ Laboratory, and/or storage recoveries.<br>➢ Laboratory control samples.<br>➢ Baseline (pre-exposure) samples.<br>➢ Biomarker stability<br>➢ Completeness of sample (i.e., creatinine, specific gravity, osmolality for urine samples)<br>**AND**<br>• No quality control issues were identified or any identified issues were minor and adequately addressed (i.e., correction for low recoveries, correction for completeness). | |
| Medium (score = 2) | • The study applied and documented quality assurance/quality control measures; however, one or more pieces of QA/QC information is not described. Missing information is unlikely to have a substantial impact on results.<br>**AND**<br>• No quality control issues were identified or any identified issues were minor and addressed (i.e., correction for low recoveries, correction for completeness). | |
| Low (score = 3) | • Quality assurance/quality control techniques and results were not directly discussed, but can be implied through the study's use of standard field and laboratory protocols.<br>**AND/OR**<br>• Deficiencies were noted in quality assurance/quality control measures that are likely to have a substantial impact on results.<br>**AND/OR**<br>• There are some inconsistencies in the quality assurance measures reported, resulting in low confidence in the quality assurance/control measures taken and results (e.g., differences between text and tables in data source). | |
| Unacceptable (score = 4) | • QA/QC issues have been identified which significantly interfere with the overall reliability of the study. | |
| Not | | |

| Confidence Level (Score) | Metric Description | Selected Score |
|---|---|---|
| rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 4. Variability and Uncertainty** | | |
| **Metric 9. Variability and Uncertainty** | | |
| High (score = 1) | • The study characterizes variability in the population/media studied.<br>**AND**<br>• Key uncertainties, limitations, and data gaps have been identified.<br>**AND**<br>• The uncertainties are minimal and have been characterized. | |
| Medium (score = 2) | • The study has limited characterization of variability in the population/media studied.<br>**AND/OR**<br>• The study has limited discussion of key uncertainties, limitations, and data gaps.<br>**AND/OR**<br>• Multiple uncertainties have been identified, but are unlikely to have a substantial impact on results. | |
| Low (score = 3) | • The characterization of variability is absent.<br>**AND/OR**<br>• Key uncertainties, limitations, and data gaps are not discussed.<br>**AND/OR**<br>• Uncertainties identified may have a substantial impact on the exposure the exposure assessment | |
| Unacceptable (score = 4) | • Estimates are highly uncertain based on characterization of variability and uncertainty. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

Notes:
ACGIH = American Conference of Governmental Industrial Hygienists
ASTM = American Society for Testing and Materials
CV = Coefficient of variation
GC = Gas chromatography
HPLC = High pressure liquid chromatography
ISO = International Organization for Standardization
LOD = Limit of detection
LOQ = Limit of quantitation
NIOSH = National Institute for Occupational Safety and Health
NIST = National Institute of Standards and Technology
QA/QC = Quality assurance/quality control
SOPs = Standard operating procedures

### E.6.6 Database Data

**Table E-18. Serious Flaws that Would Make Sources of Database Data Unacceptable for Use in the Exposure Assessment**

Optimization of the list of serious flaws may occur after pilot calibration exercises.

| Domain | Metric | Description of Serious Flaw(s) in Data Source |
|---|---|---|
| Reliability | Sampling methodology | The sampling methodologies used were not appropriate for the chemical/media of interest in the database (e.g., inappropriate sampling equipment, improper storage conditions). |
| | Analytical methodology | The analytical methodologies used were not appropriate for the chemical/media of interest in the database (e.g., method not sensitive enough, not specific to the chemical, out of date). |
| Representative | Geographic Area | Geographic location of sampling data within database is not reported, discussed, or referenced. |
| | Temporal | Timing of sample data is not reported, discussed, or referenced. |
| | Exposure Scenario | Data provided in the database are not representative of the media or population of interest. |
| Accessibility / Clarity | Availability of Database and Supporting Documents | No information is provided on the database source or availability to the public. |
| | Reporting Results | There are numerous inconsistencies or errors in the calculation and/or reporting of results, resulting in highly uncertain reported results. |
| | | The information source reporting the analysis of the database data is missing key sections or lacks enough organization and clarity to locate and extract necessary information. |
| Variability and Uncertainty | Variability and Uncertainty | Estimates are highly uncertain based on characterization of variability and uncertainty. |

**Table E-19. Evaluation Criteria for Sources of Database Data**

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 1. Reliability** | | |
| **Metric 1. Sampling methodology** | | |
| High (score = 1) | • Widely accepted sampling methodologies (i.e.,from a source generally using sound methods and/or approaches) were used to generate the data presented in the database. Example SOPs include USGS's "National Field Manual for the Collection of Water-Quality Data", EPA's "Ambient Air Sampling" (SESDPROC-303-R5), etc. | |
| Medium (score = 2) | • The sampling methodologies were consistent with sound scientific theory and/or accepted approaches based on the reported sampling information, but may not have followed published procedures from a source generally known to use sound methods and/or approaches.. | |
| Low (score = 3) | • The sampling methodology was not reported in data source or companion data source. | |
| Unacceptable (score = 4) | • The sampling methodologies used were not appropriate for the chemical/media of interest in the database (e.g., inappropriate sampling equipment, improper storage conditions). | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 2. Analytical methodology** | | |
| High (score = 1) | • Widely accepted analytical methodologies (i.e., from a source generally using sound methods and/or approaches) were used to generate the data presented in the database. Example SOPs include EPA SW-846 Methods, NIOSH Manual of Analytical Methods 5$^{th}$ Edition, etc. | |
| Medium (score = 2) | • The analytical methodologies were consistent with sound scientific theory and/or accepted approaches based on the reported analytical information, but may not have followed published procedures from a source generally known to use sound methods and/or approaches. | |
| Low (score = 3) | • The analytical methodology was not reported in data source or companion data source. | |
| Unacceptable (score = 4) | • The analytical methodologies used were not appropriate for the chemical/media of interest in the database (e.g., method not sensitive enough, not specific to the chemical, out of date). | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 2. Representative** | | |
| **Metric 3. Geographic Area** | | |
| High (score = 1) | • Geographic location(s) is reported, discussed, or referenced. | |
| Medium (score = 2) | • Not applicable. This metric is dichotomous (i.e., high versus unacceptable). | |
| Low | • Not applicable. This metric is dichotomous (i.e., high versus unacceptable). | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| (score = 3) | | |
| Unacceptable (score = 4) | • Geographic location is not reported, discussed, or referenced. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 4. Temporal** | | |
| High (score = 1) | • The data reflect current conditions (within 5 years); and/or<br>• Database contains robust historical data for spatial and temporal analyses (if applicable). | |
| Medium (score = 2) | • The data are less consistent with current or recent exposures (>5 to 15 years); and/or<br>• Database contains sufficient historical data for spatial and temporal analyses (if applicable). | |
| Low (score = 3) | • Data are not consistent with when current exposures (>15 years old) may be expected; and/or<br>• Database does not contain enough historical data for spatial and temporal analyses (if applicable). | |
| Unacceptable (score = 4) | • Timing of sample data is not reported, discussed, or referenced. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 5. Exposure Scenario** | | |
| High (score = 1) | • The data **closely represent relevant exposure scenario (i.e., the population/scenario/media** of interest). Examples include:<br>➢ amount and type of chemical / product used<br>➢ source of exposure<br>➢ method of application or by-stander exposure<br>➢ use of exposure controls<br>• microenvironment (location, time, climate) | |
| Medium (score = 2) | • The data likely represent the relevant exposure scenario (i.e., population/scenario/media of interest). **One or more key pieces of information may not be described** but the deficiencies are unlikely to have a substantial impact on the characterization of the exposure scenario.<br>**AND/OR**<br>• If surrogate data, activities seem similar to the activities within scope. | |
| Low (score = 3) | • The data lack multiple key pieces of information and the deficiencies are likely to have a substantial impact on the characterization of the exposure scenario.<br>**AND/OR**<br>• There are **some inconsistencies or possible errors** in the reporting of scenario information (e.g., differences between text and tables in data source, differences between standard method and actual procedures reported to have been used, etc.) which leads to a lower confidence in the scenario assessed.<br>**AND/OR** | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | • If surrogate data, activities have lesser similarity but are still potentially applicable to the activities within scope. | |
| Unacceptable (score = 4) | • If reported, the exposure scenario discussed in the monitored study does not represent the exposure scenario of interest for the chemical. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 3. Accessibility / Clarity** | | |
| **Metric 6. Availability of Database and Supporting Documents** | | |
| High (score = 1) | • Database is widely accepted and/or from a source generally known to use sound methods and/or approaches (e.g., NHANES, STORET). | |
| Medium (score = 2) | • The database may not be widely known or accepted (e.g., state maintained databases), but the database is adequately documented with the following information:<br>➢ Within the database, metadata is present (sample identifiers, annotations, flags, units, matrix descriptions, etc.) and data fields are generally clear and defined.<br>➢ A user manual other supporting documentation is available, or there is sufficient documentation in the data source or companion source.<br>➢ Database quality assurance and data quality control measures are defined and/or a QA/QC protocol was followed. | |
| Low (score = 3) | • The database may not be widely known or accepted and only limited database documentation is available (see the medium rating). | |
| Unacceptable (score = 4) | • No information is provided on the database source or availability to the public. | |
| Not rated/ applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 7. Reporting of Results** | | |
| High (score = 1) | • The information source reporting the analysis of the database data is well organized and understandable by the target audience.<br>**AND**<br>• Summary statistics in the data source are detailed and complete. Example parameters include:<br>➢ Description of data set summarized (i.e., location, population, dates, etc.)<br>➢ Range of concentrations or percentiles<br>➢ Number of samples in data set<br>➢ Frequency of detection<br>➢ Measure of variation (CV, standard deviation)<br>➢ Measure of central tendency (mean, geometric mean, median)<br>➢ Test for outliers (if applicable) | |
| Medium (score = 2) | • The information source reporting the analysis of the database data is well organized and understandable by the target audience.<br>**AND**<br>• Summary statistics are missing one or more parameters (see description for high). | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| Low (score = 3) | • The information source reporting the analysis of the database data is unclear or not well organized.<br>**AND/OR**<br>• Summary statistics are missing most parameters (see description for high)<br>**AND/OR**<br>• There are some inconsistencies or errors in the results reported, resulting in low confidence in the results reported (e.g., differences between text and tables in data source, less appropriate statistical methods). | |
| Unacceptable (score = 4) | • There are numerous inconsistencies or errors in the calculation and/or reporting of results, resulting in highly uncertain reported results.<br>**AND/OR**<br>• The information source reporting the analysis of the database data is missing key sections or lacks enough organization and clarity to locate and extract necessary information. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 4. Variability and Uncertainty** | | |
| **Metric 8. Variability and Uncertainty** | | |
| High (score = 1) | • Key uncertainties, limitations, and data gaps have been identified.<br>**AND**<br>• The uncertainties are minimal and have been characterized. | |
| Medium (score = 2) | • The study has limited discussion of key uncertainties, limitations, and data gaps.<br>**AND/OR**<br>• Multiple uncertainties have been identified, but are unlikely to have a substantial impact on results. | |
| Low (score = 3) | • Key uncertainties, limitations, and data gaps are not discussed.<br>**AND/OR**<br>• Uncertainties identified may have a substantial impact on the exposure the exposure assessment | |
| Unacceptable (score = 4) | • Estimates are highly uncertain based on characterization of variability and uncertainty. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

Notes:
CV = Coefficient of variation
NHANES = National Health and Nutrition Examination Survey
NIOSH = National Institute for Occupational Safety and Health
QA/QC = Quality assurance/quality control
SOPs = Standard operating procedures
STORET = Storage and Retrieval for Water Quality Data database
USGS = U.S. Geological Survey

### E.6.7 Completed Exposure Assessments and Risk Characterizations

**Table E-16. List of Serious Flaws that Would Make Completed Exposure Assessments and Risk Characterizations Unacceptable for Use in the Exposure Assessment**

Optimization of the list of serious flaws may occur after pilot calibration exercises.

| Domain | Metric | Description of Serious Flaw(s) in Data Source |
|---|---|---|
| Reliability | Methodology | The assessment uses techniques that are not appropriate (e.g., inappropriate assumptions, models not within domain of the exposure scenario, etc.). |
| | | Assumptions, extrapolations, measurements, and models are not described. |
| | | There appears to be mathematical errors or errors in logic which significantly interfere with the overall reliability of the study. |
| Representative | Exposure Scenario | If reported, the exposure scenario discussed in the monitored study does not represent the exposure scenario of interest for the chemical. |
| | | Surrogate data, if available, are not similar enough to the chemical and use of interest to be used. |
| Accessibility / Clarity | Documentation of References | The reported data, inputs, and defaults are not documented or only sparsely documented. |
| Variability and Uncertainty | Variability and Uncertainty | Estimates are highly uncertain based on characterization of variability and uncertainty. |

**Table E-17. Evaluation Criteria for Completed Exposure Assessments and Risk Characterizations**

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 1. Reliability** | | |
| **Metric 1. Methodology** | | |
| High (score = 1) | • The assessment uses technical approaches that are generally accepted by the scientific community.<br>**AND**<br>• Assumptions, extrapolations, measurements, and models have been documented and described.<br>**AND**<br>• There are no mathematical errors or errors in logic. | |
| Medium (score = 2) | • The assessment uses techniques that are from reliable sources and are generally accepted by the scientific community; however, a discussion of assumptions, extrapolations, measurements, and models is limited. | |
| Low (score = 3) | • The assessment uses techniques that may not be generally accepted by the scientific community.<br>**AND/OR** | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | • There is only a brief discussion of assumptions, extrapolations, measurements, and models, or some components may be missing.<br>**AND/OR**<br>• There are some mathematical errors or errors in logic. | |
| Unacceptable (score = 4) | • The assessment uses techniques that are not appropriate (e.g., inappropriate assumptions, models not within domain of the exposure scenario, etc.)<br>**AND/OR**<br>• Assumptions, extrapolations, measurements, and models are not described.<br>**AND/OR**<br>• There appears to be mathematical errors or errors in logic which significantly interfere with the overall reliability of the study. | |
| Not rated/applicable | | |
| Reviewer's Comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 2. Representative** | | |
| **Metric 2. Exposure Scenario** | | |
| High (score = 1) | • The data (media concentrations, doses, estimated values, exposure factors) closely represent exposure scenarios of interest. Examples include:<br>➢ geography<br>➢ temporality<br>➢ chemical/use of interest | |
| Medium (score = 2) | • The exposure activity assessed likely represents the population/scenario/media of interest; however, one or more key pieces of information may not be described.<br>**OR**<br>• If surrogate data, activities seem similar to the activities within scope. | |
| Low (score = 3) | • The study lacks multiple key pieces of information and the deficiencies are likely to have a substantial impact on the characterization of the exposure scenario.<br>**AND/OR**<br>• There are some inconsistencies or possible errors in the reporting of scenario information (e.g., differences between text and tables in data source, differences between standard method and actual procedures reported to have been used, etc.) which leads to a lower confidence in the scenario assessed.<br>**AND/OR**<br>• If surrogate data, activities have lesser similarity but are still potentially applicable to the activities within scope. | |
| Unacceptable (score = 4) | • If reported, the exposure scenario discussed in the monitored study does not represent the exposure scenario of interest for the chemical.<br>**AND/OR**<br>• Surrogate data, if available, are not similar enough to the chemical and use of interest to be used. | |
| Not rated/applicable | | |
| Reviewer's Comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 3. Accessibility / Clarity** | | |
| **Metric 3. Documentation of References** | | |
| High (score = 1) | • References are available for all reported data, inputs, and defaults.<br>**AND**<br>• References generally appear to be from publically available and peer reviewed sources. | |
| Medium (score = 2) | • References are available for all reported data, inputs, and defaults; however, some references may not be publically available or are not from peer reviewed sources (i.e., professional judgment, personal communication). | |
| Low (score = 3) | • Numerous references for reported data, inputs, and defaults appear to be missing or there are discrepancies with the references.<br>**AND/OR**<br>• Numerous references may not be publically available or are not from peer reviewed sources (i.e., professional judgment or personal communication). | |
| Unacceptable (score = 4) | • The reported data, inputs, and defaults are not documented or only sparsely documented. | |
| Not rated/applicable | | |
| Reviewer's Comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 4. Variability and Uncertainty** | | |
| **Metric 4. Variability and Uncertainty** | | |
| High (score = 1) | • The study characterizes variability in the population/media studied.<br>**AND**<br>• Key uncertainties, limitations, and data gaps have been identified.<br>**AND**<br>• The uncertainties are minimal and have been characterized. | |
| Medium (score = 2) | • The study has limited characterization of variability in the population/media studied.<br>**AND/OR**<br>• The study has limited discussion of key uncertainties, limitations, and data gaps.<br>**AND/OR**<br>• Multiple uncertainties have been identified, but are unlikely to have a substantial impact on results. | |
| Low (score = 3) | • The characterization of variability is absent.<br>**AND/OR**<br>• Key uncertainties, limitations, and data gaps are not discussed.<br>**AND/OR**<br>• Uncertainties identified may have a substantial impact on the exposure the exposure assessment | |
| Unacceptable (score = 4) | • Estimates are highly uncertain based on characterization of variability and uncertainty. | |
| Not rated/applicable | | |
| Reviewer's Comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

## E.7 References


1. ECHA. (2011). Guidance on information requirements and chemical safety assessment. (ECHA-2011-G-13-EN). https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/4262842.
2. NRC. (1991). Environmental Epidemiology, Volume 1: Public Health and Hazardous Wastes. Washington, DC: The National Academies Press. https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/4262908.
3. U.S. EPA. (2009). Guidance on the Development, Evaluation, and Application of Environmental Models. (EPA/100/K-09/003). Washington, DC: Office of the Science Advisor. https://hero.epa.gov/heronet/index.cfm/reference/download/reference_id/4262976.

# APPENDIX F: DATA QUALITY CRITERIA FOR ECOLOGICAL HAZARD STUDIES

## F.1 Types of Data Sources

The data quality will be evaluated for a variety of ecological hazard studies (Table F-1). Since the availability of information varies considerably on different chemicals, it is anticipated that some ecological hazard studies will not be available while others may be identified beyond those listed in Table F-1.

**Table F-1. Study Types that Provide Ecological Hazard Data**

| Data Category | Types of Data Sources |
|---|---|
| Ecological Hazard | Acute and chronic toxicity to aquatic invertebrates and fish (e.g., freshwater, saltwater, and sediment-based exposures); toxicity to algae, cyanobacteria, and other microorganisms; toxicity to terrestrial invertebrates; acute oral toxicity to birds; toxicity to reproduction of birds; toxicity to terrestrial plants; toxicity to mammalian wildlife |

## F.2 Data Quality Evaluation Domains

The methods for evaluation of study quality were developed after review of selected existing processes and references describing existing study quality and risk of bias evaluation tools for toxicity studies including Criteria for Reporting and Evaluating Ecotoxicity Data (CRED) and ECOTOX knowledgebase (ECOTOX) (EC, 2018; Cooper et al., 2016; Lynch et al., 2016; Moermond et al., 2016b; Samuel et al., 2016; NTP, 2015a; Hooijmans et al., 2014; Koustas et al., 2014; Kushman et al., 2013; Hartling et al., 2012; Hooijmans et al., 2010). These publications, coupled with professional judgment and experience, informed the identification of domains and metrics for consideration in the evaluation and scoring of study quality. The evaluation domains and criteria were developed by harmonizing criteria across existing processes including CRED and ECOTOX processes. Furthermore, the evaluation tool is intended to address elements of TSCA Science Standards 26(h)(1) through 26(h)(5) that EPA must address during the development process of the risk evaluations.

Ecological hazard studies will be evaluated for data quality by assessing the following seven domains: Test Substance, Test Design, Exposure Characterization, Test Organism, Outcome Assessment, Confounding/Variable Control, and Data Presentation and Analysis. The data quality within each domain will be evaluated by assessing unique metrics that pertain to each domain. For example, the Test Substance domain will be evaluated by considering the information reported by the study on the test substance identity, purity, and source. The domains are defined in Table F-2 and further information on evaluation metrics is provided in section F.3.

**Table F-2. Data Evaluation Domains and Definitions**

| Evaluation Domain | Definition |
|---|---|
| Test Substance | Metrics in this domain evaluate whether the information provided in the study provides a reliable[a] confirmation that the test substance used in a study has the same (or sufficiently similar) identity, purity, and properties as the substance of interest. |
| Test Design | Metrics in this domain evaluate whether the experimental design enables the study to distinguish the effect of exposure from other factors. This domain includes metrics related to the use of control groups and randomization in allocation to ensure that the effect of exposure is isolated. |
| Exposure Characterization | Metrics in this domain assess the validity and reliability of methods used to measure or characterize exposure. These metrics evaluate whether exposure to the test substance was characterized using a method(s) that provides valid and reliable results, whether the exposure remained consistent over the duration of the experiment, and whether the exposure levels were appropriate to the outcome of interest. |
| Test Organisms | These metrics assess the appropriateness of the population or organism(s), number of organisms used in the study, and the organism conditions to assess the outcome of interest associated with the exposure of interest. |
| Outcome Assessment | Metrics in this domain assess the validity and reliability of methods, including sensitivity of methods, that are used to measure or otherwise characterize the outcome((e.g.. immobilization as a measure of mortality in aquatic invertebrates) |
| Confounding/Variable Control | Metrics in this domain assess the potential impact of factors other than exposure that may affect the risk of outcome. The metrics evaluate whether studies identify and account for factors that are related to exposure and independently related to outcome (confounding factors) and whether appropriate experimental or analytical (statistical) methods are used to control for factors unrelated to exposure that may affect the risk of outcome (variable control). |
| Data Presentation and Analysis | Metrics in this domain assess whether appropriate statistical methods were used and if data for all outcomes are presented. |
| Other | Metrics in this domain are added as needed to incorporate chemical- or study-specific evaluations. |

Note:

[a] Reliability is defined as "the inherent property of a study or data, which includes the use of well-founded scientific approaches, the avoidance of bias within the study or data collection design and faithful study or data collection conduct and documentation" (ECHA, 2011b).

## F.3 Data Quality Evaluation Metrics

The data quality evaluation domains will be evaluated by assessing unique metrics that have been developed for ecological hazard studies. Each metric will be binned into a confidence level of high, medium, low, or unacceptable. Each confidence level is assigned a numerical score (i.e., 1 through 4) that is used in the method of assessing the overall quality of the study.

Table F-3 lists the data evaluation domains and metrics for ecological hazard studies. Each domain has between 2 and 6 metrics; however, some metrics may not apply to all study types.

A general domain for other considerations is available for metrics that are specific to a given test substance or study type.

EPA/OPPT may modify the metrics used for ecological hazard studies as the Agency acquires experience with the evaluation tool. Any modifications will be documented.

Confidence level specifications for each metric are provided in Table F-4. Table F-7 summarizes the serious flaws that would make ecological hazard studies unacceptable for use in the assessment.

**Table F-3. Data Evaluation Domains and Metrics for Ecological Hazard Studies**

| Evaluation Domain | Number of Metrics Overall | Metrics (Metric Number and Description) |
|---|---|---|
| Test Substance | 3 | • Metric 1: Test Substance Identity<br>• Metric 2: Test Substance Source<br>• Metric 3: Test Substance Purity |
| Test Design | 3 | • Metric 4: Negative Controls<br>• Metric 5: Negative Control Response<br>• Metric 6: Randomized Allocation |
| Exposure Characterization | 6 | • Metric 7: Experimental System/Test Media Preparation<br>• Metric 8: Consistency of Exposure Administration<br>• Metric 9: Measurement of Test Substance Concentration<br>• Metric 10: Exposure Duration and Frequency<br>• Metric 11: Number of Exposure Groups and Spacing of Exposure Levels<br>• Metric 12: Testing at or Below Solubility Limit |
| Test Organisms | 4 | • Metric 13: Test Organism Characteristics<br>• Metric 14: Acclimatization and Pretreatment Conditions<br>• Metric 15: Number of Organisms and Replicates per Group<br>• Metric 16: Adequacy of Test Conditions |
| Outcome Assessment | 2 | • Metric 17: Outcome Assessment Methodology<br>• Metric 18: Consistency of Outcome Assessment |
| Confounding/ Variable Control | 2 | • Metric 19: Confounding Variables in Test design and Procedures<br>• Metric 20: Outcomes Unrelated to Exposure |
| Data Presentation and Analysis | 3 | • Metric 21: Statistical Methods<br>• Metric 22: Reporting of Data<br>• Metric 23: Explanation of Unexpected Outcomes |

## F.4 Scoring Method and Determination of Overall Data Quality Level

Appendix A provides information about the evaluation method that will be applied across the various data/information sources being assessed to support TSCA risk evaluations. This section provides details about the scoring system that will be applied to ecological hazard studies, including the weighting factors assigned to each metric score of each domain.

Some metrics will be given greater weights than others, if they are regarded as key or critical metrics. Thus, EPA/OPPT will use a weighting approach to reflect that some metrics are more important than others when assessing the overall quality of the data.

### F.4.1 Weighting Factors

Each metric was assigned a weighting factor of 1 or 2, with the higher weighting factor (2) given to metrics deemed critical for the evaluation. In selecting critical metrics, EPA recognized that the relevance of an individual study to the risk analysis for a given substance is determined by its ability to inform hazard characterization and/or exposure-response assessment. Thus, the critical metrics are those that determine how well a study answers these key questions:

- Is a change in the outcome demonstrated in the study?
- Is the observed change more likely than not attributable to the substance exposure?
- At what test substance concentrations does the change occur?

EPA/OPPT assigned a weighting factor of 2 to each metric considered critical to answering these questions. Remaining metrics were assigned a weighting factor of 1. Table F-4 identifies the critical metrics (i.e., those assigned a weighting factor of 2) for ecological hazard studies and provides a rationale for selection of each metric. Table F-5 identifies the weighting factors assigned to each metric, and the ranges of possible weighted metric scores for ecological hazard studies.

### F.4.2 Calculation of Overall Study Score

A confidence level (1, 2, or 3 for *High*, *Medium*, or *Low* confidence, respectively) is assigned for each relevant metric within each domain. To determine the overall study score, the first step is to multiply the score for each metric (1, 2, or 3 for *High*, *Medium*, or *Low* confidence, respectively) by the appropriate weighting factor (as shown in Table F-5) to obtain a weighted metric score. The weighted metric scores are then summed and divided by the sum of the weighting factors (for all metrics that are scored) to obtain an overall study score between 1 and 3. The equation for calculating the overall score is shown below:

*Overall Score (range of 1 to 3) = ∑(Metric Score x Weighting Factor)/∑(Weighting Factors)*

Some metrics may not be applicable to all study types. Any metrics that are considered to be *Not rated/not applicable* to the study under evaluation will not be considered in the calculation of the study's overall quality score. These metrics will not be included in the nominator or denominator of the equation above. The overall score will be calculated using only those

metrics that receive a numerical score. Scoring samples for ecological hazard studies are given in Tables F-6 and F-7.

Studies with any single metric scored as unacceptable (score = 4) will be automatically assigned an overall quality score of 4 (*Unacceptable*). An unacceptable score means that serious flaws are noted in the domain metric that consequently make the data unusable (or invalid). If a metric is not applicable for a study type, the serious flaws would not be applicable for that metric and would not receive a score. EPA/OPPT plans to use data with an overall quality level of *High*, *Medium*, or *Low* confidence to quantitatively or qualitatively support the risk evaluations, but does not plan to use data rated as *Unacceptable*. An overall study score will not be calculated when a serious flaw is identified for any metric. If a publication reports more than one study or endpoint, each study and, as needed, each endpoint will be evaluated separately.

Detailed tables showing quality criteria for the metrics are provided in Tables F-8 and F-9, including a table that summarizes the serious flaws that would make the data unacceptable for use in the environmental hazard assessment.

**Table F-4. Ecological Hazard Metrics with Greater Importance in the Evaluation and Rationale for Selection**

| Domain | Critical Metrics with Weighting Factor of 2 (Metric Number) [a] | Rationale |
|---|---|---|
| Test substance | Test substance identity (Metric 1) | The test substance must be identified and characterized definitively to ensure that the study is relevant to the substance of interest. |
| Test design | Negative controls (Metric 4) | A concurrent negative control is required to ensure that any observed effects are attributable to substance exposure. |
| Exposure characterization | Experimental test system/test media preparation (Metric 7) | The design of the test system and methods of test media preparation must take into account the physical-chemical properties (e.g., solubility, volatility) and reactivity of the test substance (e.g., hydrolysis, biodegradation, bioaccumulation, adsorption) to ensure confidence in test substance concentrations, which will allow for determination of a concentration-response relationship and enable valid comparisons across studies. |
| Exposure characterization | Measurement of test substance concentration (Metric 9) [b] | For test substances that have poor water solubility, are volatile or unstable in the test media measurement of test substance concentrations is necessary for determination of a concentration-response relationship and to enable valid comparisons across studies. |
| Test organisms | Test organism characteristics (Metric 13) | The test organism characteristics must be reported to enable assessment of a) whether they are suitable for the endpoint of interest; and b) whether there are species, strain, sex, size, or age/lifestage differences within or between different studies. |
| Outcome assessment | Outcome assessment methodology (Metric 17) | The methods used for outcome assessment must be fully described, valid, and sensitive to ensure that effects are detected, that observed effects are true, and to enable valid comparisons across studies. |
| Confounding/variable control | Confounding variables in test design and procedures (Metric 19) | Control for confounding variables in test design and procedures are necessary to ensure that any observed effects are attributable to substance exposure and not to other factors. |
| Data presentation and analysis | Reporting of data (Metric 22) | Detailed results are necessary to determine if the study authors' conclusions are valid and to determine a exposure-response relationship. |

Notes:

[a] A weighting factor of 1 is assigned for the following metrics: test substance source (metric 2); test substance purity (metric 3); negative control response (metric 5); randomized allocation (metric 6); consistency of exposure administration (metric 8); exposure duration and frequency (metric 10); number of exposure groups and spacing of exposure levels (metric 11); testing at or below solubility limit (metric 12); acclimatization and pretreatment conditions (metric 14); number of organisms and replicates per group (metric 15); adequacy of test conditions (metric 16); consistency of outcome assessment (metric 18); outcomes unrelated to exposure (metric 20); statistical methods (metric 21); and explanation of unexpected outcomes (metric 23)

[b] This metric is applicable only to test substances that have poor water solubility or are volatile or unstable in test media

## Table F-5. Metric Weighting Factors and Range of Weighted Metric Scores for Ecological Hazard Studies

| Domain Number/ Description | Metric Number/Description | Range of Metric Scores[a] | Metric Weighting Factor | Range of Weighted Metric Scores[b] |
|---|---|---|---|---|
| 1. Test substance | 1. Test substance identity | 1 to 3 | 2 | 2 to 6 |
| | 2. Test substance source | | 1 | 1 to 3 |
| | 3.Test substance purity | | 1 | 1 to 3 |
| 2. Test design | 4. Negative controls | | 2 | 2 to 6 |
| | 5. Negative control response | | 1 | 1 to 3 |
| | 6. Randomized allocation | | 1 | 1 to 3 |
| 3. Exposure characterization | 7. Experimental system/test media preparation | | 2 | 2 to 6 |
| | 8. Consistency of exposure administration | | 1 | 1 to 3 |
| | 9. Exposure duration and frequency | | 2 | 2 to 6 |
| | 10. Measurement of test substance concentration | | 1 | 1 to 3 |
| | 11. Number of exposure groups and dose spacing | | 1 | 1 to 3 |
| | 12. Testing at or Below Solubility Limit | | 1 | 1 to 3 |
| 4. Test organisms | 13. Test organism characteristics | | 2 | 2 to 6 |
| | 14. Acclimatization and pretreatment conditions | | 1 | 1 to 3 |
| | 15. Number of organisms and replicates per group | | 1 | 1 to 3 |
| | 16. Adequacy of test conditions | | 1 | 1 to 3 |
| 5. Outcome assessment | 17. Outcome assessment methodology | | 2 | 2 to 6 |
| | 18. Consistency of outcome assessment | | 1 | 1 to 3 |
| 6. Confounding/ variable control | 19. Confounding variables in test design and procedures | | 2 | 2 to 6 |
| | 20. Outcomes unrelated to exposure | | 1 | 1 to 3 |
| 7. Data presentation and analysis | 21. Statistical methods | | 1 | 1 to 3 |
| | 22. Reporting of data | | 2 | 2 to 6 |
| | 23. Explanation of unexpected outcomes | | 1 | 1 to 3 |
| | Sum (if all metrics scored)[c] | | 31 | 31 to 93 |
| Range of Overall Scores, where<br>Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factor | | | | 31/31=1;<br>93/31=3 |
| | High: ≥1 and <1.7 / Medium: ≥1.7 and <2.3 / Low: ≥2.3 and ≤3 | | | Range of overall score = 1 to 3[d] |

Notes:

[a] For the purposes of calculating an overall study score, the range of possible metric scores is 1 to 3 for each metric, corresponding to high and low confidence. No calculations will be conducted if a study receives an "unacceptable" rating (score of "4") for any metric.

[b] The range of weighted scores for each metric is calculated by multiplying the range of metric scores (1 to 3) by the weighting factor for that metric.

[c] The sum of weighting factors and the sum of the weighted scores will differ if some metrics are not scored (not applicable).

[d] The range of possible overall scores is 1 to 3. If a study receives a score of 1 for every metric, then the overall study score will be 1. If a study receives a score of 3 for every metric, then the overall study score will be 3.

**Table F-6. Scoring Example for an Ecological Hazard Study with all Metrics Scored**

| Domain | Metric | Metric Score | Metric Weighting Factor | Weighted Score |
|---|---|---|---|---|
| Test substance | 1. Test substance identity | 2 | 2 | 4 |
| | 2. Test substance source | 3 | 1 | 3 |
| | 3.Test substance purity | 2 | 1 | 2 |
| Test design | 4. Negative controls | 1 | 2 | 2 |
| | 5. Negative control response | 2 | 1 | 2 |
| | 6. Randomized allocation | 3 | 1 | 3 |
| Exposure characterization | 7. Experimental system/test media preparation | 2 | 2 | 4 |
| | 8. Consistency of exposure administration | 1 | 1 | 1 |
| | 9. Exposure duration and frequency | 1 | 2 | 2 |
| | 10. Measurement of test substance concentration | 1 | 1 | 1 |
| | 11. Number of exposure groups and dose spacing | 1 | 1 | 1 |
| | 12. Testing at or Below Solubility Limit | 1 | 1 | 1 |
| Test organisms | 13. Test organism characteristics | 2 | 2 | 4 |
| | 14. Acclimatization and pretreatment conditions | 2 | 1 | 2 |
| | 15. Number of organisms and replicates per group | 1 | 1 | 1 |
| | 16. Adequacy of test conditions | 1 | 1 | 1 |
| Outcome assessment | 17. Outcome assessment methodology | 1 | 2 | 2 |
| | 18. Consistency of outcome assessment | 1 | 1 | 1 |
| Confounding/variable control | 19. Confounding variables in test design and procedures | 2 | 2 | 4 |
| | 20. Outcomes unrelated to exposure | 2 | 1 | 2 |
| Data presentation and analysis | 21. Statistical methods | 2 | 1 | 2 |
| | 22. Reporting of data | 1 | 2 | 2 |
| | 23. Explanation of unexpected outcomes | 2 | 1 | 2 |
| | | Sum | 31 | 49 |
| | | Overall Study Score | **1.6= High** | |

Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factor

| High | Medium | Low |
|---|---|---|
| ≥1 and <1.7 | ≥1.7 and <2.3 | ≥2.3 and ≤3 |

**Table F-7. Scoring Example for an Ecological Hazard with Some Metrics Not Rated/Not Applicable**

| Domain | Metric | Metric Score | Metric Weighting Factor | Weighted Score |
|---|---|---|---|---|
| Test substance | 1. Test substance identity | 2 | 2 | 4 |
| | 2. Test substance source | 3 | 1 | 3 |
| | 3.Test substance purity | 2 | 1 | 2 |
| Test design | 4. Negative controls | 1 | 2 | 2 |
| | 5. Negative control response | 2 | 1 | 2 |
| | 6. Randomized allocation | 3 | 1 | 3 |
| Exposure characterization | 7. Experimental system/test media preparation | 2 | 2 | 4 |
| | 8. Consistency of exposure administration | 1 | 1 | 1 |
| | 9. Exposure duration and frequency | 1 | 2 | 2 |
| | 10. Measurement of test substance concentration | 1 | 1 | 1 |
| | 11. Number of exposure groups and dose spacing | 1 | 1 | 1 |
| | 12. Testing at or Below Solubility Limit | NR | | |
| Test organisms | 13. Test organism characteristics | 3 | 2 | 6 |
| | 14. Acclimatization and pretreatment conditions | 2 | 1 | 2 |
| | 15. Number of organisms and replicates per group | 1 | 1 | 1 |
| | 16. Adequacy of test conditions | NR | | |
| Outcome assessment | 17. Outcome assessment methodology | 1 | 2 | 2 |
| | 18. Consistency of outcome assessment | NR | | |
| Confounding/variable control | 19. Confounding variables in test design and procedures | 3 | 2 | 6 |
| | 20. Outcomes unrelated to exposure | NR | | |
| Data presentation and analysis | 21. Statistical methods | 2 | 1 | 2 |
| | 22. Reporting of data | 1 | 2 | 2 |
| | 23. Explanation of unexpected outcomes | NR | | |
| NR= not rated/not applicable | | Sum | 26 | 46 |
| | | Overall Study Score | **1.8= Medium** | |

Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factor

| High | Medium | Low |
|---|---|---|
| ≥1 and <1.7 | ≥1.7 and <2.3 | ≥2.3 and ≤3 |

## F.5 Data Quality Criteria

**Table F-8. Serious Flaws that Would Make Ecological Hazard Studies Unacceptable**

Optimization of the list of serious flaws may occur after pilot calibration exercises.

| Domain | Metric | Description of Serious Flaw(s) in Data Source |
|---|---|---|
| Test substance | Test substance identity | The test substance identity and form (the latter if applicable) cannot be determined from the information provided (e.g., nomenclature was unclear and CASRN or structure were not reported)<br>**OR**<br>for mixtures, the components and ratios were not characterized. |
| | Test substance source | The test substance was not obtained from a manufacturer<br>**OR**<br>if synthesized or extracted, analytical verification of the test substance was not conducted. |
| | Test substance purity | The nature and quantity of reported impurities were such that study results were likely to be due to one or more of the impurities. |
| Test design | Negative controls | A concurrent negative control group was not included or reported<br>**OR**<br>the reported negative control group was not appropriate (e.g., age/weight of organisms differed between control and treated groups). |
| | Negative control response | The biological responses of the negative control groups were not reported<br>**OR**<br>there was unacceptable variation in biological responses between control replicates. |
| | Randomized allocation | The study reported using a biased method to allocate organisms to study groups (e.g., each study group consists of organisms from a single brood and the broods differ among study groups). |
| Exposure characterization | Experimental system/test media preparation | The physical-chemical properties of the test substance required special considerations for preparation and maintenance of test substance concentrations, but no measures were taken to appropriately prepare test concentrations and/or minimize loss of test substance before and during the exposure and/or the use of such measures was not reported. In addition, the test substance concentrations were not measured, thereby preventing characterization of a concentration-response relationship. |
| | Consistency of exposure administration | Reported information indicated that critical exposure details were inconsistent across study groups and these differences are considered serious flaws that make the study unusable (e.g., for a poorly soluble mixture, a solvent was used for some study groups while a water-accommodated fraction was used for others). |

| Domain | Metric | Description of Serious Flaw(s) in Data Source |
|---|---|---|
| | Measurement of test substance concentration | For test substances that have poor water solubility or are volatile or unstable in test media:<br>Exposure concentrations were not measured and nominal values are highly uncertain due to the nature of the test substance<br>**OR**<br>exposure concentrations were measured but analytical methods were not appropriate for the test substance resulting in serious uncertainties in measured concentrations (e.g., recovery and/or repeatability were poor). |
| | Exposure duration and frequency | The duration of exposure and/or exposure frequency were not reported<br>**OR**<br>the reported duration of exposure and/or exposure frequency were not suited to the study type and/or outcome(s) of interest (e.g., study intended to assess effects on reproduction did not expose organisms to test substance for an acceptable period of time prior to mating). |
| | Number of exposure groups and spacing of exposure levels | The number of exposure groups and spacing of exposure levels were not conducive to the purpose of the study (e.g., the range of concentrations tested was either too high or too low to observe a concentration-response relationship, a LOAEC, NOAEC, $LC_{50}$, or $EC_{50}$ could not be identified)<br>**OR**<br>no information is provided on the number of exposure groups and spacing of exposure levels. |
| | Testing at or below solubility limit | All exposure concentrations greatly exceeded the water solubility limit (or dispersibility limit if applicable) and the range of exposure concentrations tested was insufficient to characterize a concentration-response relationship<br>**AND/OR**<br>the solvent concentration exceeded an appropriate concentration and is likely to have influenced the biological response of the test organisms. |
| Test organisms | Test organism characteristics | The test organisms were not identified sufficiently or were not appropriate for the evaluation of the specific outcome(s) of interest or were not from an appropriate source (e.g., collected from a polluted field site). |
| | Acclimatization and pretreatment conditions | There were serious differences in acclimatization and/or pretreatment conditions between control and exposed groups<br>**OR**<br>organisms were previously exposed to the test substance or other unintended stressors. |
| | Number of organisms and replicates per group | The number of test organisms and/or replicates was insufficient to characterize toxicological effects and/or provided insufficient power for statistical analysis (e.g., 1-2 organisms/group). |

| Domain | Metric | Description of Serious Flaw(s) in Data Source |
|---|---|---|
| | Adequacy of test conditions | Organism housing and/or environmental conditions and/or food, water, and nutrients and/or biomass loading were not conducive to maintenance of health (e.g., overt signs of handling stress are evident). |
| Outcome assessment | Outcome assessment methodology | The outcome assessment methodology was not reported<br>**OR**<br>the reported outcome assessment methodology was not sensitive for the outcome(s) of interest (e.g., in the assessment of reproduction in a chronic daphnid test, offspring were not counted and removed until the end of the test, rather than daily). |
| | Consistency of outcome assessment | There were large inconsistencies in the execution of study protocols for outcome assessment across study groups<br>**OR**<br>outcome assessments were not adequately reported for meaningful interpretation of results. |
| Confounding/ variable control | Confounding variables in test design and procedures | The study reported significant differences among the study groups with respect to environmental conditions (e.g., differences in pH unrelated to the test substance) or other non-treatment-related factors and these prevent meaningful interpretation of the results. |
| | Outcomes unrelated to exposure | One or more study groups experienced serious test organism attrition or outcomes unrelated to exposure (e.g., infection). |
| Data presentation and analysis | Statistical methods | Statistical methods used were not appropriate (e.g., parametric test for non-normally distributed data)<br>**OR**<br>statistical analysis was not conducted<br>**AND**<br>data enabling an independent statistical analysis were not provided. |
| | Reporting of data | Data presentation was inadequate (e.g., the report does not differentiate among findings in multiple treatment groups)<br>**OR**<br>major inconsistencies were present in reporting of results. |
| | Explanation of unexpected outcomes | The occurrence of unexpected outcomes, including, but not limited to, within-study variability and/or variation from historical measures, are considered serious flaws that make the study unusable. |

## Table F-9. Data Quality Criteria for Ecological Hazard Studies

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 1. Test Substance** | | |
| **Metric 1. Test substance identity**<br>Was the test substance identified definitively (i.e., established nomenclature, CASRN, and/or structure reported, including information on the specific form tested [e.g., valence state] for substances that may vary in form)? If test substance is a mixture, were mixture components and ratios characterized? | | |
| High<br>(score = 1) | The test substance was identified definitively and the specific form was characterized (where applicable). For mixtures, the components and ratios were characterized. | |
| Medium<br>(score = 2) | The test substance and form (the latter if applicable) were identified and components and ratios of mixtures were characterized, but there were minor uncertainties (e.g., minor characterization details were omitted) that are unlikely to have a substantial impact on results. | |
| Low<br>(score = 3) | The test substance and form (the latter if applicable) were identified and components and ratios of mixtures were characterized, but there were uncertainties regarding test substance identification or characterization that are likely to have a substantial impact on results. | |
| Unacceptable<br>(score = 4) | The test substance identity and form (the latter if applicable) cannot be determined from the information provided (e.g., nomenclature was unclear and CASRN or structure were not reported)<br>**OR**<br>for mixtures, the components and ratios were not characterized. These are serious flaws that make the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 2. Test substance source**<br>Is the source of the test substance reported, including manufacturer and batch/lot number for materials that may vary in composition? If synthesized or extracted, was test substance identity verified by analytical methods? | | |
| High<br>(score = 1) | The source of the test substance was reported, including manufacturer and batch/lot number for materials that may vary in composition, and its identity was certified by manufacturer and/or verified by analytical methods (e.g., melting point, chemical analysis, etc.). | |
| Medium<br>(score = 2) | The source of the test substance and/or the analytical verification of a synthesized test substance was reported incompletely, but the omitted details are unlikely to have a substantial impact on results. | |
| Low<br>(score = 3) | Omitted details on the source of the test substance and/or the analytical verification of a synthesized test substance are likely to have a substantial impact on results. | |
| Unacceptable<br>(score = 4) | The test substance was not obtained from a manufacturer<br>**OR**<br>if synthesized or extracted, analytical verification of the test substance was not conducted. These are serious flaws that make the study unusable. | |
| Not rated/applicable[a] | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Metric 3. Test substance purity**<br>Was the purity or grade (i.e., analytical, technical) of the test substance reported and adequate to identify its toxicological effects? Were impurities identified? Were impurities present in quantities that could influence the results? | | |
| High<br>(score = 1) | The test substance purity and composition were such that any observed effects were highly likely to be due to the nominal test substance itself (e.g., highly pure or analytical-grade test substance or a formulation comprising primarily inert ingredients with small amount of active ingredient). | |
| Medium<br>(score = 2) | Minor uncertainties or limitations were identified regarding the test substance purity and composition; however, the purity and composition were such that observed effects were more likely than not due to the nominal test substance, and any identified impurities are unlikely to have a substantial impact on results. | |
| Low<br>(score = 3) | Purity and/or grade of test substance were not reported or were low enough to have a substantial impact on results (i.e., observed effects may not be due to the nominal test substance). | |
| Unacceptable<br>(score = 4) | The nature and quantity of reported impurities were such that study results were likely to be due to one or more of the impurities. This is a serious flaw that makes the study unusable. | |
| Not rated/applicable[a] | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 2. Test Design** | | |
| **Metric 4. Negative controls**<br>Was an appropriate concurrent negative control group tested? If a vehicle/solvent was used, was a vehicle (solvent) control tested in parallel? | | |
| High<br>(score = 1) | Study authors reported using an appropriate concurrent negative control group (i.e., all conditions equal except chemical exposure). | |
| Medium<br>(score = 2) | Study authors reported using a concurrent negative control group, but all conditions were not equal to those of treated groups (e.g., untreated control instead of a vehicle control); however, the identified differences are considered to be minor limitations that are unlikely to have a substantial impact on results. | |
| Low<br>(score = 3) | Study authors acknowledged using a concurrent negative control group, but details regarding the negative control group were not reported, and the lack of details is likely to have a substantial impact on results. | |
| Unacceptable<br>(score = 4) | A concurrent negative control group was not included or reported<br>**OR**<br>the reported negative control group was not appropriate (e.g., age/weight of organisms differed between control and treated groups). This is a serious flaw that makes the study unusable. | |
| Not rated/applicable[a] | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 5. Negative control response**<br>Were the biological responses (e.g., survival, growth, reproduction, etc.) of the negative control group(s) adequate? | | |
| High<br>(score = 1) | The biological responses (e.g., survival, growth, reproduction, etc.) of the negative control group(s) were adequate (e.g., mortality of control fish ≤10% in an acute test). | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| Medium (score = 2) | There were minor uncertainties or limitations regarding the biological responses of the negative control group(s) (e.g., differences in outcome between untreated and solvent controls) that are unlikely to have a substantial impact on results. | |
| Low (score = 3) | The biological responses of the negative control group(s) were reported, but there were deficiencies regarding the control responses that are likely to have a substantial impact on results (e.g., 30% mortality of control fish in an acute test). | |
| Unacceptable (score = 4) | The biological responses of the negative control groups were not reported **OR** there was unacceptable variation in biological responses between control replicates. These are serious flaws that make the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 6. Randomized allocation** Did the study explicitly report randomized allocation of organisms to study groups? | | |
| High (score = 1) | The study reported that organisms were randomly allocated into study groups (including the control group). | |
| Medium (score = 2) | The study reported methods of allocation of organisms to study groups, but there were minor limitations in the allocation method (e.g., method with a nonrandom component like assignment to minimize differences in body weight across groups) that are unlikely to have a substantial impact on results. | |
| Low (score = 3) | Researchers did not report how organisms were allocated to study groups, or there were deficiencies regarding the allocation method that are likely to have a substantial impact on results (e.g., allocation by animal number). | |
| Unacceptable (score = 4) | The study reported using a biased method to allocate organisms to study groups (e.g., each study group consists of organisms from a single brood and the broods differ among study groups). This is a serious flaw that makes the study unusable. | |
| Not rated/applicable[a] | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 3. Exposure Characterization** | | |
| Was the experimental system (e.g., static, semi-static, or flow-through regime) described in adequate detail? Were methods for test media preparation appropriate for the test substance, taking into account its physical-chemical properties (e.g., solubility, volatility) and reactivity (e.g., hydrolysis, biodegradation, bioaccumulation, adsorption)? For reactive, volatile, and/or poorly soluble test substances, were adequate measures taken to prepare and maintain test substance concentrations and minimize loss of test substance before and during the exposure?<br><br>(Based on professional judgment, the reviewer may consider this metric to be not rated/applicable for field and mesocosm studies.) | | |
| High (score = 1) | The experimental system and methods for preparation of test media were described in adequate detail and appropriately accounted for the physical-chemical properties of the test substance (e.g., use of closed, static systems with minimal headspace for volatile substances, use of water-accommodated fractions for multi-component substances that are only partially soluble in water, etc.). | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| Medium (score = 2) | The experimental system and/or test media preparation methods were adequately reported but did not completely account for physical-chemical properties (e.g., period between renewals was greater than the half-life of a test substance that degrades in the system); however, the identified limitations are unlikely to have a substantial impact on results. | |
| Low (score = 3) | The type of experimental system and/or test media preparation methods were not reported<br>**OR**<br>the study provided only limited details on the measures taken to appropriately prepare test concentrations and/or minimize loss of test substance before and during the exposure for reactive, volatile, and/or poorly soluble substances<br>**AND**<br>concentrations of test substance were not measured during the study. Therefore, the deficiencies are likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | The physical-chemical properties of the test substance required special considerations for preparation and maintenance of test substance concentrations, but no measures were taken to appropriately prepare test concentrations and/or minimize loss of test substance before and during the exposure and/or the use of such measures was not reported. In addition, the test substance concentrations were not measured, thereby preventing characterization of a concentration-response relationship. These are serious flaws that make the study unusable. | |
| Not rated/applicable[a] | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 8. Consistency of exposure administration**<br>Were exposures administered consistently across study groups (e.g., same exposure protocol; same time of day)? | | |
| High (score = 1) | Details of exposure administration were reported and exposures were administered consistently across study groups. | |
| Medium (score = 2) | Details of exposure administration were reported, but minor inconsistencies in administration of exposures among study groups were identified that are unlikely to have a substantial impact on results (e.g., slightly different solvent concentrations). | |
| Low (score = 3) | Details of exposure administration were reported, but inconsistencies in administration of exposures among study groups are considered deficiencies that are likely to have a substantial impact on results (e.g., differing periods between renewal for an unstable test substance)<br>**OR**<br>reporting omissions are likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | Reported information indicated that critical exposure details were inconsistent across study groups and these differences are considered serious flaws that make the study unusable (e.g., for a poorly soluble mixture, a solvent was used for some study groups while a water-accommodated fraction was used for others). | |
| Not rated/applicable[a] | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Metric 9. Measurement of test substance concentration**<br>If test substance has poor water solubility, is volatile or unstable in the test system (e.g., hydrolyzes or biodegrades rapidly), is bioaccumulated by biota, adsorbs to objects in the test system, or is otherwise subject to factors that are likely to cause test concentrations to change during exposure, were test substance concentrations in the exposure medium measured analytically? Were appropriate analytical methods used (i.e., recovery and repeatability were demonstrated)?<br><br>This metric is not rated/applicable if the test substance does not have poor water solubility and is not subject to any factors that are likely to cause test concentrations to change during exposure. | | |
| High<br>(score = 1) | Exposure concentrations were measured using appropriate analytical methods (i.e., recovery and repeatability were demonstrated). Endpoints were based on measured concentrations or analytically verified nominal concentrations. | |
| Medium<br>(score = 2) | Exposure concentrations were measured and measured concentrations were similar to nominal, but analytical methods were not reported<br>**OR**<br>exposure concentrations were not measured, but based on professional judgment of experimental design and nature of test substance, actual concentrations are likely to be similar to nominal concentrations. These minor uncertainties or limitations are unlikely to have a substantial impact on results. | |
| Low<br>(score = 3) | Exposure concentrations were not measured or measurements were not reported<br>**AND**<br>based on professional judgment of experimental design and nature of test substance, actual concentrations cannot be expected to be similar to nominal concentrations. This is likely to have a substantial impact on results | |
| Unacceptable<br>(score = 4) | Exposure concentrations were not measured and nominal values are highly uncertain due to the nature of the test substance<br>**OR**<br>exposure concentrations were measured but analytical methods were not appropriate for the test substance resulting in serious uncertainties in measured concentrations (e.g., recovery and/or repeatability were poor). These are serious flaws that make the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 10. Exposure duration and frequency**<br>Were the duration of exposure and/or exposure frequency reported and appropriate for the study type and/or outcome(s) of interest? | | |
| High<br>(score = 1) | The duration of exposure and/or exposure frequency were reported and appropriate for the study type and/or outcome(s) of interest (e.g., acute daphnid study of 48-hour duration). | |
| Medium<br>(score = 2) | Minor limitations in exposure frequency and duration of exposure were identified (e.g., acute daphnid toxicity study of 24-hour duration) but are unlikely to have a substantial impact on results. | |
| Low<br>(score = 3) | The duration of exposure and/or exposure frequency differed significantly from typical study designs (e.g., acute daphnid toxicity study of 8-hour duration), and these deficiencies are likely to have a substantial impact on results. | |
| Unacceptable<br>(score = 4) | The duration of exposure and/or exposure frequency were not reported<br>**OR** | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | the reported duration of exposure and/or exposure frequency were not suited to the study type and/or outcome(s) of interest (e.g., study intended to assess effects on reproduction did not expose organisms to test substance for an acceptable period of time prior to mating). These are serious flaws that make the study unusable. | |
| Not rated/applicable[a] | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 11. Number of exposure groups and spacing of exposure levels**<br>Were the number of exposure groups and spacing of exposure levels justified by study authors (e.g., based on range-finding studies) and adequate to address the purpose of the study? Did the range of concentrations/doses tested allow for identification of endpoint values (i.e., LOAEC and NOAEC, $LC_{50}$, or $EC_{50}$, depending upon duration of study)? | | |
| High (score = 1) | The number of exposure groups and spacing of exposure levels were justified by study authors, adequate to address the purpose of the study (e.g., the selected doses produce a range of responses), and allowed for identification of endpoint values. | |
| Medium (score = 2) | There were minor limitations regarding the number of exposure groups and/or spacing of exposure levels (e.g., unclear if lowest concentration was low enough), but the number of exposure groups and spacing of exposure levels were adequate to show results relevant to the outcome of interest (e.g., observation of a concentration-response relationship) and the concerns are unlikely to have a substantial impact on results. | |
| Low (score = 3) | There were deficiencies regarding the number of exposure groups and/or spacing of exposure levels (e.g., narrow spacing between exposure levels with similar responses across groups), which may include the omission of some important details (e.g., not all exposure levels are specified), and these are likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | The number of exposure groups and spacing of exposure levels were not conducive to the purpose of the study (e.g., the range of concentrations tested was either too high or too low to observe a concentration-response relationship, a LOAEC, NOAEC, $LC_{50}$, or $EC_{50}$ could not be identified)<br>**OR**<br>no information is provided on the number of exposure groups and spacing of exposure levels. These are serious flaws that make the study unusable. | |
| Not rated/applicable[a] | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 12. Testing at or below solubility limit**<br>Were exposure concentrations at or below the limit of water solubility (or dispersibility limit if applicable)? If a solvent was used, was the solvent concentration appropriate (i.e., no effects on biological responses were observed in the solvent control and no interactions were expected between the solvent and test substance)? | | |
| High (score = 1) | Exposure concentrations were at or below the water solubility limit (or dispersibility limit if applicable). The solvent concentration was appropriate. | |
| Medium (score = 2) | A subset of the exposure concentrations exceeded the water solubility limit (or dispersibility limit if applicable) but a sufficient range of exposure concentrations was tested to characterize a concentration-response relationship<br>**AND/OR** | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | the solvent concentration slightly exceeded an appropriate concentration or was not reported, but the biological response of the solvent control was acceptable and no interactions are expected between the solvent and test substance. These minor uncertainties or limitations are unlikely to have a substantial impact on results. | |
| Low (score = 3) | Reporting omissions prevented determination of whether exposure concentrations exceeded the water solubility limit (or dispersibility limit if applicable)<br>**AND/OR**<br>both the solvent concentration and biological response of the solvent control were not reported. These deficiencies are likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | All exposure concentrations greatly exceeded the water solubility limit (or dispersibility limit if applicable) and the range of exposure concentrations tested was insufficient to characterize a concentration-response relationship<br>**AND/OR**<br>the solvent concentration exceeded an appropriate concentration and is likely to have influenced the biological response of the test organisms. These are serious flaws that make the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 4. Test Organisms** | | |
| **Metric 13. Test organism characteristics**<br>Were the species, strain, sex, age, size, life stage, and/or embryonic stage of the test organisms reported and appropriate for the evaluation of the specific outcome(s) of interest (e.g., routinely used for similar study types or acceptable rationale provided for selection)? Were the test organisms from a reliable source? | | |
| High (score = 1) | The test organisms were adequately described and were obtained from a reliable source. The test organisms were appropriate for evaluation of the specific outcome(s) of interest (e.g., routinely used for similar study types or acceptable rationale provided for selection). | |
| Medium (score = 2) | There are minor reservations or uncertainties about the choice of test species, source of test organisms, or characteristics of test organisms (e.g., age, size, or sex not reported for fish) that are unlikely to have a substantial impact on results. | |
| Low (score = 3) | There were significant deficiencies or concerns regarding the choice of test species, source of test organisms, or characteristics of test organisms that are likely to have a substantial impact on study results. | |
| Unacceptable (score = 4) | The test organisms were not identified sufficiently or were not appropriate for the evaluation of the specific outcome(s) of interest or were not from an appropriate source (e.g., collected from a polluted field site). These are serious flaws that make the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Metric 14. Acclimatization and pretreatment conditions**<br>Were the test organisms acclimatized to test conditions? Were pretreatment conditions the same for control and exposed groups? | | |
| High<br>(score = 1) | The test organisms were acclimatized to test conditions and all pretreatment conditions were the same for control and exposed populations, such that the only difference was exposure to test substance. | |
| Medium<br>(score = 2) | Some acclimatization and/or pretreatment conditions differed between control and exposed populations, but the differences are unlikely to have a substantial impact on results or there are minor uncertainties or limitations in the details provided. | |
| Low<br>(score = 3) | The study did not report whether test organisms were acclimatized and/or whether pretreatment conditions were the same for control and exposed groups, and this is likely to have a substantial impact on results. | |
| Unacceptable<br>(score = 4) | There were serious differences in acclimatization and/or pretreatment conditions between control and exposed groups<br>**OR**<br>organisms were previously exposed to the test substance or other unintended stressors. These are serious flaws that make the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 15. Number of organisms and replicates per group**<br>Were the numbers of test organisms and replicates sufficient to characterize toxicological effects? | | |
| High<br>(score = 1) | The numbers of test organisms and replicates were reported and sufficient to characterize toxicological effects. | |
| Medium<br>(score = 2) | The numbers of test organisms and replicates were sufficient to characterize toxicological effects, but minor uncertainties or limitations were identified regarding the number of test organisms and/or replicates that are unlikely to have a substantial impact on results. | |
| Low<br>(score = 3) | The number of test organisms and/or replicates was not reported and this is likely to have a substantial impact on results. | |
| Unacceptable<br>(score = 4) | The number of test organisms and/or replicates was insufficient to characterize toxicological effects and/or provided insufficient power for statistical analysis (e.g., 1-2 organisms/group). These are serious flaws that make the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 16. Adequacy of test conditions**<br>Were organism housing, environmental conditions (e.g., temperature, pH, dissolved oxygen, hardness, and salinity), food, water, and nutrients conducive to maintenance of health, both before and during exposure? Was the biomass loading of the organisms in the test system appropriate? | | |
| High<br>(score = 1) | Organism housing, environmental conditions, food, water, and nutrients were conducive to maintenance of health and biomass loading was appropriate. | |
| Medium<br>(score = 2) | Minor uncertainties or limitations were identified regarding organism housing, environmental conditions, food, water, nutrients, and/or biomass loading, but these are not likely to have a substantial impact on results. | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| Low (score = 3) | Reporting of housing and/or environmental conditions and/or food, water, and nutrients and/or biomass loading was limited or unclear, and the omitted details are likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | Organism housing and/or environmental conditions and/or food, water, and nutrients and/or biomass loading were not conducive to maintenance of health (e.g., overt signs of handling stress are evident). These are serious flaws that make the study unusable. | |
| Not rated/applicable[a] | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 5. Outcome Assessment** | | |
| **Metric 17. Outcome assessment methodology**<br>Did the outcome assessment methodology address or report the intended outcome(s) of interest? Was the outcome assessment methodology (including endpoints assessed and timing of endpoint assessment) sensitive for the outcome(s) of interest (e.g., measured endpoints that were able to detect a true biological effect or hazard)?<br><br>(Note: Outcome, as addressed in this domain, refers to biological effects measured in an ecotoxicity study; e.g., reproductive toxicity.) | | |
| High (score = 1) | The outcome assessment methodology addressed or reported the intended outcome(s) of interest and was sensitive for the outcomes(s) of interest. | |
| Medium (score = 2) | The outcome assessment methodology partially addressed or reported the intended outcomes(s) of interest (e.g., total number of offspring per group reported in the absence of data on fecundity per individual), but minor uncertainties or limitations are unlikely to have a substantial impact on results. | |
| Low (score = 3) | Significant deficiencies in the reported outcome assessment methodology were identified<br>**OR**<br>due to incomplete reporting, it was unclear whether methods were sensitive for the outcome of interest. This is likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | The outcome assessment methodology was not reported<br>**OR**<br>the reported outcome assessment methodology was not sensitive for the outcome(s) of interest (e.g., in the assessment of reproduction in a chronic daphnid test, offspring were not counted and removed until the end of the test, rather than daily). These are serious flaws that make the study unusable. | |
| Not rated/applicable[a] | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 18. Consistency of outcome assessment**<br>Was the outcome assessment carried out consistently (i.e., using the same protocol) across study groups (e.g., assessment at the same time after initial exposure in all study groups)? | | |
| High (score = 1) | Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups (e.g., at the same time after initial exposure) using the same protocol in all study groups. | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| Medium (score = 2) | There were minor differences in the timing of outcome assessment across study groups, or incomplete reporting of minor details of outcome assessment protocol execution, but these uncertainties or limitations are unlikely to have substantial impact on results. | |
| Low (score = 3) | Details regarding the execution of the study protocol for outcome assessment (e.g., timing of assessment across groups) were not reported, and these deficiencies are likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | There were large inconsistencies in the execution of study protocols for outcome assessment across study groups<br>**OR**<br>outcome assessments were not adequately reported for meaningful interpretation of results. These are serious flaws that make the study unusable. | |
| Not rated/applicable[a] | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 6. Confounding/Variable Control** | | |
| **Metric 19. Confounding variables in test design and procedures**<br>Were all variables consistent across experimental groups or appropriately controlled for in the analysis, including, but not limited to, size and age of test organisms, environmental conditions (e.g., temperature, pH, and dissolved oxygen), and protective or toxic factors that could mask or enhance effects? | | |
| High (score = 1) | There were no reported differences among the study groups in environmental conditions or other factors that could influence the outcome assessment. | |
| Medium (score = 2) | The study reported minor differences among the study groups with respect to environmental conditions or other non-treatment-related factors, but these are unlikely to have a substantial impact on results. | |
| Low (score = 3) | The study did not provide enough information to allow a comparison of environmental conditions or other non-treatment-related factors across study groups, and the omitted information is likely to have a substantial impact on study results. | |
| Unacceptable (score = 4) | The study reported significant differences among the study groups with respect to environmental conditions (e.g., differences in pH unrelated to the test substance) or other non-treatment-related factors and these prevent meaningful interpretation of the results. These are serious flaws that make the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 20. Outcomes unrelated to exposure**<br>Were there differences among the study groups in test organism attrition or outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment? | | |
| High (score = 1) | Details regarding test organism attrition and outcomes unrelated to exposure (e.g., infection) were reported for each study group and there were no differences among groups that could influence the outcome assessment. | |
| Medium (score = 2) | Authors reported that one or more study groups experienced disproportionate test organism attrition or outcomes unrelated to exposure (e.g., infection), but data from the remaining exposure groups were valid and the low incidence of attrition is unlikely to have a substantial impact on | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | results<br>**OR**<br>data on attrition and/or outcomes unrelated to exposure for each study group were not reported because only substantial differences among groups were noted (as indicated by study authors). | |
| Low<br>(score = 3) | Data on attrition and/or outcomes unrelated to exposure were not reported for each study group, and this deficiency is likely to have a substantial impact on results. | |
| Unacceptable<br>(score = 4) | One or more study groups experienced serious test organism attrition or outcomes unrelated to exposure (e.g., infection). This is a serious flaw that makes the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 7. Data Presentation and Analysis** | | |
| **Metric 21. Statistical methods**<br>Were statistical methods clearly described and appropriate for dataset(s) (e.g., parametric test for normally distributed data)? | | |
| High<br>(score = 1) | Statistical methods were clearly described and appropriate for dataset(s) (e.g., parametric test for normally distributed data).<br>**OR**<br>no statistical analyses, calculation methods, and/or data manipulation were conducted but sufficient data were provided to conduct an independent statistical analysis. | |
| Medium<br>(score = 2) | Not applicable for this metric | |
| Low<br>(score = 3) | Statistical analysis was not described clearly, and this deficiency is likely to have a substantial impact on results. | |
| Unacceptable<br>score = 4) | Statistical methods used were not appropriate (e.g., parametric test for non-normally distributed data)<br>**OR**<br>statistical analysis was not conducted<br>**AND**<br>data enabling an independent statistical analysis were not provided. These are serious flaws that make the study unusable. | |
| Not rated/applicable[a] | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 22. Reporting of data**<br>Were the data for all outcomes presented? Were data reported for each treatment and control group? Were reported data sufficient to determine values for the endpoint(s) of interest (e.g., LOEC, NOEC, $LC_{50}$, and $EC_{50}$)? | | |
| High<br>(score = 1) | Data for exposure-related findings were presented for each treatment and control group and were adequate to determine values for the endpoint(s) of interest. Negative findings were reported qualitatively or quantitatively. | |
| Medium<br>(score = 2) | Data for exposure-related findings were reported for most, but not all, outcomes by study group and/or data were not reported for outcomes with negative findings, but these minor uncertainties or limitations are unlikely to have a substantial impact on results. | |
| Low | Data for exposure-related findings were not shown for each study group, but | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| (score = 3) | results were described in the text and/or data were only reported for some outcomes. These deficiencies are likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | Data presentation was inadequate (e.g., the report does not differentiate among findings in multiple treatment groups)<br>**OR**<br>major inconsistencies were present in reporting of results. These are serious flaws that make the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 23. Explanation of unexpected outcomes**<br>Did the author provide a suitable explanation for unexpected outcomes (including excessive within-study variability)? | | |
| High (score = 1) | There were no unexpected outcomes, or unexpected outcomes were satisfactorily explained. | |
| Medium (score = 2) | Minor uncertainties or limitations were identified in how the study characterized unexpected outcomes, including within-study variability and/or variation from historical measures, but those are not likely to have a substantial impact on results. | |
| Low (score = 3) | The study did not report any measures of variability (e.g., SE, SD, confidence intervals) and/or insufficient information was provided to determine if excessive variability or unexpected outcomes occurred. This is likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | The occurrence of unexpected outcomes, including, but not limited to, within-study variability and/or variation from historical measures, are considered serious flaws that make the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 8. Other (Apply as Needed)** | | |
| Metric | | |
| High (score = 1) | | |
| Medium (score = 2) | | |
| Low (score = 3) | | |
| Unacceptable (score = 4) | | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

Note:
[a]These metrics should be scored as *Not rated/applicable* if the study cited a secondary literature source for the description of testing methodology; if the study is not classified as unacceptable in the initial review, the secondary source will be reviewed during a subsequent evaluation step and the metric will be rated at that time.

## F.6 References


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# APPENDIX G: DATA QUALITY CRITERIA FOR STUDIES ON ANIMAL AND *IN VITRO* TOXICITY

## G.1 Types of Data Sources

The data quality will be evaluated for a variety of animal and *in vitro* toxicity studies. Table G-1 provides examples of types of studies falling into these two broad categories. Since the availability of information varies considerably on different chemicals, it is anticipated that some study types will not be available while others may be identified beyond those listed in Table G-1.

**Table G-1. Types of Animal and *In Vitro* Toxicity Data**

| Data Category | Type of Data Sources |
|---|---|
| Animal Toxicity | Oral, dermal, and inhalation routes: lethality, irritation, sensitization, reproduction, fertility, developmental, neurotoxicity, carcinogenicity, systemic toxicity, metabolism, pharmacokinetics, absorption, immunotoxicity, genotoxicity, mutagenicity, endocrine disruption |
| *In Vitro* Toxicity Studies | Irritation, corrosion, sensitization, genotoxicity, dermal absorption, phototoxicity, ligand binding, steroidogenesis, developmental, organ toxicity, mechanisms, high throughput, immunotoxicity |

Mechanistic evidence is highly heterogeneous and may come from human, animal or *in vitro* toxicity studies. Mechanistic evidence may provide support for biological plausibility and help explain differences in tissue sensitivity, species, gender, life-stage or other factors (U.S. EPA, 2006). Although highly preferred, the availability of a fully elucidated mode of action (MOA) or adverse outcome pathway (AOP) is not required to conduct the human health hazard assessment for a given chemical.

EPA/OPPT plans to prioritize the evaluation of mechanistic evidence instead of evaluating all of the identified evidence upfront. This approach has the advantage of conducting a focused review of those mechanistic studies that are most relevant to the hazards under evaluation. The prioritization approach is generally initiated during the data screening step. For example, many of the human health PECOs for the first ten TSCA risk evaluation excluded mechanistic evidence during full text screening. Excluding the mechanistic evidence during full text screening does not mean that the data cannot be accessed later. The assessor can eventually mine the database of mechanistic references when specific questions or hypotheses arise related to the chemical's MOA/AOP.

Moreover, EPA/OPPT anticipates that some chemicals undergoing TSCA risk evaluations may have physiologically based pharmacokinetic (PBPK) models that could be used for predicting internal dose at a target site as well as interspecies, intraspecies, route-to-route extrapolations or other types of extrapolations. These models should be carefully evaluated to determine if they can be used for risk assessment purposes. Although EPA/OPPT is not including an evaluation strategy for PBPK models in this document, when necessary, it plans to document

the model evaluation process based on the list of considerations described in U.S. EPA (2006) and IPCS (2010). EPA/OPPT plans to use the evaluation strategies for animal and *in vitro* toxicity data to assess the quality of mechanistic and pharmacokinetic data supporting the model. EPA/OPPT may tailor the criteria to capture the inherent characteristics of particular studies that are not captured in the current criteria (e.g., optimization of criteria to evaluate the quality of new approach methodologies or NAMs).

## G.2 Data Quality Evaluation Domains

The methods for evaluation of study quality were developed after review of selected references describing existing study quality and risk of bias evaluation tools for toxicity studies (EC, 2018; Cooper et al., 2016; Lynch et al., 2016; Moermond et al., 2016b; Samuel et al., 2016; NTP, 2015a; Hooijmans et al., 2014; Koustas et al., 2014; Kushman et al., 2013; Hartling et al., 2012; Hooijmans et al., 2010). These publications, coupled with professional judgment and experience, informed the identification of domains and metrics for consideration in the evaluation and scoring of study quality. Furthermore, the evaluation tool is intended to address elements of TSCA Science Standards 26(h)(1) through 26(h)(5) that EPA must address during the development process of the risk evaluations.

The data quality of animal toxicity studies and *in vitro* toxicity studies is evaluated by assessing the following seven domains: Test Substance, Test Design, Exposure Characterization, Test Organism/Test Model, Outcome Assessment, Confounding/Variable Control, and Data Presentation and Analysis. The data quality within each domain will be evaluated by assessing unique metrics that pertain to each domain. The domains are defined in Table G-2 and further information on evaluation metrics is provided in section G.3. Relevance of the studies will also be checked in continuance with relevance identification that began during the data screening process.

**Table G-2. Data Evaluation Domains and Definitions**

| Evaluation Domain | Definition |
|---|---|
| Test Substance | Metrics in this domain evaluate whether the information provided in the study provides a reliable[a] confirmation that the test substance used in a study has the same (or sufficiently similar) identity, purity, and properties as the substance of interest. |
| Test Design | Metrics in this domain evaluate whether the experimental design enables the study to distinguish the effect of exposure from other factors. This domain includes metrics related to the use of control groups and randomization in allocation to ensure that the effect of exposure is isolated. |
| Exposure Characterization | Metrics in this domain assess the validity and reliability of methods used to measure or characterize exposure. These metrics evaluate whether exposure to the test substance was characterized using a method(s) that provides valid and reliable results, whether the exposure remained consistent over the duration of the experiment, and whether the exposure levels were appropriate to the outcome of interest. |
| Test Organism/Test Model | These metrics assess the appropriateness of the population or organism(s), group sizes used in the study (i.e., number of organisms and/or number of replicates per exposure group), and the organism conditions to assess the outcome of interest associated with the exposure of interest. |

| Evaluation Domain | Definition |
|---|---|
| Outcome Assessment | Metrics in this domain assess the validity and reliability of methods, including sensitivity of methods, that are used to measure or otherwise characterize the outcome(s) of interest. |
| Confounding/Variable Control | Metrics in this domain assess the potential impact of factors other than exposure that may affect the risk of outcome. The metrics evaluate whether studies identify and account for factors that are related to exposure and independently related to outcome (confounding factors) and whether appropriate experimental or analytical (statistical) methods are used to control for factors unrelated to exposure that may affect the risk of outcome (variable control). |
| Data Presentation and Analysis | Metrics in this domain assess whether appropriate statistical methods were used and if data for all outcomes are presented. |
| Other | Metrics in this domain are added as needed to incorporate chemical- or study-specific evaluations. |

Note:

[a] Reliability is defined as "the inherent property of a study or data, which includes the use of well-founded scientific approaches, the avoidance of bias within the study or data collection design and faithful study or data collection conduct and documentation" (ECHA, 2011a).

## G.3 Data Quality Evaluation Metrics

The data quality evaluation domains are evaluated by assessing unique metrics that have been developed for animal and *in vitro* studies. Each metric is binned into a confidence level of *High*, *Medium*, *Low*, or *Unacceptable*. Each confidence level is assigned a numerical score (i.e., 1 through 4) that is used in the method of assessing the overall quality of the study.

Table G-3 lists the data evaluation domains and metrics for animal toxicity studies including metrics that inform risk of bias and types of bias, and Table G-4 lists the data evaluation domains and metrics for *in vitro* toxicity studies. Each domain has between 2 and 6 metrics; however, some metrics may not apply to all study types. A general domain for other considerations is available for metrics that are specific to a given test substance or study type.

EPA may modify the metrics used for animal toxicity and *in vitro* toxicity studies as the Agency acquires experience with the evaluation tool. Any modifications will be documented.

**Table G-3. Data Evaluation Domains and Metrics for Animal Toxicity Studies**

| Evaluation Domain | Number of Metrics Overall | Metrics (Metric Number and Description, Type of Bias) |
|---|---|---|
| Test Substance | 3 | • Metric 1: Test Substance Identity<br>• Metric 2: Test Substance Source<br>• Metric 3: Test Substance Purity (*information bias[a]) (*detection bias[b]) |
| Test Design | 3 | • Metric 4: Negative and Vehicle Controls (*performance bias[b])<br>• Metric 5: Positive Controls (*information bias[a])<br>• Metric 6: Randomized Allocation (*selection bias[a,b]) |
| Exposure Characterization | 6 | • Metric 7: Preparation and Storage of Test Substance<br>• Metric 8: Consistency of Exposure Administration<br>• Metric 9: Reporting of Doses/Concentrations<br>• Metric 10: Exposure Frequency and Duration<br>• Metric 11: Number of Exposure Groups and Dose Spacing<br>• Metric 12: Exposure Route and Method |
| Test Organism | 3 | • Metric 13: Test Animal Characteristics<br>• Metric 14: Adequacy and Consistency of Animal Husbandry Conditions<br>• Metric 15: Number per Group (*missing data bias[a]) |
| Outcome Assessment | 5 | • Metric 16: Outcome Assessment Methodology (*information bias[a]) (*detection bias[b])<br>• Metric 17: Consistency of Outcome Assessment<br>• Metric 18: Sampling Adequacy<br>• Metric 19: Blinding of Assessors (*selection bias[a]) (*performance bias[b])<br>• Metric 20: Negative Control Response |
| Confounding/ Variable Control | 2 | • Metric 21: Confounding Variables in Test Design and Procedures (*other bias[b])<br>• Metric 22: Health Outcomes Unrelated to Exposure (*attrition/exclusion bias[b]) |
| Data Presentation and Analysis | 2 | • Metric 23: Statistical Methods (*information bias[a]) (*other bias[b])<br>• Metric 24: Reporting of Data (*selective reporting bias[b]) |

Notes:
Items marked with an asterisk (*) are examples of items that can be used to assess internal validity/risk of bias.
[a]National Academies of Sciences, Engineering, and Medicine. 2017. *Application of Systematic Review Methods in an Overall Strategy for Evaluating Low-Dose Toxicity from Endocrine Active Chemicals*. Washington, DC: The National Academies Press. doi: https://doi.org/10.17226/24758
[b]National Toxicology Program, Office of Health Assessment and Translation (OHAT). 2015. OHAT Risk of Bias Rating Tool for Human and Animal Studies. https://ntp.niehs.nih.gov/ntp/ohat/pubs/riskofbiastool_508.pdf

**Table G-4. Data Evaluation Domains and Metrics for *In Vitro* Toxicity Studies**

| Evaluation Domain | Number of Metrics Overall | Metrics (Metric Number and Description, Type of Bias) |
|---|---|---|
| Test Substance | 3 | • Metric 1: Test Substance Identity<br>• Metric 2: Test Substance Source<br>• Metric 3: Test Substance Purity |
| Test Design | 4 | • Metric 4: Negative Controls [a]<br>• Metric 5: Positive Controls [a]<br>• Metric 6: Assay Procedures<br>• Metric 7: Standards for Test |
| Exposure Characterization | 6 | • Metric 8: Preparation and Storage of Test Substance<br>• Metric 9: Consistency of Exposure Administration<br>• Metric 10: Reporting of Doses/Concentrations<br>• Metric 11: Exposure Duration<br>• Metric 12: Number of Exposure Groups and Dose Spacing<br>• Metric 13: Metabolic Activation |
| Test Model | 2 | • Metric 14: Test Model<br>• Metric 15: Number per Group |
| Outcome Assessment | 4 | • Metric 16: Outcome Assessment Methodology<br>• Metric 17: Consistency of Outcome Assessment<br>• Metric 18: Sampling Adequacy<br>• Metric 19: Blinding of Assessors |
| Confounding/ Variable Control | 2 | • Metric 20: Confounding Variables in Test Design and Procedures<br>• Metric 21: Outcomes Unrelated to Exposure |
| Data Presentation and Analysis | 4 | • Metric 22: Data Analysis<br>• Metric 23: Data Interpretation<br>• Metric 24: Cytotoxicity Data<br>• Metric 25: Reporting of Data |

Note:

[a] These are for the assay performance, not necessarily for the "validation" of extrapolating to a particular apical outcome (i.e., assay performance vs assay validation).

## G.4 Scoring Method and Determination of Overall Data Quality Level

Appendix A provides information about the evaluation method that will be applied across the various data/information sources being assessed to support TSCA risk evaluations. This section provides details about the scoring system that will be applied to animal and *in vitro* toxicity studies, including the weighting factors assigned to each metric score of each domain.

Some metrics will be given greater weights than others, if they are regarded as key or critical metrics. Thus, EPA will use a weighting approach to reflect that some metrics are more important than others when assessing the overall quality of the data.

### G.4.1 Weighting Factors

Each metric was assigned a weighting factor of 1 or 2, with the higher weighting factor (2) given to metrics deemed critical for the evaluation. The critical metrics were identified based on professional judgment in conjunction with consideration of the factors that are most frequently included in other study quality/risk of bias tools for animal toxicity studies [reviewed by Lynch et al. (2016); Samuel et al. (2016)]. In selecting critical metrics, EPA recognized that the relevance of an individual study to the risk analysis for a given substance is determined by its ability to inform hazard identification and/or dose-response assessment. Thus, the critical metrics are those that determine how well a study answers these key questions:

- Is a change in health outcome demonstrated in the study?
- Is the observed change more likely than not attributable to the substance exposure?
- At what substance dose(s) does the change occur?

EPA/OPPT assigned a weighting factor of 2 to each metric considered critical to answering these questions. Remaining metrics were assigned a weighting factor of 1. Tables G-5 and G-6 identify the critical metrics (i.e., those assigned a weighting factor of 2) for animal toxicity and *in vitro* toxicity studies, respectively, and provides a rationale for selection of each metric. Tables G-7 and G-8 identify the weighting factors assigned to each metric for animal toxicity and *in vitro* toxicity studies, respectively.

**Table G-5. Animal Toxicity Metrics with Greater Importance in the Evaluation and Rationale for Selection**

| Domain | Critical Metrics with Weighting Factor of 2 (Metric Number) [a] | Rationale |
|---|---|---|
| Test substance | Test substance identity (Metric 1) | The test substance must be identified and characterized definitively to ensure that the study is relevant to the substance of interest. |
| Test design | Negative and vehicle controls (Metric 4) | A concurrent negative control and vehicle control (when indicated) are required to ensure that any observed effects are attributable to substance exposure. Note that more than one negative control may be necessary in some studies. |
| Exposure characterization | Reporting of doses/concentrations (Metric 9) | Dose levels must be defined without ambiguity to allow for determination of the dose-response relationship and to enable valid comparisons across studies. |
| Test organisms | Test animal characteristics (Metric 13) | The test animal characteristics must be reported to enable assessment of a) whether they are suitable for the endpoint of interest; b) whether there are species, strain, sex, or age/lifestage differences within or between different studies; and c) to enable consideration of approaches for extrapolation to humans. |
| Outcome assessment | Outcome assessment methodology (Metric 16) | The methods used for outcome assessment must be fully described, valid, and sensitive to ensure that effects are detected, that observed effects are true, and to enable valid comparisons across studies. |
| Confounding/ variable control | Confounding variables in test design and procedures (Metric 21) | Control for confounding variables in test design and procedures is necessary to ensure that any observed effects are attributable to substance exposure and not to other factors. |
| Data presentation and analysis | Reporting of data (Metric 24) | Detailed results are necessary to determine if the study authors' conclusions are valid and to enable dose-response modeling. |

Note:
[a]A weighting factor of 1 is assigned for the remaining metrics.

**Table G-6. *In Vitro* Toxicity Metrics with Greater Importance in the Evaluation and Rationale for Selection**

| Domain | Critical Metrics with Weighting Factor of 2 (Metric Number) [a] | Rationale |
|---|---|---|
| Test Substance | Test Substance Identity (Metric 1) | The test substance must be identified and characterized definitively to ensure that the study is relevant to the substance of interest. |
| Test Design | Negative and Vehicle Controls (Metric 4) | A concurrent negative control and vehicle control (when indicated) are required for comparison of results between exposed and unexposed models to allow determination of treatment-related effects. |
| | Positive Controls (Metric 5) | A concurrent positive control or proficiency control (when applicable) is required to determine if the chemical of interest produces the intended outcome for the study type. |
| Exposure Characterization | Reporting of concentrations (Metric 10) | Dose levels must be defined without ambiguity to allow for determination of an accurate dose-response relationship or and to ensure valid comparisons across studies. |
| | Exposure duration (Metric 11) | The exposure duration during the study must be defined to accurately assess potential risk. |
| Test Model | Test Model (Metric 14) | The identity of the test model must be reported and suitable for the evaluation of outcome(s) of interest. |
| Outcome Assessment | Outcome assessment methodology (Metric 16) | The methods used for outcome assessment must be fully described, valid, and sensitive to ensure that effects are detected and that observed effects are true. |
| | Sampling adequacy (Metric 18) | The number of samples evaluated must be sufficient to allow data interpretation and analysis. |
| Confounding/Variable Control | Confounding variables in test design and procedures (Metric 20) | Control for confounding variables in test design and procedures are necessary to ensure that any observed effects are attributable to substance exposure and not to other factors. |
| Data Presentation and Analysis | Data interpretation (Metric 23) | The criteria for scoring and/or evaluation criteria are necessary so that the correct categorization (e.g., positive, negative, equivocal) can be determined for the chemical of interest. |
| | Reporting of data (Metric 25) | Detailed results are necessary to determine if the study authors' conclusions are valid and to enable dose-response modeling. |

Note:
[a] A weighting factor of 1 is assigned for the remaining metrics.

### G.4.2 Calculation of Overall Study Score

A confidence level (1, 2, or 3 for *High, Medium*, or *Low* confidence, respectively) is assigned for each relevant metric within each domain. To determine the overall study score, the first step is to multiply the score for each metric (1, 2, or 3 for *High, Medium*, or *Low* confidence, respectively) by the appropriate weighting factor (as shown in Tables G-7 and G-8 for animal toxicity and *in vitro* studies, respectively) to obtain a weighted metric score. The weighted metric scores are then summed and divided by the sum of the weighting factors (for all metrics that are scored) to obtain an overall study score between 1 and 3. The equation for calculating the overall score is shown below:

$$\textit{Overall Score (range of 1 to 3)} = \sum (\textit{Metric Score} \times \textit{Weighting Factor}) / \sum (\textit{Weighting Factors})$$

Some metrics may not be applicable to all study types. These metrics will not be included in the nominator or denominator of the equation above. The overall score will be calculated using only those metrics that receive a numerical score. Scoring examples for animal toxicity and *in vitro* toxicity studies are in tables G-9 through G-12.

Studies with any single metric scored as unacceptable (score = 4) will be automatically assigned an overall quality score of 4 (*Unacceptable*). An unacceptable score means that serious flaws are noted in the domain metric that consequently make the data unusable. If a metric is not applicable for a study type, the serious flaws would not be applicable for that metric and would not receive a score. EPA/OPPT plans to use data with an overall quality level of High, Medium, or Low confidence to quantitatively or qualitatively support the risk evaluations, but does not plan to use data rated as *Unacceptable.* An overall study score will not be calculated when a serious flaw is identified for any metric. If a publication reports more than one study or endpoint, each study and, as needed, each endpoint will be evaluated separately.

Detailed tables showing quality criteria for the metrics are provided in Tables G-13 through G-16 for animal toxicity and *in vitro* toxicity studies, including a table that summarizes the serious flaws that would make the data unacceptable for use in the environmental hazard assessment

**Table G-7. Metric Weighting Factors and Range of Weighted Metric Scores for Animal Toxicity Studies**

| Domain Number/ Description | Metric Number/Description | Range of Metric Scores[a] | Metric Weighting Factor | Range of Weighted Metric Scores[b] |
|---|---|---|---|---|
| 1. Test Substance | 1. Test Substance Identity | 1 to 3 | 2 | 2 to 6 |
| | 2. Test Substance Source | | 1 | 1 to 3 |
| | 3. Test Substance Purity | | 1 | 1 to 3 |
| 2. Test Design | 4. Negative and Vehicle Controls | | 2 | 2 to 6 |
| | 5. Positive Controls | | 1 | 1 to 3 |
| | 6. Randomized Allocation | | 1 | 1 to 3 |
| 3. Exposure Characterization | 7. Preparation and Storage of Test Substance | | 1 | 1 to 3 |
| | 8. Consistency of Exposure Administration | | 1 | 1 to 3 |
| | 9. Reporting of Doses/Concentrations | | 2 | 2 to 6 |
| | 10. Exposure Frequency and Duration | | 1 | 1 to 3 |
| | 11. Number of Exposure Groups and Dose Spacing | | 1 | 1 to 3 |
| | 12. Exposure Route and Method | | 1 | 1 to 3 |
| 4. Test Organisms | 13. Test Animal Characteristics | | 2 | 2 to 6 |
| | 14. Adequacy and Consistency of Animal Husbandry Conditions | | 1 | 1 to 3 |
| | 15. Number per Group | | 1 | 1 to 3 |
| 5. Outcome Assessment | 16. Outcome Assessment Methodology | | 2 | 2 to 6 |
| | 17. Consistency of Outcome Assessment | | 1 | 1 to 3 |
| | 18. Sampling Adequacy | | 1 | 1 to 3 |
| | 19. Blinding of Assessors | | 1 | 1 to 3 |
| | 20. Negative Control Response | | 1 | 1 to 3 |
| 6. Confounding/ Variable Control | 21. Confounding Variables in Test Design and Procedures | | 2 | 2 to 6 |
| | 22. Health Outcomes Unrelated to Exposure | | 1 | 1 to 3 |
| 7. Data Presentation and Analysis | 23. Statistical Methods | | 1 | 1 to 3 |
| | 24. Reporting of Data | | 2 | 2 to 6 |
| | Sum (if all metrics scored)[c] | | 31 | 31 to 93 |
| Range of Overall Scores, where Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factor | | | | 31/31=1; 93/31=3 |
| | High: ≥1 and <1.7 | Medium: ≥1.7 and <2.3 | Low: ≥2.3 and ≤3 | Range of overall score = 1 to 3[d] |

Notes:

[a] For the purposes of calculating an overall study score, the range of possible metric scores is 1 to 3 for each metric, corresponding to high and low confidence. No calculations will be conducted if a study receives an "unacceptable" rating (score of "4") for any metric.

[b] The range of weighted scores for each metric is calculated by multiplying the range of metric scores (1 to 3) by the weighting factor for that metric.

[c] The sum of weighting factors and the sum of the weighted scores will differ if some metrics are not scored (not applicable).

[d] The range of possible overall scores is 1 to 3. If a study receives a score of 1 for every metric, then the overall study score will be 1. If a study receives a score of 3 for every metric, then the overall study score will be 3.

**Table G-8. Metric Weighting Factors and Range of Weighted Metric Scores for *In Vitro* Toxicity Studies**

| Domain Number/ Description | Metric Number/Description | Range of Metric Scores[a] | Metric Weighting Factor | Range of Weighted Metric Scores[b] |
|---|---|---|---|---|
| 1. Test Substance | 1. Test Substance Identity | 1 to 3 | 2 | 2 to 6 |
| | 2. Test Substance Source | | 1 | 1 to 3 |
| | 3. Test Substance Purity | | 1 | 1 to 3 |
| 2. Test Design | 4. Negative and Vehicle Controls | | 2 | 2 to 6 |
| | 5. Positive Controls | | 2 | 2 to 6 |
| | 6. Assay Procedures | | 1 | 1 to 3 |
| | 7. Standards for Test | | 1 | 1 to 3 |
| 3. Exposure Characterization | 8. Preparation and Storage of Test Substance | | 1 | 1 to 3 |
| | 9. Consistency of Exposure Administration | | 1 | 1 to 3 |
| | 10. Reporting of Concentrations | | 2 | 2 to 6 |
| | 11. Exposure Duration | | 2 | 2 to 6 |
| | 12. Number of Exposure Groups and Dose Spacing | | 1 | 1 to 3 |
| | 13. Metabolic Activation | | 1 | 1 to 3 |
| 4. Test model | 14. Test Model | | 2 | 2 to 6 |
| | 15. Number per Group | | 1 | 1 to 3 |
| 5. Outcome Assessment | 16. Outcome Assessment Methodology | | 2 | 2 to 6 |
| | 17. Consistency of Outcome Assessment | | 1 | 1 to 3 |
| | 18. Sampling Adequacy | | 2 | 2 to 6 |
| | 19. Blinding of Assessors | | 1 | 1 to 3 |
| 6. Confounding/ Variable Control | 20. Confounding Variables in Test design and Procedures | | 2 | 2 to 6 |
| | 21. Outcomes Unrelated to Exposure | | 1 | 1 to 3 |
| 7. Data Presentation and Analysis | 22. Data Analysis | | 1 | 1 to 3 |
| | 23. Data Interpretation | | 2 | 2 to 6 |
| | 24. Cytotoxicity Data | | 1 | 1 to 3 |
| | 25. Reporting of Data | | 2 | 2 to 6 |
| | Sum (if all metrics scored)[c] | | 36 | 36 - 108 |
| Range of Overall Scores, where<br>Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factor | | | | 36/36=1;<br>108/36=3<br><br>Range of overall score = 1 to 3[d] |

| High | Medium | Low |
|---|---|---|
| ≥1 and <1.7 | ≥1.7 and <2.3 | ≥2.3 and ≤3 |

Notes:

[a] For the purposes of calculating an overall study score, the range of possible metric scores is 1 to 3 for each metric, corresponding to high and low confidence. No calculations will be conducted if a study receives an "unacceptable" rating (score of "4") for any metric.

[b] The range of weighted scores for each metric is calculated by multiplying the range of metric scores (1 to 3) by the weighting factor for that metric.

[c] The sum of weighting factors and the sum of the weighted scores will differ if some metrics are not scored (not applicable).

[d] The range of possible overall scores is 1 to 3. If a study receives a score of 1 for every metric, then the overall study score will be 1. If a study receives a score of 3 for every metric, then the overall study score will be 3.

**Table G-9. Scoring Example for Animal Toxicity Study with all Metrics Scored**

| Domain | Metric | Metric Score | Metric Weighting Factor | Weighted Score |
|---|---|---|---|---|
| Test substance | 1. Test substance identity | 2 | 2 | 4 |
| | 2. Test substance source | 3 | 1 | 3 |
| | 3. Test substance purity | 2 | 1 | 2 |
| Test design | 4. Negative and vehicle controls | 1 | 2 | 2 |
| | 5. Positive controls | 2 | 1 | 2 |
| | 6. Randomized allocation | 3 | 1 | 3 |
| Exposure characterization | 7. Preparation and storage of test substance | 2 | 1 | 2 |
| | 8. Consistency of exposure administration | 2 | 1 | 2 |
| | 9. Reporting of doses/concentrations | 1 | 2 | 2 |
| | 10. Exposure frequency and duration | 2 | 1 | 2 |
| | 11. Number of exposure groups and dose spacing | 1 | 1 | 1 |
| | 12. Exposure route and method | 1 | 1 | 1 |
| Test organisms | 13. Test animal characteristics | 2 | 2 | 4 |
| | 14. Consistency of animal conditions | 2 | 1 | 2 |
| | 15. Number per group | 1 | 1 | 1 |
| Outcome assessment | 16. Outcome assessment methodology | 2 | 2 | 4 |
| | 17. Consistency of outcome assessment | 3 | 1 | 3 |
| | 18. Sampling adequacy | 2 | 1 | 2 |
| | 19. Blinding of assessors | 3 | 1 | 3 |
| | 20. Negative control responses | 2 | 1 | 2 |
| Confounding/variable control | 21. Confounding variables in test design and procedures | 2 | 2 | 4 |
| | 22. Health outcomes unrelated to exposure | 2 | 1 | 2 |
| Data presentation and analysis | 23. Statistical methods | 2 | 1 | 2 |
| | 24. Reporting of data | 2 | 2 | 4 |
| NR= not rated/not applicable | | Sum of scores | 31 | 59 |
| | | Overall Study Score | **1.9 = Medium** | |

Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors

| High | Medium | Low |
|---|---|---|
| ≥1 and <1.7 | ≥1.7 and <2.3 | ≥2.3 and ≤3 |

**Table G-10. Scoring Example for Animal Toxicity Study with Some Metrics Not Rated/Not Applicable**

| Domain | Metric | Metric Score | Metric Weighting Factor | Weighted Score |
|---|---|---|---|---|
| Test substance | 1. Test substance identity | 2 | 2 | 4 |
| | 2. Test substance source | 3 | 1 | 3 |
| | 3. Test substance purity | 2 | 1 | 2 |
| Test design | 4. Negative and vehicle controls | 1 | 2 | 2 |
| | 5. Positive controls | NR | | |
| | 6. Randomized allocation | 3 | 1 | 3 |
| Exposure characterization | 7. Preparation and storage of test substance | 2 | 1 | 2 |
| | 8. Consistency of exposure administration | NR | | |
| | 9. Reporting of doses/concentrations | 1 | 2 | 2 |
| | 10. Exposure frequency and duration | 2 | 1 | 2 |
| | 11. Number of exposure groups and dose spacing | 1 | 1 | 1 |
| | 12. Exposure route and method | 1 | 1 | 1 |
| Test organisms | 13. Test animal characteristics | 2 | 2 | 4 |
| | 14. Consistency of animal conditions | 2 | 1 | 2 |
| | 15. Number per group | 1 | 1 | 1 |
| Outcome assessment | 16. Outcome assessment methodology | 2 | 2 | 4 |
| | 17. Consistency of outcome assessment | NR | | |
| | 18. Sampling adequacy | 2 | 1 | 2 |
| | 19. Blinding of assessors | NR | | |
| | 20. Negative control responses | 2 | 1 | 2 |
| Confounding/variable control | 21. Confounding variables in test design and procedures | 2 | 2 | 4 |
| | 22. Health outcomes unrelated to exposure | 2 | 1 | 2 |
| Data presentation and analysis | 23. Statistical methods | 2 | 1 | 2 |
| | 24. Reporting of data | 2 | 2 | 4 |
| NR= not rated/not applicable | Sum | | 27 | 49 |
| | Overall Study Score | | **1.8 = Medium** | |

Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factor

| High | Medium | Low |
|---|---|---|
| ≥1 and <1.7 | ≥1.7 and <2.3 | ≥2.3 and ≤3 |

**Table G-11. Scoring Example for *In Vitro* Study with all Metrics Scored**

| Domain | Metric | Metric Score | Metric Weighting Factor | Weighted Score |
|---|---|---|---|---|
| Test substance | 1. Test substance identity | 1 | 2 | 2 |
| | 2. Test substance source | 2 | 1 | 2 |
| | 3. Test substance purity | 2 | 1 | 2 |
| Test design | 4. Negative controls | 1 | 2 | 2 |
| | 5. Positive controls | 1 | 2 | 2 |
| | 6. Assay procedures | 2 | 1 | 2 |
| | 7. Standards for test | 3 | 1 | 3 |
| Exposure characterization | 8. Preparation and storage of test substance | 2 | 1 | 2 |
| | 9. Consistency of exposure administration | 2 | 1 | 2 |
| | 10. Reporting of concentrations | 1 | 2 | 2 |
| | 11. Exposure duration | 1 | 2 | 2 |
| | 12. Number of exposure groups and dose spacing | 1 | 1 | 1 |
| | 13. Metabolic activation | 3 | 1 | 3 |
| Test Model | 14. Test model | 2 | 2 | 4 |
| | 15. Number per group | 2 | 1 | 2 |
| Outcome assessment | 16. Outcome assessment methodology | 3 | 2 | 6 |
| | 17. Consistency of outcome assessment | 2 | 1 | 2 |
| | 18. Sampling adequacy | 1 | 2 | 2 |
| | 19. Blinding of assessors | 2 | 1 | 2 |
| Confounding/variable control | 20. Confounding variables in test design and procedures | 3 | 2 | 6 |
| | 21. Outcomes unrelated to exposure | 2 | 1 | 2 |
| Data presentation and analysis | 22. Data analysis | 1 | 1 | 1 |
| | 23. Data interpretation | 2 | 2 | 4 |
| | 24. Cytotoxicity data | 2 | 1 | 2 |
| | 25. Reporting of data | 3 | 2 | 6 |
| NR= not rated/not applicable | | Sum | 36 | 66 |
| | | Overall Study Score | **1.8 = Medium** | |

Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factor

| High | Medium | Low |
|---|---|---|
| ≥1 and <1.7 | ≥1.7 and <2.3 | ≥2.3 and ≤3 |

**Table G-12. Scoring Example for *In Vitro* Study with Some Metrics Not Rated/Not Applicable**

| Domain | Metric | Metric Score | Metric Weighting Factor | Weighted Score |
|---|---|---|---|---|
| Test substance | 1. Test substance identity | 1 | 2 | 2 |
| | 2. Test substance source | 2 | 1 | 2 |
| | 3. Test substance purity | 2 | 1 | 2 |
| Test design | 4. Negative controls | 1 | 2 | 2 |
| | 5. Positive controls | 1 | 2 | 2 |
| | 6. Assay procedures | 2 | 1 | 2 |
| | 7. Standards for test | 3 | 1 | 3 |
| Exposure characterization | 8. Preparation and storage of test substance | NR | | |
| | 9. Consistency of exposure administration | 2 | 1 | 2 |
| | 10. Reporting of concentrations | 1 | 2 | 2 |
| | 11. Exposure duration | 1 | 2 | 2 |
| | 12. Number of exposure groups and dose spacing | 1 | 1 | 1 |
| | 13. Metabolic activation | NR | | |
| Test Model | 14. Test model | 2 | 2 | 4 |
| | 15. Number per group | 3 | 1 | 3 |
| Outcome assessment | 16. Outcome assessment methodology | 3 | 2 | 6 |
| | 17. Consistency of outcome assessment | 2 | 1 | 2 |
| | 18. Sampling adequacy | 1 | 2 | 2 |
| | 19. Blinding of assessors | NR | | |
| Confounding/variable control | 20. Confounding variables in test design and procedures | 3 | 2 | 6 |
| | 21. Outcomes unrelated to exposure | 2 | 1 | 2 |
| Data presentation and analysis | 22. Data analysis | 1 | 1 | 1 |
| | 23. Data interpretation | 2 | 2 | 4 |
| | 24. Cytotoxicity data | NR | | |
| | 25. Reporting of data | 3 | 2 | 6 |
| NR= not rated/not applicable | Sum | | 32 | 58 |
| | Overall Study Score | | **1.8 = Medium** | |

Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factor

| High | Medium | Low |
|---|---|---|
| ≥1 and <1.7 | ≥1.7 and <2.3 | ≥2.3 and ≤3 |

## G.5 Data Quality Criteria

### G.5.1 Animal Toxicity Studies

Optimization of the list of serious flaws may occur after pilot calibration exercises.

**Table G-13. Serious Flaws that Would Make Animal Toxicity Studies Unacceptable**

| Domain | Metric | Description of Serious Flaw(s) in Data Source |
|---|---|---|
| Test substance | Test substance identity | The test substance identity and form (the latter if applicable) cannot be determined from the information provided (e.g., nomenclature was unclear and CASRN or structure were not reported)<br>**OR**<br>for mixtures, the components and ratios were not characterized. |
| | Test substance source | The test substance was not obtained from a manufacturer<br>**OR**<br>if synthesized or extracted, analytical verification of the test substance was not conducted. |
| | Test substance purity | The nature and quantity of reported impurities were such that study results were likely to be due to one or more of the impurities. |
| Test design | Negative and vehicle controls | A concurrent negative control group was not included or reported<br>**OR**<br>the reported negative control group was not appropriate (e.g., age/ weight of animals differed between control and treated groups). |
| | Positive controls | For study types that require a concurrent positive control group:<br>When applicable, an appropriate concurrent positive control (i.e., inducing a positive response) was not used and its omission is a serious flaw that makes the study unusable. |
| | Randomized allocation of animals | The study reported using a biased method to allocate animals to study groups (e.g., judgement of investigator). |
| Exposure characterization | Preparation and storage of test substance | Information on preparation and storage was not reported<br>**OR**<br>serious flaws reported with test substance preparation and/or storage conditions will have critical impacts on dose/concentration estimates and make the study unusable (e.g., instability of test substance in exposure medium was reported, or there was heterogeneous distribution of test substance in exposure matrix [e.g., aerosol deposition in exposure chamber, insufficient mixing of dietary matrix]). For inhalation studies, there was no mention of the method and equipment used to generate the test substance, or the method used is atypical and inappropriate. |

| Domain | Metric | Description of Serious Flaw(s) in Data Source |
|---|---|---|
| | Consistency of exposure administration | Critical exposure details (e.g., methods for generating atmosphere in inhalation studies) were not reported<br>**OR**<br>reported information indicated that exposures were not administered consistently across study groups (e.g., differing particle size), resulting in serious flaws that make the study unusable. |
| | Reporting of doses/concentrations | The reported exposure levels could not be validated (e.g., lack of food or water intake data for dietary or water exposures in conjunction with evidence of palatability differences, lack of body weight data in conjunction with qualitative evidence for body weight differences across groups, inconsistencies in reporting, etc.). For inhalation studies, actual concentrations not reported along with animal responses (or lack of responses) that indicate exposure problems due to faulty test substance generation. Animals were exposed to an aerosol but no particle size data were reported. |
| | Exposure frequency and duration | The exposure frequency or duration of exposure were not reported<br>**OR**<br>the reported exposure frequency and duration were not suited to the study type and/or outcome(s) of interest (e.g., study length inadequate to evaluate tumorigenicity). |
| | Number of exposure groups and dose/concentration spacing | The number of exposure groups and spacing were not reported<br>**OR**<br>dose groups and spacing were not relevant for the assessment (e.g., all doses in a developmental toxicity study produced overt maternal toxicity). |
| | Exposure route and method | The route or method of exposure was not reported<br>**OR**<br>an inappropriate route or method (e.g., administration of a volatile organic compound via the diet) was used for the test substance without taking steps to correct the problem (e.g., mixing fresh diet, replacing air in static chambers). For inhalation studies, there is no description of the inhalation chamber used, or an atypical exposure method was used, such as allowing a container of test substance to evaporate in a room. |
| Test organisms | Test animal characteristics | The test animal species was not reported<br>**OR**<br>the test animal (species, strain, sex, life-stage, source) was not appropriate for the evaluation of the specific outcome(s) of interest (e.g., genetically modified animals, strain was uniquely susceptible or resistant to one or more outcome of interest). |
| | Adequacy and consistency of animal husbandry conditions | There were significant differences in husbandry conditions between control and exposed groups (e.g., temperature, humidity, light-dark cycle)<br>**OR** |

| Domain | Metric | Description of Serious Flaw(s) in Data Source |
|---|---|---|
| | | animal husbandry conditions deviated from customary practices in ways likely to impact study results (e.g., injuries and stress due to cage overcrowding). |
| | Number of animals per group | The number of animals per study group was not reported<br>**OR**<br>the number of animals per study group was insufficient to characterize toxicological effects (e.g., 1-2 animals in each group). |
| Outcome assessment | Outcome assessment methodology | The outcome assessment methodology was not reported<br>**OR**<br>the reported outcome assessment methodology was not sensitive for the outcome(s) of interest (e.g., evaluation of endpoints outside the critical window of development, a systemic toxicity study that evaluated only grossly observable endpoints, such as clinical signs and mortality, etc.). |
| | Consistency of outcome assessment | There were large inconsistencies in the execution of study protocols for outcome assessment across study groups<br>**OR**<br>outcome assessments were not adequately reported for meaningful interpretation of results. |
| | Sampling adequacy | Sampling was not adequate for the outcome(s) of interest (e.g., histopathology was performed on exposed groups, but not controls). |
| | Blinding of assessors | Information in the study report did not report whether assessors were blinded to treatment group for subjective outcomes and suggested that the assessment of subjective outcomes (e.g., functional observational battery, qualitative neurobehavioral endpoints, histopathological re-evaluations) was performed in a biased fashion (e.g., assessors of subjective outcomes were aware of study groups). This is a serious flaw that makes the study unusable. |
| | Negative control responses | The biological responses of the negative control groups were not reported<br>**OR**<br>there was unacceptable variation in biological responses between control replicates. |
| Confounding/ variable control | Confounding variables in test design and procedures | The study reported significant differences among the study groups with respect to initial body weight, decreased drinking water/food intake due to palatability issues (≥20% difference from control) that could lead to dehydration and/or malnourishment, or reflex bradypnea that could lead to decreased oxygenation of the blood. |
| | Health outcomes unrelated to exposure | One or more study groups experienced serious animal attrition or health outcomes unrelated to exposure (e.g., infection). |

| Domain | Metric | Description of Serious Flaw(s) in Data Source |
|---|---|---|
| Data presentation and analysis | Statistical methods | Statistical methods used were not appropriate (e.g., parametric test for non-normally distributed data)<br>**OR**<br>statistical analysis was not conducted<br>**AND**<br>data were not provided preventing an independent statistical analysis. |
| | Reporting of data | Data presentation was inadequate (e.g., the report does not differentiate among findings in multiple exposure groups)<br>**OR**<br>major inconsistencies were present in reporting of results. |

## Table G-14. Data Quality Criteria for Animal Toxicity Studies

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 1. Test Substance** | | |
| **Metric 1. Test substance identity**<br>Was the test substance identified definitively (i.e., established nomenclature, CASRN, and/or structure reported, including information on the specific form tested [particle characteristics for solid-state materials, salt or base, valence state, hydration state, isomer, radiolabel, etc.] for materials that may vary in form)? If test substance is a mixture, were mixture components and ratios characterized? | | |
| High<br>(score = 1) | The test substance was identified definitively and the specific form was characterized (where applicable). For mixtures, the components and ratios were characterized. | |
| Medium<br>(score = 2) | The test substance and form (the latter if applicable) were identified and components and ratios of mixtures were characterized, but there were minor uncertainties (e.g., minor characterization details were omitted) that are unlikely to have a substantial impact on results. | |
| Low<br>(score = 3) | The test substance and form (the latter if applicable) were identified and components and ratios of mixtures were characterized, but there were uncertainties regarding test substance identification or characterization that are likely to have a substantial impact on results. | |
| Unacceptable<br>(score = 4) | The test substance identity and form (the latter if applicable) cannot be determined from the information provided (e.g., nomenclature was unclear and CASRN or structure were not reported)<br>**OR**<br>for mixtures, the components and ratios were not characterized. These are serious flaws that make the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 2. Test substance source**<br>Was the source of the test substance reported, including manufacturer and batch/lot number for materials that may vary in composition? If synthesized or extracted, was test substance identity verified by analytical methods? | | |
| High<br>(score = 1) | The source of the test substance was reported, including manufacturer and batch/lot number for materials that may vary in composition, and its identity was certified by manufacturer and/or verified by analytical methods (melting point, chemical analysis, etc.). | |
| Medium<br>(score = 2) | The source of the test substance and/or the analytical verification of a synthesized test substance was reported incompletely, but the omitted details are unlikely to have a substantial impact on results. | |
| Low<br>(score = 3) | Omitted details on the source of the test substance and/or the analytical verification of a synthesized test substance are likely to have a substantial impact on results. | |
| Unacceptable<br>(score = 4) | The test substance was not obtained from a manufacturer<br>**OR**<br>if synthesized or extracted, analytical verification of the test substance was not conducted. These are serious flaws that makes the study unusable. | |
| Not rated/applicable | | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 3. Test substance purity**<br>Was the purity or grade (i.e., analytical, technical) of the test substance reported and adequate to identify its toxicological effects? Were impurities identified? Were impurities present in quantities that could influence the results? | | |
| High<br>(score = 1) | The test substance purity and composition were such that any observed effects were highly likely to be due to the nominal test substance itself (e.g., highly pure or analytical-grade test substance or a formulation comprising primarily inert ingredients with small amount of active ingredient). | |
| Medium<br>(score = 2) | Minor uncertainties or limitations were identified regarding the test substance purity and composition; however, the purity and composition were such that observed effects were more likely than not due to the nominal test substance, and any identified impurities are unlikely to have a substantial impact on results. Alternately, purity was not reported but given other information purity was not expected to be of concern. | |
| Low<br>(score = 3) | Purity and/or grade of test substance were not reported or were low enough to have a substantial impact on results (i.e., observed effects may not be due to the nominal test substance). | |
| Unacceptable<br>(score = 4) | The nature and quantity of reported impurities were such that study results were likely to be due to one or more of the impurities. This is a serious flaw that makes the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 2. Test Design** | | |
| **Metric 4. Negative and vehicle controls**<br>Was an appropriate concurrent negative control group included? If a vehicle was used, was the control group exposed to the vehicle? For inhalation and gavage studies, were controls sham-exposed? | | |
| High<br>(score = 1) | Study authors reported using an appropriate concurrent negative control group (i.e., all conditions equal except chemical exposure). If gavage or inhalation study, a vehicle and/or sham-treated control group was included. | |
| Medium<br>(score = 2) | Study authors reported using a concurrent negative control group, but all conditions were not equal to those of treated groups; however, the identified differences are considered to be minor limitations that are unlikely to have a substantial impact on results. | |
| Low<br>(score = 3) | Study authors acknowledged using a concurrent negative control group, but details regarding the negative control group were not reported, and the lack of details is likely to have a substantial impact on results. | |
| Unacceptable<br>(score = 4) | A concurrent negative control group was not included or reported<br>**OR**<br>the reported negative control group was not appropriate (e.g., age/ weight of animals differed between control and treated groups). This is a serious flaw that makes the study unusable. | |
| Not rated/applicable | | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 5. Positive controls**<br>Was an appropriate concurrent positive control group included if necessary based on study type (e.g., certain neurotoxicity studies)?<br><br>This metric is not rated/applicable if positive control was not indicated by study type. | | |
| High<br>(score = 1) | When applicable, A concurrent positive control was used (if necessary for the study type) and a positive response was observed. | |
| Medium<br>(score = 2) | When applicable, A concurrent positive control was used, but there were minor uncertainties (e.g., minor details regarding control exposure or response were omitted) that are unlikely to have a substantial impact on results. | |
| Low<br>(score = 3) | When applicable, A concurrent positive control was used, but there were deficiencies regarding the control exposure or response that are likely to have a substantial impact on results (e.g., the control response was not described). | |
| Unacceptable<br>(score = 4) | When applicable, an appropriate concurrent positive control (i.e., inducing a positive response) was not used and its omission is a serious flaw that makes the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 6. Randomized allocation of animals**<br>Did the study explicitly report randomized allocation of animals to study groups? | | |
| High<br>(score = 1) | The study reported that animals were randomly allocated into study groups (including the control group). | |
| Medium<br>(score = 2) | The study reported methods of allocation of animals to study groups, but there were minor limitations in the allocation method (e.g., method with a nonrandom component like assignment to minimize differences in body weight across groups) that are unlikely to have a substantial impact on results. | |
| Low<br>(score = 3) | The study did not report how animals were allocated to study groups, or there were deficiencies regarding the allocation method that are likely to have a substantial impact on results (e.g., allocation by animal number). | |
| Unacceptable<br>(score = 4) | The study reported using a biased method to allocate animals to study groups (e.g., judgement of investigator). This is a serious flaw that makes the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
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| | | |
| **Domain 3. Exposure Characterization** | | |
| **Metric 7. Preparation and storage of test substance**<br>Did the study characterize the test substance preparation and storage conditions (e.g., test substance stability, homogeneity, mixing temperature, stock concentration, stirring methods, centrifugation/filtration)? Were the frequency of preparation and/or storage conditions appropriate to the test substance stability? For inhalation studies, was the aerosol/vapor generation method appropriate? | | |
| High<br>(score = 1) | The test substance preparation and storage conditions were reported and appropriate for the test substance (e.g., test substance well-mixed in diet). For inhalation studies, the method and equipment used to generate the test substance as a gas, vapor, or aerosol were reported and appropriate. | |
| Medium<br>(score = 2) | The test substance preparation and storage conditions were reported, but there were only minor limitations in the test substance preparation and/or storage conditions were identified (i.e., diet was not mixed fresh daily) or omission of details that are unlikely to have a substantial impact on results. For inhalation studies, the method and equipment used to generate the test substance were incomplete or confusing but there is no reason to believe there was an impact on animal exposure. | |
| Low<br>(score = 3) | Deficiencies in reporting of test substance preparation and/or storage conditions are likely to have a substantial impact on results (e.g., available information on physical-chemical properties suggested that stability and/or solubility of test substance in vehicle may be poor). For inhalation studies, there is reason to question the validity of the method used for generating the test substance. | |
| Unacceptable<br>(score = 4) | Information on preparation and storage was not reported<br>**OR**<br>serious flaws reported with test substance preparation and/or storage conditions will have critical impacts on dose/concentration estimates and make the study unusable (e.g., instability of test substance in exposure medium was reported, or there was heterogeneous distribution of test substance in exposure matrix [e.g., aerosol deposition in exposure chamber, insufficient mixing of dietary matrix]). For inhalation studies, there was no mention of the method and equipment used to generate the test substance, or the method used is atypical and inappropriate. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 8. Consistency of exposure administration**<br>Were exposures administered consistently across study groups (e.g., same exposure frequency; same time of day; consistent gavage volumes or diet compositions in oral studies; consistent chamber designs, animals/chamber, and comparable particle size characteristics in inhalation studies; consistent application methods and volumes in dermal studies)? | | |
| High<br>(score = 1) | Details of exposure administration were reported and exposures were administered consistently across study groups in a scientifically sound manner (e.g., gavage volume was not excessive). | |
| Medium<br>(score = 2) | Details of exposure administration were reported, but minor limitations in administration of exposures (e.g., accidental mistakes in dosing) were | |

| Confidence Level (Score) | Description | Selected Score |
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| | identified that are unlikely to have a substantial impact on results. | |
| Low (score = 3) | Details of exposure administration were reported, but deficiencies in administration of exposures (e.g., exposed at different times of day) are likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | Critical exposure details (e.g., methods for generating atmosphere in inhalation studies) were not reported<br>**OR**<br>reported information indicated that exposures were not administered consistently across study groups (e.g., differing particle size), resulting in serious flaws that make the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 9. Reporting of doses/concentrations**<br>Were doses/concentrations reported without ambiguity (e.g., point estimate in addition to a range)? In oral studies, if doses were not reported, was information reported that enabled dose estimation (e.g., test animal dietary intake and body weight monitoring data in dietary studies)? In inhalation studies, was test substance vapor/aerosol concentration measured analytically along with nominal and target concentrations? | | |
| High (score = 1) | For oral and dermal studies, administered doses/concentrations, or the information to calculate them, were reported without ambiguity.<br><br>For inhalation studies, several specific considerations apply: Analytical, nominal and target chamber concentrations were all reported, with high confidence in the accuracy of the actual concentrations; the range of concentrations within a treatment group did not deviate widely (range should be within ±10% for gases and vapors and within ±20% for liquid and solid aerosols).<br><br>The analytical method (HPLC, GC, IR spectrophotometry, etc.) used to measure chamber test substance and vehicle concentration was reported and appropriate. Actual chamber measurements using gravimetric filters are acceptable when testing dry aerosols and non-volatile liquid aerosols.<br><br>The particle size distribution data, mass median aerodynamic diameter (MMAD), and geometric standard deviation were reported for all exposed groups (including vehicle controls, when used). | |
| Medium (score = 2) | For oral and dermal studies, minor uncertainties in reporting of administered doses/concentrations occurred (e.g., dietary or air concentrations were not measured analytically) but are unlikely to have a substantial impact on results.<br><br>For inhalation studies, several specific considerations apply:<br>With gases only, actual concentrations were not reported but there is high confidence that the animals were exposed at approximately the reported target concentrations. [There is no comparable medium result for aerosols and vapors if analytical concentrations are not reported.]<br><br>For inhalation studies (gas, vapor, aerosol), the analytical method used was less than ideal or subject to interference but nevertheless yielded fairly reliable measurements of chamber concentrations. | |

| Confidence Level (Score) | Description | Selected Score |
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| | Particle size distribution data were not reported, but mass median aerodynamic diameter (MMAD), and geometric standard deviation values were reported for all exposed groups (including vehicle controls, when used). | |
| Low (score = 3) | For oral and dermal studies, deficiencies in reporting of administered doses/concentrations occurred (e.g., no information on animal body weight or intake were provided) that are likely to have a substantial impact on results.<br><br>For inhalation studies, several considerations apply: Using aerosols and vapors, a score of low is indicated if actual concentrations are not reported or the analytical method used, such as sampling tubes (e.g., Draeger tubes) provided imprecise measurements.<br><br>An MMAD is reported but no geometric standard deviation or particle size distribution data were reported. | |
| Unacceptable (score = 4) | The reported exposure levels could not be validated (e.g., lack of food or water intake data for dietary or water exposures in conjunction with evidence of palatability differences, lack of body weight data in conjunction with qualitative evidence for body weight differences across groups, inconsistencies in reporting, etc.). This is a serious flaw that makes the study unusable.<br><br>For inhalation studies, actual concentrations were not reported along with animal responses (or lack of responses) that indicate exposure problems due to faulty test substance generation.<br><br>Animals were exposed to an aerosol but no MMAD or particle size data were reported. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 10. Exposure frequency and duration**<br>Were the exposure frequency (hours/day and days/week) and duration of exposure reported and appropriate for this study type and/or outcome(s) of interest? | | |
| High (score = 1) | The exposure frequency and duration of exposure were reported and appropriate for this study type and/or outcome(s) of interest (e.g., inhalation exposure 6 hours/day, gavage 5 days/week, 2-year duration for cancer bioassays). | |
| Medium (score = 2) | Minor limitations in exposure frequency and duration of exposure were identified (e.g., inhalation exposure of 4 hours/day instead of 6 hours/day in a repeated exposure study), but are unlikely to have a substantial impact on results. | |
| Low (score = 3) | The duration of exposure and/or exposure frequency differed significantly from typical study designs (e.g., gavage 1 day/week) and these deficiencies are likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | The exposure frequency or duration of exposure were not reported<br>**OR** | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | the reported exposure frequency and duration were not suited to the study type and/or outcome(s) of interest (e.g., study length inadequate to evaluate tumorigenicity). These are serious flaws that make the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 11. Number of exposure groups and dose/concentration spacing**<br>Were the number of exposure groups and dose/concentration spacing justified by study authors (e.g., based on range-finding studies) and adequate to address the purpose of the study (e.g., to evaluate dose-response relationships, identify points of departure, inform MOA/AOP, etc.)? | | |
| High (score = 1) | The number of exposure groups and dose/concentration spacing were justified by study authors and considered adequate to address the purpose of the study (e.g., the selected doses produce a range of responses). | |
| Medium (score = 2) | There were minor limitations regarding the number of exposure groups and/or dose/concentration spacing (e.g., unclear if lowest dose was low enough or the highest dose was high enough), but the number of exposure groups and spacing of exposure levels were adequate to show results relevant to the outcome of interest (e.g., observation of a dose-response relationship) and the concerns are unlikely to have a substantial impact on results. | |
| Low (score = 3) | There were deficiencies regarding the number of exposure groups and/or dose/concentration spacing (e.g., narrow spacing between doses with similar responses across groups), and these are likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | The number of exposure groups and spacing were not reported<br>**OR**<br>dose groups and spacing were not relevant for the assessment (e.g., all doses in a developmental toxicity study produced overt maternal toxicity). These are serious flaws that make the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 12. Exposure route and method**<br>Were the route and method of exposure reported and suited to the test substance (e.g., was the test substance non-volatile in dietary studies)? | | |
| High (score = 1) | The route and method of exposure were reported and were suited to the test substance.<br><br>For inhalation studies, a dynamic chamber was used. While dynamic nose-only (or head-only) studies are generally preferred, dynamic whole-body chambers are acceptable for gases and for vapors that do not condense. | |
| Medium (score = 2) | There were minor limitations regarding the route and method of exposure, but the researchers took appropriate steps to mitigate the problem (e.g., mixed diet fresh each day for volatile compounds). These limitations are unlikely to have a substantial impact on results.<br><br>For inhalation studies, a dynamic whole-body chamber was used for vapors | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | that may condense or for aerosols.[28] | |
| Low (score = 3) | There were deficiencies regarding the route and method of exposure that are likely to have a substantial effect on results. Researchers may have attempted to correct the problem, but the success of the mitigating action was unclear.<br><br>For inhalation studies, there are significant flaws in the design or operation of the inhalation chamber, such as uneven distribution of test substance in a whole-body chamber, having less than 15 air changes/hour in a whole-body chamber, or using a whole-body chamber that is too small for the number and volume of animals exposed. | |
| Unacceptable (score = 4) | The route or method of exposure was not reported<br>**OR**<br>an inappropriate route or method (e.g., administration of a volatile organic compound via the diet) was used for the test substance without taking steps to correct the problem (e.g., mixing fresh diet). These are serious flaws that makes the study unusable.<br><br>For inhalation studies, either a static chamber was used, there is no description of the inhalation chamber, or an atypical exposure method was used, such as allowing a container of test substance to evaporate in a room. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 4. Test Animals** | | |
| **Metric 13. Test animal characteristics**<br>Were the test animal species, strain, sex, health status, age, and starting body weight reported? Was the test animal from a commercial source or in-house colony? Was the test species and strain an appropriate animal model for the evaluation of the specific outcome(s) of interest (e.g., routinely used for similar study types)? | | |
| High (score = 1) | The test animal species, strain, sex, health status, age, and starting body weight were reported, and the test animal was obtained from a commercial source or laboratory-maintained colony. The test species and strain were an appropriate animal model for the evaluation of the specific outcome(s) of interest (e.g., routinely used for similar study types). | |
| Medium (score = 2) | Minor uncertainties in the reporting of test animal characteristics (e.g., health status, age, or starting body weight) are unlikely to have a substantial impact on results. The test animals were obtained from a commercial source or in-house colony, and the test species/strain/sex was an appropriate animal model for the evaluation of the specific outcome(s) of interest (e.g., routinely used for similar study types). | |
| Low (score = 3) | The source of the test animal was not reported<br>**OR**<br>the test animal strain or sex was not reported. These deficiencies are likely to | |

[28] This results in a medium score because in addition to inhalation exposure to the test substance, there may also be significant oral exposure due to rodents grooming test substance that adheres to their fur. The combined oral and inhalation exposure results in a lower POD, which makes a test substance appear more toxic than it really is by the inhalation route.

| Confidence Level (Score) | Description | Selected Score |
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| | have a substantial impact on results. | |
| Unacceptable (score = 4) | The test animal species was not reported<br>**OR**<br>the test animal (species, strain, sex, life-stage, source) was not appropriate for the evaluation of the specific outcome(s) of interest (e.g., genetically modified animals, strain was uniquely susceptible or resistant to one or more outcome of interest). These are serious flaws that make the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 14. Adequacy and consistency of animal husbandry conditions**<br>Were all husbandry conditions (e.g., housing, temperature) adequate and the same for control and exposed populations, such that the only difference was exposure to the test substance? | | |
| High (score = 1) | All husbandry conditions were reported (e.g., temperature, humidity, light-dark cycle) and were adequate and the same for control and exposed populations, such that the only difference was exposure. | |
| Medium (score = 2) | Most husbandry conditions were reported and were adequate and similar for all groups. Some differences in conditions were identified among groups, but these differences were considered minor uncertainties or limitations that are unlikely to have a substantial impact on results. | |
| Low (score = 3) | Husbandry conditions were not sufficiently reported to evaluate if husbandry was adequate and if differences occurred between control and exposed populations. These deficiencies are likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | There were significant differences in husbandry conditions between control and exposed groups (e.g., temperature, humidity, light-dark cycle)<br>**OR**<br>animal husbandry conditions deviated from customary practices in ways likely to impact study results (e.g., injuries and stress due to cage overcrowding). These are serious flaws that makes the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 15. Number of animals per group**<br>Was the number of animals per study group appropriate for the study type and outcome analysis? | | |
| High (score = 1) | The number of animals per study group was reported, appropriate for the study type and outcome analysis, and consistent with studies of the same or similar type (e.g., 50/sex/group for rodent cancer bioassay, 10/sex/group for rodent subchronic study, etc.). | |
| Medium (score = 2) | The reported number of animals per study group was lower than the typical number used in studies of the same or similar type (e.g., 30/sex/group for rodent cancer bioassay, 8/sex/group for rodent subchronic study, etc.), but sufficient for statistical analysis and this minor limitation is unlikely to have a substantial impact on results. | |
| Low (score = 3) | The reported number of animals per study group was not sufficient for statistical analysis (e.g., varying numbers per group with some groups consisting of only one animal) and this deficiency is likely to have a substantial impact on results. | |

| Confidence Level (Score) | Description | Selected Score |
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| Unacceptable (score = 4) | The number of animals per study group was not reported<br>**OR**<br>the number of animals per study group was insufficient to characterize toxicological effects (e.g., 1-2 animals in each group). These are serious flaws that makes the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 5. Outcome Assessment** | | |
| **Metric 16. Outcome assessment methodology**<br>Did the outcome assessment methodology address or report the intended outcome(s) of interest? Was the outcome assessment methodology (including endpoints and timing of assessment) sensitive for the outcome(s) of interest (e.g., measured endpoints that are able to detect a true health effect or hazard)?<br><br>Note: Outcome, as addressed in this domain, refers to health effects measured in an animal study (e.g., organ-specific toxicity, reproductive and developmental toxicity). | | |
| High (score = 1) | The outcome assessment methodology addressed or reported the intended outcome(s) of interest and was sensitive for the outcomes(s) of interest. | |
| Medium (score = 2) | The outcome assessment methodology partially addressed or reported the intended outcomes(s) of interest (e.g., serum chemistry and organ weight evaluated in the absence of histology), but minor uncertainties are unlikely to have a substantial impact on results. | |
| Low (score = 3) | Significant deficiencies in the reported outcome assessment methodology were identified<br>**OR**<br>due to incomplete reporting, it was unclear whether methods were sensitive for the outcome of interest. This is likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | The outcome assessment methodology was not reported<br>**OR**<br>the reported outcome assessment methodology was not sensitive for the outcome(s) of interest (e.g., evaluation of endpoints outside the critical window of development, a systemic toxicity study that evaluated only grossly observable endpoints, such as clinical signs and mortality, etc.). These are serious flaws that make the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 17. Consistency of outcome assessment**<br>Was the outcome assessment carried out consistently (i.e., using the same protocol) across study groups (e.g., assessment at the same time after initial exposure in all study groups)? | | |
| High (score = 1) | Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups (e.g., at the same time after initial exposure) using the same protocol in all study groups. | |
| Medium (score = 2) | There were minor differences in the timing of outcome assessment across study groups, or incomplete reporting of minor details of outcome assessment protocol execution, but these uncertainties or limitations are unlikely to have substantial impact on results. | |

| Confidence Level (Score) | Description | Selected Score |
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| Low (score = 3) | Details regarding the execution of the study protocol for outcome assessment (e.g., timing of assessment across groups) were not reported, and these deficiencies are likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | There were large inconsistencies in the execution of study protocols for outcome assessment across study groups<br>**OR**<br>outcome assessments were not adequately reported for meaningful interpretation of results. These are serious flaws that make the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 18. Sampling adequacy**<br>Was sampling adequate for the outcome(s) of interest, including experimental unit (e.g., litter vs. individual animal weight), number of evaluations per dose group, and endpoint (e.g., number of slides evaluated per organ)? | | |
| High (score = 1) | Details regarding sampling for the outcome(s) of interest were reported and the study used adequate sampling for the outcome(s) of interest (e.g., litter data provided for developmental studies; endpoints were evaluated in an adequate number of animals in each group). | |
| Medium (score = 2) | Details regarding sampling for the outcome(s) of interest were reported, but minor limitations were identified in the sampling of the outcome(s) of interest (e.g., histopathology was performed for high-dose group and controls only, and treatment-related changes were observed at the high dose) that are unlikely to have a substantial impact on results. | |
| Low (score = 3) | Details regarding sampling of outcomes were not reported and this deficiency is likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | Sampling was not adequate for the outcome(s) of interest (e.g., histopathology was performed on exposed groups, but not controls). This is a serious flaw that makes the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 19. Blinding of assessors**<br>Were investigators assessing subjective outcomes (i.e., those evaluated using human judgment, including functional observational battery, qualitative neurobehavioral endpoints, histopathological re-evaluations) blinded to treatment group? If blinding was not applied, were quality control/quality assurance procedures for endpoint evaluation cited?<br><br>Note that blinding is not required for initial histopathology review in accordance with Best Practices recommended by the Society of Toxicologic Pathology. This should be considered when rating this metric.[a]<br><br>This metric is not rated/applicable for initial histopathology review or if no subjective outcomes were assessed (i.e., only automated measurements were included and/or human judgment was not applied). | | |
| High (score = 1) | The study explicitly reported that investigators assessing subjective outcomes (i.e., those evaluated using human judgment, including functional observational battery, qualitative neurobehavioral endpoints, histopathological re-evaluations) were blinded to treatment group or that quality control/quality assurance methods were followed in the absence of blinding. | |

| Confidence Level (Score) | Description | Selected Score |
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| Medium (score = 2) | The study reported that blinding was not possible, but steps were taken to minimize bias (e.g., knowledge of study group was restricted to personnel not assessing subjective outcome) and this minor uncertainty is unlikely to have a substantial impact on results. Alternately, blinding was not reported; however, lack of blinding is not expected to have a substantial impact on results. | |
| Low (score = 3) | The study did not report whether assessors were blinded to treatment group for subjective outcomes, and this deficiency is likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | Information in the study report did not report whether assessors were blinded to treatment group for subjective outcomes or suggested that the assessment of subjective outcomes (e.g., functional observational battery, qualitative neurobehavioral endpoints, histopathological re-evaluations) was performed in a biased fashion (e.g., assessors of subjective outcomes were aware of study groups). This is a serious flaw that makes the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 20. Negative control response**<br>Were the biological responses (e.g., histopathology, litter size, pup viability, etc.) of the negative control group(s) adequate? | | |
| High (score = 1) | The biological responses of the negative control group(s) were adequate (e.g., no/low incidence of histopathological lesions). | |
| Medium (score = 2) | There were minor uncertainties or limitations regarding the biological responses of the negative control group(s) (e.g., differences in outcome between untreated and solvent controls) that are unlikely to have a substantial impact on results. | |
| Low (score = 3) | The biological responses of the negative control group(s) were reported, but there were deficiencies regarding the control responses that are likely to have a substantial impact on results (e.g., elevated incidence of histopathological lesions). | |
| Unacceptable (score = 4) | The biological responses of the negative control groups were not reported<br>**OR**<br>there was unacceptable variation in biological responses between control replicates. These are serious flaws that make the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 6. Confounding/Variable Control** | | |
| **Metric 21 Confounding variables in test design and procedures**<br>Were there confounding differences among the study groups in initial body weight or test substance palatability that could influence the outcome assessment (e.g., did palatability issues lead to dehydration and/or malnourishment)? Did reflex bradypnea (i.e., reduced respiration and reduced test substance exposure) induced by respiratory irritants influence outcome assessment? Were normal signs of reflex bradypnea misinterpreted as neurologic, behavioral, or developmental effects (e.g. hypothermia, lethargy, unconsciousness, poor performance in behavioral studies, delayed pup development)? | | |
| High (score = 1) | There were no reported differences among the study groups in initial body weight, food or water intake, or respiratory rate that could influence the outcome assessment. | |
| Medium (score = 2) | The study reported minor differences among the study groups (<20% difference from control) with respect to initial body weight, drinking water and/or food consumption due to palatability issues, or respiratory rate due to reflex bradypnea. These minor uncertainties are unlikely to have a substantial impact on results. Alternately, the lack of reporting of initial body weights, food/water intake, and/or respiratory rate is not likely to have a significant impact on results. | |
| Low (score = 3) | Initial body weight, food/water intake, and respiratory rate were not reported. These deficiencies are likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | The study reported significant differences among the study groups with respect to initial body weight, decreased drinking water/food intake due to palatability issues (≥20% difference from control) that could lead to dehydration and/or malnourishment, or reflex bradypnea that could lead to decreased oxygenation of the blood. These are serious flaws that makes the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 22. Health outcomes unrelated to exposure**<br>Were there differences among the study groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment? Professional judgement should be used to determine whether or not signs of infection would invalidate the study. Criteria for High, Medium and Low are used when the study is still usable. | | |
| High (score = 1) | Details regarding animal attrition and health outcomes unrelated to exposure (e.g., infection) were reported for each study group and there were no differences among groups that could influence the outcome assessment. | |
| Medium (score = 2) | Authors reported that one or more study groups experienced disproportionate animal attrition or health outcomes unrelated to exposure (e.g., infection), but data from the remaining exposure groups were valid and the low incidence of attrition is unlikely to have a substantial impact on results<br>**OR**<br>data on attrition and/or health outcomes unrelated to exposure for each study group were not reported because only substantial differences among groups were noted (as indicated by study authors). | |
| Low (score = 3) | Data on attrition and/or health outcomes unrelated to exposure were not reported for each study group and this deficiency is likely to have a substantial impact on results. **OR** data on attrition and/or health outcomes | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | are reported and could have substantial impact on results. | |
| Unacceptable (score = 4) | One or more study groups experienced serious animal attrition or health outcomes unrelated to exposure (e.g., infection). This is a serious flaw that makes the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 7. Data Presentation and Analysis** | | |
| **Metric 23. Statistical methods**<br>Were statistical methods clearly described and appropriate for dataset(s) (e.g., parametric test for normally distributed data)? | | |
| High (score = 1) | Statistical methods were clearly described and appropriate for dataset(s) (e.g., parametric test for normally distributed data).<br>**OR**<br>no statistical analyses, calculation methods, and/or data manipulation were conducted but sufficient data were provided to conduct an independent statistical analysis. | |
| Medium (score = 2) | Statistical analysis was described with some omissions that would unlikely have a substantial impact on results. | |
| Low (score = 3) | Statistical analysis was not described clearly, and this deficiency is likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | Statistical methods were not appropriate (e.g., parametric test for non-normally distributed data)<br>**OR**<br>statistical analysis was not conducted<br>**AND**<br>data were not provided preventing an independent statistical analysis. These are serious flaws that make the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 24. Reporting of data**<br>Were the data for all outcomes presented? Were data reported by exposure group and sex (if applicable), with numbers of animals affected and numbers of animals evaluated (for quantal data) or group means and variance (for continuous data)? If severity scores were used, was the scoring system clearly articulated? | | |
| High (score = 1) | Data for exposure-related findings were presented for all outcomes by exposure group and sex (if applicable) with quantal and/or continuous presentation and description of severity scores if applicable. Negative findings were reported qualitatively or quantitatively. | |
| Medium (score = 2) | Data for exposure-related findings were reported for most, but not all, outcomes by exposure group and sex (if applicable) with quantal and/or continuous presentation and description of severity scores if applicable. The minor uncertainties in outcome reporting are unlikely to have substantial impact on results. | |
| Low (score = 3) | Data for exposure-related findings were not shown for each study group, but results were described in the text and/or data were only reported for some outcomes. These deficiencies are likely to have a substantial impact on | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | results. | |
| Unacceptable (score = 4) | Data presentation was inadequate (e.g., the report does not differentiate among findings in multiple exposure groups)<br>**OR**<br>major inconsistencies were present in reporting of results. These are serious flaws that make the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 8. Other (Apply as Needed)** | | |
| Metric: | | |
| High (score = 1) | | |
| Medium (score = 2) | | |
| Low (score = 3) | | |
| Unacceptable (score = 4) | | |
| Not rated/applicable | | |
| Reviewer's comments | *Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

[a] Crissman et al. (2004)

### G.5.2 *In Vitro* Toxicity Studies

**Table G-15. Serious Flaws that Would Make *In Vitro* Toxicity Studies Unacceptable**

Optimization of the list of serious flaws may occur after pilot calibration exercises.

| Domain | Metric | Description of Serious Flaw(s) in Data Source[a] |
|---|---|---|
| Test Substance | Test Substance Identity | The test substance identity and form (if applicable) could not be determined from the information provided (e.g., nomenclature was unclear and CASRN or structure were not reported)<br>**OR**<br>the components and ratios of mixtures were not characterized. |
| | Test Substance Source | The test substance was not obtained from a manufacturer<br>**OR**<br>if synthesized or extracted, analytical verification of the test substance was not conducted. |
| | Test Substance Purity | The nature and quantity of reported impurities were such that study results were likely to be due to one or more of the impurities. |
| Test Design | Negative Controls | A concurrent negative control group was not included or reported<br>**OR**<br>the reported negative control group was not appropriate (e.g., different cell lines used for controls and test substance exposure). |
| | | |
| | Positive Controls | A concurrent positive control or proficiency group was not used (when applicable). |
| | Assay Procedures | Assay methods and procedures were not reported<br>**OR**<br>assay methods and procedures were not appropriate for the study type (e.g., *in vitro* skin corrosion protocol used for *in vitro* skin irritation assay). |
| | Standards for Testing | QC criteria were not reported and/or inadequate data were provided to demonstrate validity, acceptability, and reliability of the test when compared with current standards and guidelines. |
| Exposure Characterization | Preparation and Storage of Test Substance | Information on preparation and storage was not reported<br>**OR**<br>serious flaws reported with test substance preparation and/or storage conditions will have critical impacts on dose/concentration estimates and make the study unusable (e.g., instability of test substance in exposure media, test substance volatilized rapidly from the open containers that were used as test vessels). |
| | Consistency of Administration | Critical exposure details (e.g., amount of test substance used) were not reported<br>**OR**<br>exposures were not administered consistently across and/or within study groups (e.g., 75 mg/cm$^2$ and 87 mg/cm$^2$ administered to reconstructed corneas replicate 1 and replicate 2, respectively, in *in vitro* eye irritation test) resulting in serious flaws that make the study unusable. |
| | Reporting of Concentrations | The exposure doses/concentrations or amounts of test substance were not reported resulting in serious flaws. |

| Domain | Metric | Description of Serious Flaw(s) in Data Source[a] |
|---|---|---|
| | Exposure Duration | No information on exposure duration(s) was reported<br>**OR**<br>the exposure duration was not appropriate for the study type and/or outcome of interest (e.g., 5 hours for reconstructed epidermis in skin irritation test, 24 hours exposure for bacterial reverse mutation test). |
| | Number of Exposure Groups and Concentrations Spacing | The number of exposure groups and dose/concentration spacing were not reported<br>**OR**<br>the number of exposure groups and dose/concentration spacing were not relevant for the assessment (e.g., all concentrations used in an *in vitro* mammalian cell micronucleus test were cytotoxic). |
| | Metabolic Activation | No information on the characterization and use of a metabolic activation system was reported. |
| Test Model | Test Model | The test model and descriptive information were not reported<br>**OR**<br>the test model was not appropriate for evaluation of the specific outcome of interest (e.g., bacterial reverse mutation assay to evaluate chromosome aberrations). |
| | Number per Group | The number of organisms or tissues per study group and/or replicates per study group were not reported<br>**OR**<br>the number of organisms or tissues per study group and/or replicates per study group were insufficient to characterize toxicological effects (e.g., one tissue/test concentration/one exposure time for *in vitro* skin corrosion test, one replicate/strain of bacteria exposed in bacterial reverse mutation assay). |
| Outcome Assessment | Outcome Assessment Methodology | The outcome assessment methodology was not reported<br>**OR**<br>the assessment methodology was not appropriate for the outcome(s) of interest (e.g., cells were evaluated for chromosomal aberrations immediately after exposure to the test substance instead of after post-exposure incubation period, cytotoxicity not determined prior to CD86/CD expression measurement assay, and labeling antibodies were not tested on proficiency substances in an *in vitro* skin sensitization test in h-CLAT cells). |
| | Consistency of Outcome Assessment | There were large inconsistencies in the execution of study protocols for outcome assessment across study groups<br>**OR**<br>outcome assessments were not adequately reported for meaningful interpretation of results. |
| | Sampling Adequacy | Reported sampling was not adequate for the outcome(s) of interest and/or serious uncertainties or limitations were identified in how the study carried out the sampling of the outcome(s) of interest (e.g., replicates from control and test concentrations were evaluated at different times). |
| | Blinding of Assessors | Information in the study report suggested that the assessment of subjective outcomes was performed in a biased fashion (e.g., assessors of subjective outcomes were aware of study groups). |
| Confounding/ Variable Control | Confounding Variables in Test Design and | There were significant differences among the study groups with respect to the strain/batch/lot number of organisms or models used per group or size and/or quality of tissues exposed (e.g., initial |

| Domain | Metric | Description of Serious Flaw(s) in Data Source[a] |
|---|---|---|
| | Procedures | number of viable bacterial cells were different for each replicate [$10^5$ cells in replicate 1, $10^8$ cell in replicate 2, and $10^3$ cells in replicate 3], tissues from two different lots were used for *in vitro* skin corrosion test, but the control batch quality for one lot was outside of the acceptability range). |
| | Confounding Variables in Outcomes Unrelated to Exposure | One or more replicates or groups (i.e., negative and positive controls experienced disproportionate growth or reduction in growth unrelated to exposure (e.g., contamination) such that no outcomes could be assessed. |
| Data Presentation and Analysis | Data Analysis | Statistical methods, calculation methods, or data manipulation were not appropriate (e.g., Student's t-test used to compare 2 groups in a multi-group study, parametric test for non-normally distributed data)<br>**OR**<br>statistical analysis was not conducted<br><br>**AND**<br>data enabling an independent statistical analysis were not provided. |
| | Data Interpretation | The reported scoring and/or evaluation criteria were inconsistent with established practices resulting in the interpretation of data results that are seriously flawed. |
| | Cytotoxicity Data | Cytotoxicity endpoints were not defined, methods were not described, and it could not be determined that cytotoxicity was accounted for in the interpretation of study results. |
| | Reporting of Data | Data presentation was inadequate (e.g., the report did not differentiate among findings in multiple exposure groups, no scores or frequencies were reported), or major inconsistencies were present in reporting of results. |

Note:

[a] If the metric does not apply to the study type, the flaw will not be applied to determine unacceptability.

## Table G-16. Data Quality Criteria for *In Vitro* Toxicity Studies

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 1. Test Substance** | | |
| **Metric 1. Test substance identity**<br>Was the test substance identified definitively (i.e., established nomenclature, CASRN, physical nature, physiochemical properties, and/or structure reported, including information on the specific form tested [e.g., salt or base, valence state, isomer, if applicable] for materials that may vary in form)? If test substance was a mixture, were mixture components and ratios characterized? | | |
| High<br>(score = 1) | The test substance was identified definitively (i.e., established nomenclature, CASRN, physical nature, physiochemical properties, and/or structure reported, including information on the specific form tested (e.g., salt or base, valence state, isomer, [if applicable]) for materials that may vary in form. For mixtures, the components and ratios were characterized. | |
| Medium<br>(score = 2) | The test substance and form (if applicable) were identified, and components and ratios of mixtures were characterized, but there were minor uncertainties (e.g., minor characterization details were omitted) that are unlikely to have a substantial impact on results. | |
| Low<br>(score = 3) | The test substance and form (if applicable) were identified, and components and ratios of mixtures were characterized, but there were uncertainties regarding test substance identification or characterization that are likely to have a substantial impact on the results. | |
| Unacceptable<br>(score = 4) | The test substance identity and form (if applicable) could not be determined from the information provided (e.g., nomenclature was unclear and CASRN or structure were not reported)<br>**OR**<br>the components and ratios of mixtures were not characterized. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 2. Test substance source**<br>Was the source of the test substance reported, including manufacturer and batch/lot number for materials that may vary in composition? If synthesized or extracted, was test substance identity verified by analytical methods? | | |
| High<br>(score = 1) | The source of the test substance was reported, including manufacturer and batch/lot number for materials that may vary in composition, and its identity was certified by manufacturer and/or verified by analytical methods (melting point, chemical analysis, etc.). | |
| Medium<br>(score = 2) | The source of the test substance and/or the analytical verification of a synthesized test substance was reported incompletely, but the omitted details are unlikely to have a substantial impact on the results. | |
| Low<br>(score = 3) | Omitted details on the source of the test substance and/or analytical verification of a synthesized test substance are likely to have a substantial impact on the results. | |
| Unacceptable<br>(score = 4) | The test substance was not obtained from a manufacturer<br>**OR**<br>if synthesized or extracted, analytical verification of the test substance was not conducted. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | *additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 3. Test substance purity**<br>Was the purity or grade (i.e., analytical, technical) of the test substance reported and adequate to identify its toxicological effects? Were impurities identified? Were impurities present in quantities that could influence the results? | | |
| High<br>(score = 1) | The test substance purity and composition were such that any observed effects were highly likely to be due to the nominal test substance itself (e.g., ACS grade, analytical grade, reagent grade test substance or a formulation comprising primarily inert ingredients with small amount of active ingredient). Impurities, if identified, were not present in quantities that could influence the results. | |
| Medium<br>(score = 2) | Minor uncertainties or limitations were identified regarding the test substance purity and composition; however, the purity and composition were such that observed effects were more likely than not to be due to the nominal test substance and impurities, if identified, were unlikely to have a substantial impact on the results. | |
| Low<br>(score = 3) | Purity and/or grade of test substance were not reported<br>**OR**<br>the percentage of the reported purity was such that the observed effects may not have been due to the nominal test substance. | |
| Unacceptable<br>(score = 4) | The nature and quantity of reported impurities were such that study results were likely to be due to one or more of the impurities. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 2. Test Design** | | |
| **Metric 4. Negative controls**<br>Was a concurrent negative (untreated, sham-treated, and/or vehicle, as necessary) control group included? | | |
| High<br>(score = 1) | Study authors reported using a concurrent negative control group (untreated, sham-treated, and/or vehicle, as applicable) in which all conditions equal except exposure to test substance. | |
| Medium<br>(score = 2) | Study authors reported using a concurrent negative control group, but all conditions were not equal to those of treated groups; however, the identified differences are considered to be minor limitations that are unlikely to have substantial impact on results. | |
| Low<br>(score = 3) | Study authors acknowledged using a concurrent negative control group, but details regarding the negative control group were not reported, and the lack of details is likely to have a substantial impact on the results. | |
| Unacceptable<br>(score = 4) | A concurrent negative control group was not included or reported<br>**OR**<br>the reported negative control group was not appropriate (e.g., different cell lines used for controls and test substance exposure). | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | *elements such as relevance]* | |
| **Metric 5. Positive controls**<br>Was a concurrent positive or proficiency control group included, *if applicable*, based on study type, and was the response appropriate in this group (e.g., induction of positive effect)?<br>*This metric is applicable studies that require a concurrent positive control. | | |
| High<br>(score = 1) | A concurrent positive control or proficiency control group, if applicable, was used and the intended positive response was induced. | |
| Medium<br>(score = 2) | A concurrent positive control or proficiency control was used, but there were minor uncertainties (e.g., minor details regarding control exposure or response were omitted) that are unlikely to have a substantial impact on results. | |
| Low<br>(score = 3) | A concurrent positive control or proficiency control was used, but there were uncertainties regarding the control exposure or response that are likely to have a substantial impact on results (e.g., the control response was not described). | |
| Unacceptable<br>(score = 4) | A concurrent positive control or proficiency group was not used. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 6. Assay procedures**<br>Were assay methods and procedures (e.g., test conditions, cell density culture media and volumes, pre- and post-incubation temperatures, humidity, reaction mix, washing/rinsing methods, incubation with amino acids, slide preparation, instrument used and calibration, wavelengths measured) described in detail and applicable to the study type? | | |
| High<br>(score = 1) | Study authors described the methods and procedures (e.g., test conditions, cell density culture media and volumes, pre- and post-incubation temperatures, humidity, reaction mix, washing/rinsing methods, incubation with amino acids, slide preparation, instrument used and calibration, wavelengths measured) used for the test in detail and they were applicable for the study type (e.g., protocol for *in vitro* skin irritation test was reported). | |
| Medium<br>(score = 2) | Methods and procedures were partially described and/or cited in another publication(s), but appeared to be appropriate (e.g., reporting that "calculations were used for enumerating viable and mutant cells" in a mammalian cell gene mutation test using *Hprt* and *xprt* genes instead of inclusion of the equations) to the study type, so the omission is unlikely to have a substantial impact on results. | |
| Low<br>(score = 3) | The methods and procedures were not well described or deviated from customary practices (e.g., post-incubation time was not stated in a mammalian cell gene mutation test using *Hprt* and *xprt* genes) and this is likely to have a substantial impact on results. | |
| Unacceptable<br>(score = 4) | Assay methods and procedures were not reported<br>**OR**<br>assay methods and procedures were not appropriate for the study type (e.g., | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | *in vitro* skin corrosion protocol used for *in vitro* skin irritation assay). | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 7. Standards for tests**<br>For assays with established criteria, were the test validity, acceptability, reliability, and/or QC criteria reported and consistent with current standards and guidelines? Example acceptability and QC criteria for an *in vitro* skin corrosion test using the EpiSkin™ (SM) model: Acceptability criteria: negative control OD values between ≥0.6 and ≤1.5, variability of the positive control replicates should be ≤20% of negative control, difference of viability between 2 tissue replicates should not exceed 30% in the range of 20-100% viability and for EDs≥0.3; QC criteria: Only QC-accepted tissue batches having an $IC_{50}$ range of 1.0-3.0 mg/mL were used.)<br><br>* This metric is generally applicable to studies using reconstructed human cells and may not be applicable to other studies. | | |
| High (score = 1) | The test validity, acceptability, reliability, and/or QC criteria were reported and consistent with current standards and guidelines,[a] if applicable. | |
| Medium (score = 2) | Not applicable for this metric. | |
| Low (score = 3) | Not applicable for this metric. | |
| Unacceptable (score = 4) | QC criteria were not reported and/or inadequate data were provided to demonstrate validity, acceptability, and reliability of the test when compared with current standards and guidelines. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 3. Exposure Characterization** | | |
| **Metric 8. Preparation and storage of test substance**<br>Did the study characterize preparation of the test substance and storage conditions? Were the frequency of preparation and/or storage conditions appropriate to the test substance stability and solubility (if applicable)? | | |
| High (score = 1) | The test substance preparation and/or storage conditions (e.g., test substance stability, homogeneity, mixing temperature, stock concentration, stirring methods, centrifugation/filtration, aerosol/vapor generation method, storage conditions) were reported and appropriate (e.g., stability in exposure media confirmed, volatile test substances prepared and stored in sealed containers) for the test substance. | |
| Medium (score = 2) | The test substance preparation and storage conditions were reported, but minor limitations in the test substance preparation and/or storage conditions were identified (e.g., test substance formulations were stirred instead of centrifuged for a specific number of rotations per minute) that are unlikely to have a substantial impact on results. | |
| Low (score = 3) | Deficiencies in reporting of test substance preparation, and/or storage conditions are likely to have a substantial impact on results (e.g., available information on physical-chemical properties suggests that stability and/or solubility of test substance in vehicle or culture media may be poor). | |
| Unacceptable (score = 4) | Information on preparation and storage was not reported<br>**OR** | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | serious flaws reported with test substance preparation and/or storage conditions will have critical impacts on dose/concentration estimates and make the study unusable (e.g., instability of test substance in exposure media, test substance volatilized rapidly from the open containers that were used as test vessels). | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 9. Consistency of administration**<br>Were exposures administered consistently across study groups (e.g., consistent application methods and volumes, control for evaporation)? | | |
| High (score = 1) | Details of exposure administration were reported and exposures were administered consistently across study groups in a scientifically sound manner (e.g., consistent application methods and volumes, control for evaporation). | |
| Medium (score = 2) | Details of exposure administration were reported or inferred from the text, but the minor limitations in administration of exposures (e.g., accidental mistakes in dosing) that were identified are unlikely to have a substantial impact on results. | |
| Low (score = 3) | Details of exposure administration were reported, but deficiencies in administration of exposures (e.g., non-calibrated instrument used to administer test substance) that were reported or inferred from the text are likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | Critical exposure details (e.g., amount of test substance used) were not reported<br>**OR**<br>exposures were not administered consistently across and/or within study groups (e.g., 75 mg/cm$^2$ and 87 mg/cm$^2$ administered to reconstructed corneas replicate 1 and replicate 2, respectively, in *in vitro* eye irritation test) resulting in serious flaws that make the study unusable. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 10. Reporting of concentrations**<br>Were exposure doses/concentrations or amounts of test substance reported without ambiguity (e.g., point estimate instead of range, analytical instead of nominal)? | | |
| High (score = 1) | The exposure doses/concentrations or amounts of test substance were reported without ambiguity (e.g., point estimate instead of range, analytical instead of nominal). | |
| Medium (score = 2) | Not applicable for this metric. | |
| Low (score = 3) | Not applicable for this metric. | |
| Unacceptable (score = 4) | The exposure doses/concentrations or amounts of test substance were not reported resulting in serious flaws. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | *additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 11. Exposure duration**<br>Was the exposure duration (e.g., minutes, hours, days) reported and appropriate for this study type and/or outcome(s) of interest? | | |
| High<br>(score = 1) | The exposure duration (e.g., min, hours, days) was reported and appropriate for the study type and/or outcome(s) of interest (e.g., 60-minute exposure for reconstructed epidermis in skin irritation test, 48-72-hour exposure for bacterial reverse mutation assay). | |
| Medium<br>(score = 2) | Duration(s) of exposure differed slightly from current standards and guidelines[a] for studies of this type (e.g., 65 minutes for reconstructed epidermis in skin irritation test), but the differences are unlikely to have a substantial impact on results. | |
| Low<br>(score = 3) | Duration(s) of exposure were not clearly stated (e.g., exposure duration was described only in qualitative terms) or duration(s) differed significantly from studies of the same or similar types. These deficiencies are likely to have a substantial impact on results. | |
| Unacceptable<br>(score = 4) | No information on exposure duration(s) was reported<br>**OR**<br>the exposure duration was not appropriate for the study type and/or outcome of interest (e.g., 5 hours for reconstructed epidermis in skin irritation test, 24 hours exposure for bacterial reverse mutation test). | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 12. Number of exposure groups and concentrations spacing**<br>Were the number of exposure groups and dose/concentration spacing justified by study authors (e.g., based on study type, range-finding study, and/or cytotoxicity studies) and adequate to address the purpose of the study (e.g., to evaluate dose-response relationships, inform MOA/AOP)? | | |
| High<br>(score = 1) | The number of exposure groups and dose/concentration spacing were justified by study authors (e.g., based on study type, range-finding study, and/or cytotoxicity studies) and considered adequate to address the purpose of the study (e.g., to evaluate dose-response relationships, inform MOA/AOP). | |
| Medium<br>(score = 2) | There were minor limitations regarding the number of exposure groups and/or dose/concentration spacing, but the number of exposure groups and spacing of exposure levels were adequate to show results relevant to the outcome of interest (e.g., observation of a dose-response relationship) and the concerns are unlikely to have a substantial impact on results. | |
| Low<br>(score = 3) | There were deficiencies regarding the number of exposure groups and/or dose/concentration spacing (e.g., one bacterial strain exposed to 2 concentrations of the test substance in bacterial reverse mutation assay) and these concerns were likely had a substantial impact on interpretation of the results. | |
| Unacceptable<br>(score = 4) | The number of exposure groups and dose/concentration spacing were not reported<br>**OR**<br>the number of exposure groups and dose/concentration spacing were not | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | relevant for the assessment (e.g., all concentrations used in an *in vitro* mammalian cell micronucleus test were cytotoxic). | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 13. Metabolic activation (if applicable)**<br>Were exposures conducted in the presence and absence of a metabolic activation system, if applicable, for the study type? Were the source, method of preparation, concentration or volume in final culture, and quality control information on the metabolic activation system reported? | | |
| High (score = 1) | Study authors reported exposures were conducted in the presence of metabolic activation and the type and source, method of preparation, concentration or volume in final culture, and quality control information of the metabolic activation system were described. | |
| Medium (score = 2) | The presence of a commonly used metabolic activation system (e.g., aroclor-, ethanol-, or phenobarbitial/β-naphthoflavone-induced rat, hamster, or mice liver cells) was reported in the study; however, some details regarding type, composition mix, concentration, or quality control information were not described. These omissions are unlikely to have a substantial impact on the results. | |
| Low (score = 3) | The presence of a metabolic activation system was reported in the study, but the system described was not validated (e.g., rigorous testing to ensure that it suitable for the purpose for which it is used) or comparable to commonly used systems (e.g., aroclor-, ethanol-, or phenobarbitial/β-naphthoflavone-induced rat, hamster, or mice liver cells). | |
| Unacceptable (score = 4) | No information on the characterization and use of a metabolic activation system was reported. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 4. Test Model** | | |
| **Metric 14. Test model**<br>Were the test models (e.g., cell types or lines, tissue models) and descriptive information (e.g., tissue origin, number of passages, karyotype features, doubling times, donor information, biomarkers) reported? Was the test model from a commercial source or an in-house culture? Was the model routinely used for the outcome of interest (e.g., Chinese hamster ovary cells for micronucleus formation)? | | |
| High (score = 1) | The test model (e.g., cell types or lines, tissue models) and descriptive information (e.g., tissue origin, number of passages, karyotype features, doubling times, donor information, biomarkers) were reported, the test model was obtained from a commercial source or laboratory-maintained culture, and the test model was routinely used for the outcome of interest (e.g., Chinese hamster ovary cells for micronucleus formation). | |
| Medium (score = 2) | The test model was reported along with limited descriptive information. The test model was routinely used for the outcome of interest. Reporting limitations are unlikely to have a substantial impact on results. | |
| Low (score = 3) | The test model was reported but no additional details were reported **AND/OR** | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | the test model was not routinely used for the outcome of interest (e.g., feline cell line for micronucleus formation). This is likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | The test model and descriptive information were not reported<br>**OR**<br>the test model was not appropriate for evaluation of the specific outcome of interest (e.g., bacterial reverse mutation assay to evaluate chromosome aberrations). | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 15. Number per group**<br>Was the number of organisms or tissues per study group and/or replicates per study group reported and appropriate for the study type and outcome analysis? | | |
| High (score = 1) | The number of organisms or tissues per study group and/or number of replicates per study group were reported and were appropriate[a] for the study type and outcome analysis, and consistent with studies of the same or similar type (e.g., at least two replicates/test substance/3 different exposure times for *in vitro* skin corrosion test, 3 replicates/strain of bacteria in bacterial reverse mutation assay). | |
| Medium (score = 2) | The number of organisms or tissues per study group and/or replicates per study group were reported but were lower than the typical number used in studies of the same or similar type (e.g., 3 replicates/strain of bacteria in bacterial reverse mutation assay), but were sufficient for analysis and unlikely to have a substantial impact on results. | |
| Low (score = 3) | The number of organisms or tissues per study group and/or replicates per study group were reported but were less than recommended by current standards and guidelines[a] (e.g., one tissue/test concentration/exposure time for *in vitro* skin corrosion test). This is likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | The number of organisms or tissues per study group and/or replicates per study group were not reported<br>**OR**<br>the number of organisms or tissues per study group and/or replicates per study group were insufficient to characterize toxicological effects (e.g., one tissue/test concentration/one exposure time for *in vitro* skin corrosion test, one replicate/strain of bacteria exposed in bacterial reverse mutation assay). | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 5. Outcome Assessment** | | |
| **Metric 16. Outcome assessment methodology**<br>Did the outcome assessment methodology address or report the intended outcome(s) of interest? Was the outcome assessment methodology (including endpoints and timing of assessment) sensitive for the outcome(s) of interest (e.g., measured endpoints that are able to detect a true effect)? | | |
| High (score = 1) | The outcome assessment methodology addressed or reported the intended outcome(s) of interest and was sensitive for the outcome(s) of interest. | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| Medium (score = 2) | The outcome assessment methodology used only partially addressed or reported the intended outcomes(s) of interest (e.g., mutation frequency evaluated in the absence of cytotoxicity in a gene mutation test), but minor uncertainties are unlikely to have a substantial impact on results. | |
| Low (score = 3) | Significant deficiencies in the reported outcome assessment methodology were identified (e.g., optimum time for expression of chromosomal aberrations after exposure to test compound was not determined)<br>**OR**<br>due to incomplete reporting, it was unclear whether methods were sensitive for the outcome of interest. This is likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | The outcome assessment methodology was not reported<br>**OR**<br>the assessment methodology was not appropriate for the outcome(s) of interest (e.g., cells were evaluated for chromosomal aberrations immediately after exposure to the test substance instead of after post-exposure incubation period). | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 17. Consistency of outcome assessment**<br>Was the outcome assessment carried out consistently (i.e., using the same protocol) across study groups (e.g., assessment at the same time after initial exposure in all study groups)? | | |
| High (score = 1) | Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups (e.g., at the same time after initial exposure) using the same protocol in all study groups. | |
| Medium (score = 2) | There were minor differences in the timing of outcome assessment across study groups, or incomplete reporting of minor details of outcome assessment protocol execution, but these uncertainties or limitations are unlikely to have substantial impact on results. | |
| Low (score = 3) | Details regarding the execution of the study protocol for outcome assessment (e.g., timing of assessment across groups) were not reported, and these deficiencies are likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | There were large inconsistencies in the execution of study protocols for outcome assessment across study groups<br>**OR**<br>outcome assessments were not adequately reported for meaningful interpretation of results. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 18. Sampling adequacy**<br>Was the reported sampling adequate for the outcome(s) of interest, including number of evaluations per exposure group, and endpoint (e.g., number of replicates/slides/cells/metaphases evaluated per test concentration)? | | |
| High (score = 1) | The study reported adequate sampling for the outcome(s) of interest including number of evaluations per exposure group, and endpoint (e.g., number of replicates/slides/cells/metaphases [at least 300 well-spread | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | metaphases scored/concentration in a chromosome aberration test]). | |
| Medium (score = 2) | Details regarding sampling for the outcome(s) of interest were reported, but minor limitations were identified in the reported sampling of the outcome(s) of interest, but those are unlikely to have a substantial impact on results. | |
| Low (score = 3) | Details regarding sampling of outcomes were not fully reported and the omissions are likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | Reported sampling was not adequate for the outcome(s) of interest and/or serious uncertainties or limitations were identified in how the study carried out the sampling of the outcome(s) of interest (e.g., replicates from control and test concentrations were evaluated at different times). | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 19. Blinding of assessors**<br>Were investigators assessing subjective outcomes (i.e., those evaluated using human judgment) blinded to treatment group?<br><br>This metric is not rated/applicable if no subjective outcomes were assessed (i.e., only automated measurements were included and human judgment was not applied). | | |
| High (score = 1) | The study explicitly reported that investigators assessing subjective outcomes (i.e., those evaluated using human judgment) were blinded to treatment group or that quality control/quality assurance methods were followed in the absence of blinding. | |
| Medium (score = 2) | The study reported that blinding was not possible, but steps were taken to minimize bias (e.g., knowledge of study group was restricted to personnel not assessing subjective outcome) and this minor uncertainty is unlikely to have a substantial impact on results. | |
| Low (score = 3) | The study did not report whether assessors were blinded to treatment group for subjective outcomes, and this deficiency is likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | Information in the study report suggested that the assessment of subjective outcomes was performed in a biased fashion (e.g., assessors of subjective outcomes were aware of study groups). | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 6. Confounding/Variable Control** | | |
| **Metric 20. Confounding variables in test design and procedures**<br>Were there confounding differences among the study groups in the strain/batch/lot number of organisms or models used per group, size, and/or quality of tissues exposed, or lot of test substance used that could influence the outcome assessment? | | |
| High (score = 1) | There were no differences reported among study group parameters (e.g., test substance lot or batch, strain/batch/ lot number of organisms or models used per group or size, and/or quality of tissues exposed) that could influence the outcome assessment. | |
| Medium | Minor differences were reported in initial conditions that are unlikely to have | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| (score = 2) | a substantial impact on results (e.g., tissues from two different lots were used for *in vitro* skin corrosion test, and QC data were similar for both lots). | |
| Low (score = 3) | Initial strain/batch/lot number of organisms or models used per group, size, and/or quality of tissues exposed was not reported. These deficiencies are likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | There were significant differences among the study groups with respect to the strain/batch/lot number of organisms or models used per group or size and/or quality of tissues exposed (e.g., initial number of viable bacterial cells were different for each replicate [$10^5$ cells in replicate 1, $10^8$ cell in replicate 2, and $10^3$ cells in replicate 3], tissues from two different lots were used for *in vitro* skin corrosion test, but the control batch quality for one lot was outside of the acceptability range). | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 21. Confounding variables in outcomes unrelated to exposure**<br>Were there differences among the study groups unrelated to exposure to test substance (e.g., contamination) that could influence the outcome assessment? Did the test material interfere in the assay (e.g., altering fluorescence or absorbance, signal quenching by heavy metals, altering pH, solubility or stability issues)? | | |
| High (score = 1) | There were no reported differences among the study replicates or groups in test model unrelated to exposure (e.g., contamination) and the test substance did not interfere with the assay (e.g., signal quenching by heavy metals). | |
| Medium (score = 2) | Authors reported that one or more replicates or groups experienced disproportionate outcomes unrelated to exposure (e.g., contamination), but data from the remaining exposure replicates or groups were valid and is unlikely to have a substantial impact on results<br>**OR**<br>data on experienced disproportionate outcomes unrelated to exposure were not reported because only substantial differences among groups were noted (as indicated by study authors).<br>**OR**<br>the test material interfered in the assay, but the interference did not cause substantial differences among the groups.. | |
| Low (score = 3) | Data on outcome differences unrelated to exposure were not reported for each study replicate or group. Assay interference was present or inferred resulting in large variabilities among the groups. The absence of this information is likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | One or more replicates or groups (i.e., negative and positive controls experienced disproportionate growth or reduction in growth unrelated to exposure (e.g., contamination), or assay interference occurred such that no outcomes could be assessed. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 7. Data Presentation and Analysis** | | |
| **Metric 22. Data analysis**<br>Were statistical methods, calculations methods, and/or data manipulation clearly described and appropriate for dataset(s)? | | |
| High<br>(score = 1) | Statistical methods, calculation methods, and/or data manipulation were clearly described and presented for dataset(s) (e.g., frequencies of chromosomal aberrations were statistically analyzed across groups, trend test used to determine dose relationships, or results compared to historical negative control data).<br>**OR**<br>no statistical analyses, calculation methods, and/or data manipulation were conducted but sufficient data were provided to conduct an independent statistical analysis. | |
| Medium<br>(score = 2) | Statistical analysis was described with some omissions that would unlikely have a substantial impact on results. | |
| Low<br>(score = 3) | Statistical analysis was not described clearly, and this deficiency is likely to have a substantial impact on results. | |
| Unacceptable<br>(score = 4) | Statistical methods were not appropriate (e.g., Student's t-test used to compare 2 groups in a multi-group study, parametric test for non-normally distributed data)<br>**OR**<br>statistical analysis was not conducted<br>**AND**<br>data were not provided preventing an independent statistical analysis. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 23. Data interpretation**<br>Were the scoring and/or evaluation criteria reported and consistent with standards and guidelines? | | |
| High<br>(score = 1) | Study authors reported the scoring and/or evaluation criteria (e.g., for determining negative, positive, and equivocal outcomes) for the test and these were consistent with established practices.[a] | |
| Medium<br>(score = 2) | Scoring and/or evaluation criteria were partially reported (e.g., evaluation criteria were reported following 3- and 60-minute exposures, but not for 240-minute exposure in *in vitro* skin corrosion test), but the omissions are unlikely to have a substantial impact on results. | |
| Low<br>(score = 3) | Scoring and/or evaluation criteria were not reported and the omissions are likely to have a substantial impact on interpretation of the results. | |
| Unacceptable<br>(score = 4) | The reported scoring and/or evaluation criteria were inconsistent with established practices. resulting in the interpretation of data results that are seriously flawed. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Metric 24. Cytotoxicity data**<br>Were cytotoxicity endpoints defined, if necessitated by study type, and were methods for measuring cytotoxicity described and commonly used for assessment[a]? | | |
| High (score = 1) | Study authors defined cytotoxicity endpoints (e.g., cell integrity, apoptosis, necrosis, color induction, cell viability, mitotic index) and the methods for measuring cytotoxicity were clearly described and commonly used for assessment. | |
| Medium (score = 2) | Cytotoxicity endpoints were defined and methods of measurement were partially reported, but the omissions are unlikely to have substantial impact on study results. | |
| Low (score = 3) | Cytotoxicity endpoints were defined, but the methods of measurements were not fully described or reported, and the omissions are likely to have a substantial impact on the study results. | |
| Unacceptable (score = 4) | Cytotoxicity endpoints were not defined, methods were not described, and it could not be determined that cytotoxicity was accounted for in the interpretation of study results. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 25. Reporting of data**<br>Were the data for all outcomes presented? Were data reported by exposure group? | | |
| High (score = 1) | Data for exposure-related findings were presented for all outcomes by exposure group. Negative findings were reported qualitatively or quantitatively. | |
| Medium (score = 2) | Data for exposure-related findings were reported for most, but not all, outcomes by exposure group (e.g., sensitization percentages reported in the absence of incidence data). The minor uncertainties in outcome reporting are unlikely to have substantial impact on results. | |
| Low (score = 3) | Data for exposure-related findings were not shown for each study group, but results were described in the text and/or data were only reported for some outcomes. These deficiencies are likely to have a substantial impact on results. | |
| Unacceptable (score = 4) | Data presentation was inadequate (e.g., the report did not differentiate among findings in multiple exposure groups, no scores or frequencies were reported), or major inconsistencies were present in reporting of results. | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 8. Other (Apply as Needed)** | | |
| **Metric:** | | |
| High (score = 1) | | |
| Medium (score = 2) | | |
| Low (score = 3) | | |
| Unacceptable | | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| (score = 4) | | |
| Not rated/applicable | | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

Note:
[a] For comparison purposes, current standards and guidelines may be reviewed at http://www.oecd-ilibrary.org/environment/oecd-guidelines-for-the-testing-of-chemicals-section-4-health-effects_20745788; https://www.epa.gov/test-guidelines-pesticides-and-toxic-substances; https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/IngredientsAdditivesGRASPackaging/ucm2006826.htm#TOC.

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# APPENDIX H: DATA QUALITY CRITERIA FOR EPIDEMIOLOGICAL STUDIES

## H.1 Types of Data Sources

The data quality will be evaluated for the epidemiological studies listed in Table H-1.

**Table H-1. Types of Epidemiological Studies**

| Data Category | Types of Data Sources |
|---|---|
| Epidemiological Studies | Controlled exposure, cohort, case-control, cross-sectional, case-crossover |

## H.2 Data Quality Evaluation Domains

The data sources will be evaluated against the following six data quality evaluation domains: study participation, exposure characterization, outcome assessment, potential confounding/variability control, analysis, and other. These domains, as defined in Table H-2, address elements of TSCA Science Standards 26(h)(1) through 26(h)(5).

**Table H-2. Data Evaluation Domains and Definitions**

| Evaluation Domain | Definition |
|---|---|
| Study Participation | Study design elements characterizing the selection of participants in or out of the study (or analysis sample), which influence whether the exposure-outcome distribution among participants is representative of the exposure-outcome distribution in the overall population of eligible persons. |
| Exposure Characterization | Evaluation of exposure assessment methodology that includes consideration of methodological quality, sensitivity, and validation of the methods used, degree of variation in participants, and an established time order between exposure and outcome. |
| Outcome Assessment | Evaluation of outcome (effect) assessment methodology that includes consideration of diagnostic methods, training of interviewers, data sources including registries, blinding to exposure status or level, and reporting of all results. |
| Potential Confounding / Variability Control | Valid and reliable methods to reduce research-specific bias, including standardization, matching, adjustment in multivariate models, and stratification. This includes control of potential co-exposures when it is known that there is potential for co-exposure to occur and the co-exposure could influence the outcome of interest. |
| Analysis | Appropriate study design chosen for the research question with evaluation of statistical power, reproducibility, and statistical or modelling approaches. |
| Other / Consideration for Biomarker Selection and Measurement | Measures of biomarker (exposure and/or effect) data reliability. This includes but is not limited to evaluations of storage, stability and contamination of samples, validity and limits of detection of methods, method requirements, inclusion of matrix-specific considerations, and relationship of biomarker with external exposure, internal dose, or target dose. |

## H.3 Data Quality Evaluation Metrics

The data quality evaluation domains are evaluated by assessing two to seven unique metrics. Each metric is binned into a confidence level of *High*, *Medium*, *Low*, and/or Unacceptable. Each confidence level is assigned a numerical score (i.e., 1 through 4) that is used in the method of assessing the overall quality of the study.

A summary of the number of metrics and metric name for each data type is provided in Table H-3. Each domain has between 2 and 7 metrics. Metrics may be modified as EPA/OPPT acquires experience with the evaluation tool to support fit-for-purpose TSCA risk evaluations. Any modifications will be documented.

Detailed tables showing confidence level specifications of the metrics are provided in Tables H-6 through H-8 for each data type, including separate tables which summarize the serious flaws which would make the data source unacceptable for use in the hazard assessment.

**Table H-3. Summary of Metrics for the Seven Data Types**

| Evaluation Domain | Number of Metrics Overall | Metrics (Metric Number and Description) |
|---|---|---|
| Study Participation | 3 | • Metric 1: Participant Selection<br>• Metric 2: Attrition<br>• Metric 3: Comparison Group |
| Exposure Characterization | 3 | • Metric 4: Measurement of Exposure<br>• Metric 5: Exposure Levels<br>• Metric 6: Temporality |
| Outcome Assessment | 2 | • Metric 7: Outcome Measurement or Characterization,<br>• Metric 8: Reporting Bias |
| Potential Confounding / Variability Control | 3 | • Metric 9: Covariate Adjustment<br>• Metric 10: Covariate Characterization<br>• Metric 11: Co-exposure Counfounding/Moderation/Mediation |
| Analysis | 4 | • Metric 12: Study Design and Methods<br>• Metric 13: Statistical Power<br>• Metric 14: Reproducibility of Analyses<br>• Metric 15: Statistical Models |
| Other / Consideration for Biomarker Selection and Measurement | 7 | • Metric 16: Use of Biomarker of Exposure<br>• Metric 17: Effect Biomarker<br>• Metric 18: Method Sensitivity<br>• Metric 19: Biomarker Stability<br>• Metric 20: Sample Contamination<br>• Metric 21: Method Requirements<br>• Metric 22: Matrix Adjustment |

## H.4 Scoring Method and Determination of Overall Data Quality Level

A scoring system is used to assign the overall quality of the data source, as discussed in Appendix A. Each data source is assigned an overall qualitative confidence level of *High*, *Medium*, *Low*, or *Unacceptable*. This section provides details about the scoring system that will be applied to epidemiologic studies, including the weighting factors assigned to each metric score of each domain.

### H.4.1 Weighting Factors

The weighting method assumes that each domain carries an equal amount of weight of 1. However, some metrics within a given domain are given greater weights than others in the same domain, if they are regarded as key or critical metrics. Thus, EPA will use a weighting approach to reflect that some metrics are more important than others when assessing the overall quality of the epidemiologic data.

Each key or critical metric is assigned a higher weighting factor. The critical metrics are identified based on professional judgment in conjunction with consideration of the factors that are most frequently included in other study quality/risk of bias tools for epidemiologic literature. In developing metrics for each domain, several basic elements for epidemiologic studies were incorporated to form the structure of the 6 domains (Blumentthal et al. 2001), each of which are considered to be equally important aspects of an epidemiologic study.

The critical metrics within each domain are those that cover the most important aspects of the domain and are those that more directly evaluate the role of confounding and bias. After pilot testing the evaluation tool, EPA recognized that more attention (or weight) should be given to studies that measure exposure and disease accurately and allow for the consideration of potential confounding factors. Therefore, metrics deemed as critical metrics are those that identify the major biases associated with the domain, evaluate the measurement of exposure and disease, and/or address any potential confounding.

EPA/OPPT assigned a weighting factor that is twice the value of the other metrics within the same domain to each critical metric. Remaining metrics are assigned a weighting factor of 0.5 times the weighting factor assigned to the critical metric(s) in the domain. The sum of the weighting factors for each domain equals one. Tables H-4 identifies the critical metrics for epidemiologic studies, respectively, and provides a rationale for why the metrics are considered to be of greater importance than others within the domain. Table H-5 identifies the weighting factors assigned to each metric for epidemiologic studies, respectively.

**Table H-4. Epidemiology Metrics with Greater Importance in the Evaluation and Rationale for Selection**

| Domain | Critical Metrics with Higher Weighting Factors (Metric Number) [a] | Rationale |
|---|---|---|
| Study Participation Study Participation | Participant Selection (Metric 1) | The participants selected for the study must be representative of the target population. Differences between participants and nonparticipants determines the amount of bias present, and differences should be well-described (Galea and Tracy 2007). |
| | Attrition (Metric 2) | Study attrition threatens the internal validity of studies, affects sample size, and compromises the precision of the measured associations (Kristman et al. 2004). |
| Exposure characterization | Measurement of Exposure (Metric 4) | The exposure of interest of should be well-defined and measured in a manner that is accurate, precise, and reliable to ensure the internal and external validity of the study findings (Blumenthal et al. 2001, Nieuwenhuijsen 2015). |
| | Temporality (Metric 6) | Temporality is essential to causal inference. Details must be provided to ensure the exposure sufficiently preceded the outcome and that enough time has passed since the exposure to observed said effect (Fedak et al. 2015). |
| Outcome assessment | Outcome Measurement or Characterization (Metric 7) | The methods used for outcome assessment must be fully described, valid, and sensitive to ensure that the observed effects are true, and to enable valid comparisons across studies (Blumenthal et al. 2001). |
| Potential Confounding/ variable control | Covariate Adjustment (Metric 9) | Control for confounding variables either through study design or analysis is considered important to ensure that any observed effects are attributable to the chemical exposure of interest and not to other factors (Blumenthal et al. 2001). |
| Analysis | Study Design and Methods (Metric 12) | The study design selected and applied analytical techniques for the collected data must be suitable to address the research question at hand (Checkoway et al. 2007). |

[a]For the remaining metrics within the same domain, a weighting factor of 0.5*the key metric weighting factor is assigned

### H.4.2 Calculation of Overall Study Score

A confidence level (1, 2, or 3 for High, Medium, or Low confidence, respectively) is assigned for each relevant metric within each domain. To determine the overall study score, the first step is to multiply the score for each metric (1, 2, or 3 for High, Medium, or Low confidence, respectively) by the appropriate weighting factor to obtain a weighted metric score. The weighted metric scores are then summed and divided by the sum of the weighting factors (for all metrics that are scored) to obtain an overall study score between 1 and 3. The equation for calculating the overall score is shown below:

$$\textit{Overall Score (range of 1 to 3)} = \sum (\textit{Metric Score} \times \textit{Weighting Factor}) / \sum (\textit{Weighting Factors})$$

Tables H-5 and H-6 present a summary of the domain, metrics and weighting approach for epidemiological studies with or without biomarkers, respectively. Table H-7 provides a scoring example for epidemiological studies where sample size is not applicable.

EPA/OPPT plans to use data with an overall quality level of *High, Medium*, or *Low* confidence to quantitatively or qualitatively support the risk evaluations, but does not plan to use data rated as *Unacceptable*. Studies with any single metric scored as 4 will be automatically assigned an overall quality score of *Unacceptable* and further evaluation of the remaining metrics is not necessary. An *Unacceptable* score means that serious flaws are noted in the domain metric that consequently make the data unusable (or invalid).

Any metrics that are *Not rated/not applicable* to the study under evaluation are not considered in the calculation of the study's overall quality score. These metrics are not included in the nominator or denominator of the *overall score* equation. The overall score is calculated using only those metrics that receive a numerical score. In addition, if a publication reports more than one study or endpoint, each study and, as needed, each endpoint will be evaluated separately.

Detailed tables showing quality criteria for the metrics are provided in Tables H-8 and H-9, including a table that summarizes the serious flaws that would make the data unacceptable for use in the human health hazard assessment.

**Table H-5. Summary of Domain, Metrics, and Weighting Approach with Biomarkers**

| Domain | Metric | Range of Metric Scores | Metric weighting Factor | Domain Weight | Range of Weighted Metric Scores |
|---|---|---|---|---|---|
| Study Participation | Participant Selection | 1 to 3 | 0.4 | 1 | 0.4 to 1.2 |
| | Attrition | 1 to 3 | 0.4 | | 0.4 to 1.2 |
| | Comparison Group | 1 to 3 | 0.2 | | 0.2 to 0.6 |
| Exposure Characterization | Measurement of Exposure | 1 to 3 | 0.4 | 1 | 0.4 to 1.2 |
| | Exposure Levels | 1 to 3 | 0.2 | | 0.2 to 0.6 |
| | Temporality | 1 to 3 | 0.4 | | 0.4 to 1.2 |
| Outcome Assessment | Outcome measurement or characterization | 1 to 3 | 0.67 | 1 | 0.67 to 2.01 |
| | Reporting Bias | 1 to 3 | 0.33 | | 0.33 to 0.99 |
| Potential Confounding/ Variable Control | Covariate Adjustment | 1 to 3 | 0.5 | 1 | 0.5 to 1.5 |
| | Covariate Characterization | 1 to 3 | 0.25 | | 0.25 to 0.75 |
| | Co-exposure Confounding/Moderation/ Mediation | 1 to 3 | 0.25 | | 0.25 to 0.75 |
| Analysis | Study Design and Methods | 1 to 3 | 0.4 | 1 | 0.4 to 1.2 |
| | Statistical Power | 1 to 3 | 0.2 | | 0.2 to 0.6 |
| | Reproducibility of Analyses | 1 to 3 | 0.2 | | 0.2 to 0.6 |
| | Statistical Models | 1 to 3 | 0.2 | | 0.2 to 0.6 |
| Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al., 2014) | Use of Biomarker of Exposure | 1 to 3 | 0.143 | 1 | 0.143 to 0.429 |
| | Effect Biomarker | 1 to 3 | 0.143 | | |
| | Method Sensitivity | 1 to 3 | 0.143 | | |
| | Biomarker Stability | 1 to 3 | 0.143 | | |
| | Sample Contamination | 1 to 3 | 0.143 | | |
| | Method Requirements | 1 to 3 | 0.143 | | |
| | Matrix Adjustment | 1 to 3 | 0.143 | | |
| *Equation:* Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factor | | | | *Sum of Weighted Scores = 6 to 18*<br><br>*Sum of Metric Weighting Factors= 6*<br>6/6=1;<br>18/6=3<br><br>Range of overall score = 1 to 3 | |

**Table H-6. Summary of Domain, Metrics, and Weighting Approach for Studies without Biomarkers**

| Domain | Metric | Range of Metric Scores | Metric weighting Factor | Domain Weight | Range of Weighted Metric Scores |
|---|---|---|---|---|---|
| Study Participation | Participant Selection | 1 to 3 | 0.4 | 1 | 0.4 to 1.2 |
| | Attrition | | 0.4 | | 0.4 to 1.2 |
| | Comparison Group | | 0.2 | | 0.2 to 0.6 |
| Exposure Characterization | Measurement of Exposure | | 0.4 | 1 | 0.4 to 1.2 |
| | Exposure Levels | | 0.2 | | 0.2 to 0.6 |
| | Temporality | | 0.4 | | 0.4 to 1.2 |
| Outcome Assessment | Outcome measurement or characterization | | 0.67 | 1 | 0.67 to 2.01 |
| | Reporting Bias | | 0.33 | | 0.33 to 0.99 |
| Potential Confounding/ Variable Control | Covariate Adjustment | | 0.5 | 1 | 0.5 to 1.5 |
| | Covariate Characterization | | 0.25 | | 0.25 to 0.75 |
| | Co-exposure Confounding/Moderation/Mediation | | 0.25 | | 0.25 to 0.75 |
| Analysis | Study Design and Methods | | 0.4 | 1 | 0.4 to 1.2 |
| | Statistical Power | | 0.2 | | 0.2 to 0.6 |
| | Reproducibility of Analyses | | 0.2 | | 0.2 to 0.6 |
| | Statistical Models | | 0.2 | | 0.2 to 0.6 |
| *Equation:*<br>Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factor | | | | *Sum of Weighted Scores = 5 to 15*<br><br>Sum of Metric Weighting Factors= 5<br><br>5/5=1;<br>15/5=3<br><br>Range of overall score = 1 to 3 | |

**Table H-7. Example of Scoring for Epidemiologic Studies where Sample Size is Not Applicable**

| Domain | Metric | Metric Score | Metric Weighting Factor | Weighted Score |
|---|---|---|---|---|
| Study Participation | 1. Participant Selection | 1 | 0.4 | 0.4 |
| | 2. Attrition | 3 | 0.4 | 1.2 |
| | 3. Comparison Group | 2 | 0.2 | 0.4 |
| Exposure Characterization | 4. Measurement of Exposure | 1 | 0.4 | 0.4 |
| | 5. Exposure Levels | 1 | 0.2 | 0.2 |
| | 6. Temporality | 1 | 0.4 | 0.8 |
| Outcome Assessment | 7. Outcome measurement or characterization | 3 | 0.67 | 2.01 |
| | 8. Reporting Bias | 2 | 0.33 | 0.33 |
| Potential Confounding/ Variable Control | 9. Covariate Adjustment | 1 | 0.67 | 0.67 |
| | 10. Covariate Characterization | 1 | 0.33 | 0.33 |
| | 11. Co-exposure Confounding/Moderation/Mediation | NR | NR | NR |
| Analysis | 12. Study Design and Methods | 1 | 0.4 | 1.2 |
| | 13. Statistical Power | 1 | 0.2 | 0.4 |
| | 14. Reproducibility of Analyses | 3 | 0.2 | 0.2 |
| | 15. Statistical Models | 3 | 0.2 | 0.6 |
| | | Sum of scores | 5 | 8.47 |
| | | Overall Study Score | **1.7 = Medium** | |

NR= not rated/not applicable

*Equation:*

Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factor

| High | Medium | Low |
|---|---|---|
| ≥1 and <1.7 | ≥1.7 and <2.3 | ≥2.3 and ≤3 |

## H.5 Data Quality Criteria

**Table H-8. Serious Flaws that Would Make Epidemiological Studies Unacceptable for Use in the Hazard Assessment**

Optimization of the list of serious flaws may occur after pilot calibration exercises.

| Domain | Metric | Description of Serious Flaw(s) in Data Source |
|---|---|---|
| Study Participation | Participant Selection | For all study types: The reported information indicates that selection in or out of the study (or analysis sample) and participation was likely to be significantly biased (i.e., the exposure-outcome distribution of the participants is likely not representative of the exposure-outcome distributions in the overall population of eligible persons.) |
| | Attrition | For cohort studies: The loss of subjects (i.e., incomplete outcome data) was large and unacceptably handled (as described above in the low confidence category) (Source: OHAT).<br>OR<br>Numbers of individuals were not reported at important stages of study (e.g., numbers of eligible participants included in the study or analysis sample, completing follow-up, and analyzed). Reasons were not provided for non-participation at each stage [STROBE Checklist Item 13 (Von Elm et al., 2008)]. |
| | | For case-control and cross-sectional studies: The exclusion of subjects from analyses was large and unacceptably handled (as described above in the low confidence category).<br>OR<br>Reasons were not provided for non-participation at each stage [STROBE Checklist Item 13 (Von Elm et al., 2008)]. |
| | Comparison Group | For cohort studies: Subjects in all exposure groups were not similar, recruited within very different time frames, or had the very different participation/ response rates (NTP, 2015a).<br>OR<br>Information was not reported to determine if participants in all exposure groups were similar [STROBE Checklist 6 (Von Elm et al., 2008)] |
| | | For case-control studies: Controls were drawn from a very dissimilar population than cases or recruited within very different time frames (NTP, 2015a).<br>OR<br>Rationale and/or methods for case and control selection, matching criteria including number of controls per case (if relevant) were not reported [STROBE Checklist 6 (Von Elm et al., 2008)]. |
| | | For cross-sectional studies: Subjects in all exposure groups were not similar, recruited within very different time frames, or had the very different participation/response rates (NTP, 2015a). |

| Domain | Metric | Description of Serious Flaw(s) in Data Source |
|---|---|---|
| | | OR<br>Sources and methods of selection of participants in all exposure groups were not reported [STROBE Checklist 6 (Von Elm et al., 2008)]. |
| Exposure Characterization | Measurement of Exposure | For all study types: Exposure variables were not well defined, and sources of data and detailed methods of exposure assessment were not reported [STROBE Checklist 7 and 8 (Von Elm et al., 2008)].<br>OR<br>Exposure was assessed using methods known or suspected to have poor validity (Source: OHAT).<br>OR<br>There is evidence of substantial exposure misclassification that would significantly alter results. |
| | Exposure Levels | For all study types: The levels of exposure are not sufficient or adequate (as defined above) to detect an effect of exposure (Cooper et al., 2016).<br>OR<br>No description is provided on the levels or range of exposure. |
| | Temporality | For all study types: Study lacks an established time order, such that exposure is not likely to have occurred prior to outcome (Lakind et al., 2014).<br>OR<br>Exposures clearly fell outside of relevant exposure window for the outcome of interest.<br>OR<br>For each variable of interest (outcome and predictor), sources of data and details of methods of assessment were not reported (e.g., periods of exposure, dates of outcome ascertainment, etc.) [STROBE Checklist 8 (Von Elm et al., 2008)]. |
| Outcome Assessment | Outcome measurement or characterization | For all study types: Numbers of outcome events or summary measures, or diagnostic criteria were not defined or reported [STROBE Checklist 15 (Von Elm et al., 2008)]. |
| Potential Confounding/Variable Control | Covariate adjustment | For cohort and cross-sectional studies: The distribution of primary covariates (excluding co-exposures) and known confounders differed significantly between the exposure groups<br>OR<br>Confounding was demonstrated and was not appropriately adjusted for in the final analyses (NTP, 2015a). |
| | | For case-control studies: The distribution of primary covariates (excluding co-exposures) and known confounders differed significantly between cases and controls.<br>OR<br>Confounding was demonstrated and was not appropriately adjusted for in the final analyses (NTP, 2015a). |

| Domain | Metric | Description of Serious Flaw(s) in Data Source |
|---|---|---|
| | Covariate characterization | For all study types: Primary covariates (excluding co-exposures) and confounders were not assessed. |
| | Co-exposure Confounding/ Moderation/ Mediation | For cohort and cross-sectional studies: There is direct evidence that there was an unbalanced provision of additional co-exposures across the primary study groups, which were not appropriately adjusted for. |
| | | For case-control studies: There is direct evidence that there was an unbalanced provision of additional co-exposures across cases and controls, which were not appropriately adjusted for, and significant indication a biased exposure-outcome association. |
| Analysis | Study design and methods | For all study types: The study design chosen was not appropriate for the research question.<br>OR<br>Inappropriate statistical analyses were applied to assess the research questions. |
| | Statistical power (sensitivity) | For cohort and cross-sectional studies: The number of participants are inadequate to detect an effect in the exposed population and/or subgroups of the total population. |
| | | For case-control studies: The number of cases and controls are inadequate to detect an effect in the exposed population and/or subgroups of the total population. |
| Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al., 2014) | Use of Biomarker of Exposure | Biomarker in a specified matrix is a poor surrogate (low accuracy and precision) for exposure/dose. |
| | Effect biomarker | Biomarker has undetermined consequences (e.g., biomarker is not specific to a health outcome). |
| | Method sensitivity | Frequency of detection too low to address the research hypothesis.<br>OR<br>LOD/LOQ (value or %) are not stated. |
| | Biomarker stability | Samples with either unknown storage history and/or no stability data for target analytes and high likelihood of instability for the biomarker under consideration. |
| | Sample contamination | There are known contamination issues and no documentation that the issues were addressed. |
| | Method requirements | Instrumentation that only allows for possible quantification of the biomarker, but the method has known interferants (e.g., GC–FID, spectroscopy). |
| | Matrix adjustment | If applicable for the biomarker under consideration, no established method for matrix adjustment was conducted. |

## Table H-9. Evaluation Criteria for Epidemiological Studies

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Domain 1. Study Participation** | | |
| **Metric 1. Participant selection (selection, performance biases)** | | |
| **Instructions: To meet criteria for confidence ratings for metrics where 'AND' is included, studies must address both of the conditions where "AND" is stipulated. To meet criteria for confidence ratings for metrics where 'OR' is included studies must address at least one of the conditions stipulated.** | | |
| High (score = 1) | • ***For all study types:*** All key elements of the study design are reported (i.e., setting, participation rate described at all steps of the study, inclusion and exclusion criteria, and methods of participant selection or case ascertainment)<br>**AND**<br>The reported information indicates that selection in or out of the study (or analysis sample) and participation was not likely to be biased (i.e., the exposure-outcome distribution of the participants is likely representative of the exposure-outcome distributions in the overall population of eligible persons.) | |
| Medium (score = 2) | • ***For all study types:*** Some key elements of the study design were not present but available information indicates a low risk of selection bias (i.e., the exposure-outcome distribution of the participants is likely representative of the exposure-outcome distributions in the overall population of eligible persons.) | |
| Low (score = 3) | • ***For all study types:*** Key elements of the study design and information on the comparison group (i.e., setting, participation rate described at most steps of the study, inclusion and exclusion criteria, and methods of participant selection or case ascertainment) are not reported [STROBE checklist 4, 5 and 6 (Von Elm et al., 2008)]. | |
| Unacceptable (score = 4) | • ***For all study types:*** The reported information indicates that selection in or out of the study (or analysis sample) and participation was likely to be significantly biased (i.e., the exposure-outcome distribution of the participants are likely not representative of the exposure-outcome distributions in the overall population of eligible persons.) | |
| Not rated/applicable | • Do not select for this metric. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 2. Attrition (missing data/attrition/exclusion, reporting biases)** | | |
| High (score = 1) | • ***For cohort studies:*** There was minimal subject attrition during the study (or exclusion from the analysis sample) and outcome data were largely complete.<br>**OR**<br>• Any loss of subjects (i.e., incomplete outcome data) was adequately* addressed (as described above) and reasons were documented when human subjects were removed from a study (NTP, 2015a).<br>**OR**<br>• Missing data have been imputed using appropriate methods (e.g., random regression imputation), and characteristics of subjects lost to follow up or with unavailable records are described in identical way and are not significantly different from those of the study participants (NTP, 2015a).<br>• ***For case-control studies and cross-sectional studies:*** There was minimal subject | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | withdrawal from the study (or exclusion from the analysis sample) and outcome data were largely complete.<br>**OR**<br>• Any exclusion of subjects from analyses was adequately* addressed (as described above), and reasons were documented when subjects were removed from the study or excluded from analyses (NTP, 2015a).<br><br>***NOTE for all study types:*** Adequate handling of subject attrition includes: very little missing outcome data; reasons for missing subjects unlikely to be related to outcome (for survival data, censoring was unlikely to introduce bias); missing outcome data balanced in numbers across study groups, with similar reasons for missing data across groups. | |
| Medium (score = 2) | • ***For cohort studies:*** There was moderate subject attrition during the study (or exclusion from the analysis sample).<br>**AND**<br>• Any loss or exclusion of subjects was adequately addressed (as described in the acceptable handling of subject attrition in the high confidence category) and reasons were documented when human subjects were removed from a study.<br>• ***For case-control studies and cross-sectional studies:*** There was moderate subject withdrawal from the study (or exclusion from the analysis sample), but outcome data were largely complete.<br>**AND**<br>• Any exclusion of subjects from analyses was adequately addressed (as described above), and reasons were documented when subjects were removed from the study or excluded from analyses (NTP, 2015a). | |
| Low (score = 3) | • ***For cohort studies:*** There was large subject attrition during the study (or exclusion from the analysis sample).<br>**OR**<br>• Unacceptable handling of subject attrition: reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across study groups; or potentially inappropriate application of imputation (Source: OHAT).<br>• ***For case-control and cross-sectional studies:*** There was large subject withdrawal from the study (or exclusion from the analysis sample).<br>**OR**<br>• Unacceptable handling of subject attrition: reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across study groups; or potentially inappropriate application of imputation. | |
| Unacceptable (score = 4) | • ***For cohort studies:*** The loss of subjects (i.e., incomplete outcome data) was large and unacceptably handled (as described above in the low confidence category) (Source: OHAT).<br>**OR**<br>• Numbers of individuals were not reported at important stages of study (e.g., numbers of eligible participants included in the study or analysis sample, completing follow-up, and analyzed). Reasons were not provided for non-participation at each stage [STROBE Checklist Item 13 (Von Elm et al., 2008)].<br>• ***For case-control and cross-sectional studies:*** The exclusion of subjects from | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | analyses was large and unacceptably handled (as described above in the low confidence category).<br>**OR**<br>• Reasons were not provided for non-participation at each stage [STROBE Checklist Item 13 (Von Elm et al., 2008)]. | |
| Not rated/applicable | • Do not select for this metric. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 3. Comparison Group (selection, performance biases)** | | |
| High (score = 1) | • ***For cohort and cross-sectional studies:*** Key elements of the study design are reported (i.e., setting, inclusion and exclusion criteria, and methods of participant selection), and indicate that subjects (in all exposure groups) were similar (e.g., recruited from the same eligible population with the same method of ascertainment and within the same time frame using the same inclusion and exclusion criteria, and were of similar age and health status) (NTP, 2015a).<br>• ***For case-control studies:*** Key elements of the study design are reported (i.e., setting, inclusion and exclusion criteria, and methods of case ascertainment or control selection), and indicate that that cases and controls were similar (e.g., recruited from the same eligible population with appropriate matching criteria, such as age, gender, and ethnicity, the number of controls described, and eligibility criteria other than outcome of interest as appropriate), recruited within the same time frame, and controls are described as having no history of the outcome (NTP, 2015a).<br>**OR**<br>• ***For all study types:*** Baseline characteristics of groups differed ***but*** these differences were considered as potential confounding or stratification variables, and were thereby controlled by statistical analysis (Source: OHAT). | |
| Medium (score = 2) | • ***For cohort studies:*** There is indirect evidence (e.g., stated by the authors without providing a description of methods) that subjects (in all exposure groups) are similar (as described above for the high confidence rating).<br>**AND**<br>• The baseline characteristics for subjects (in all exposure groups) reported in the study are similar (NTP, 2015a).<br>• ***For case-control studies***: There is indirect evidence (i.e., stated by the authors without providing a description of methods) that that cases and controls are similar (as described above for the high confidence rating).<br>**AND**<br>• The characteristics of case and controls reported in the study are similar (NTP, 2015a).<br>• ***For cross-sectional studies:*** There is indirect evidence (i.e., stated by the authors without providing a description of methods) that subjects (in all exposure groups) are similar (as described above for the high confidence rating) (Source: OHAT).<br>**AND**<br>• The characteristics of participants (in all exposure groups) reported in the study are similar. | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | | |
| Low (score = 3) | • ***For cohort studies***: There is indirect evidence (i.e., stated by the authors without providing a description of methods) that subjects (in all exposure groups) were similar (as described above for the high confidence rating).<br>**AND**<br>• The baseline characteristics for subjects (in all exposure groups) are not reported (NTP, 2015a).<br>• ***For case-control studies***: There is indirect evidence (i.e., stated by the authors without providing a description of methods) that that cases and controls were similar (as described above for the high confidence rating).<br>**AND**<br>• The characteristics of case and controls are not reported (Source: (NTP, 2015a).<br>• ***For cross-sectional studies:*** There is indirect evidence (i.e., stated by the authors without providing a description of method) that subjects (in all exposure groups) were similar (as described above for the high confidence rating).<br>**AND**<br>• The characteristics of participants (in all exposure groups) are not reported (Source: OHAT). | |
| Unacceptable (score = 4) | • ***For cohort studies:*** Subjects in all exposure groups were not similar, recruited within very different time frames, or had the very different participation/ response rates (NTP, 2015a).<br>**OR**<br>• Information was not reported to determine if participants in all exposure groups were similar [STROBE Checklist 6 (Von Elm et al., 2008)]<br>• ***For case-control studies:*** Controls were drawn from a very dissimilar population than cases or recruited within very different time frames (NTP, 2015a).<br>**OR**<br>• Rationale and/or methods for case and control selection, matching criteria including number of controls per case (if relevant) were not reported [STROBE Checklist 6 (Von Elm et al., 2008)].<br>• ***For cross-sectional studies:*** Subjects in all exposure groups were not similar, recruited within very different time frames, or had the very different participation/response rates (NTP, 2015a).<br>**OR**<br>• Sources and methods of selection of participants in all exposure groups were not reported [STROBE Checklist 6 (Von Elm et al., 2008)]. | |
| Not rated/applicable | • Do not select for this metric. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 2. Exposure Characterization** | | |
| **Metric 4. Measurement of Exposure (Detection/measurement/information, performance biases)** | | |
| High (score = 1) | • ***For all study types:*** Exposure was consistently assessed (i.e., under the same method and time-frame) using well-established methods (e.g., personal and/or industrial hygiene data used to determine levels of exposure, a frequently used biomarker of exposure) that directly measure exposure (e.g., measurement of the chemical in the environment (air, drinking water, consumer product, etc.) or | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | measurement of the chemical concentration in a biological matrix such as blood, plasma, urine, etc.) (NTP, 2015a). | |
| Medium (score = 2) | • ***For all study types:*** Exposure was directly measured and assessed using a method that is not well-established (e.g., newly developed biomarker of exposure), ***but*** is validated against a well-established method and demonstrated a high agreement between the two methods. | |
| Low (score = 3) | • ***For all study types:*** A less-established method (e.g., newly developed biomarker of exposure) was used and no method validation was conducted against well-established methods, but there was little to no evidence that the method had poor validity and little to no evidence of significant exposure misclassification (e.g., differential recall of self-reported exposure) (Source: OHAT). | |
| Unacceptable (score = 4) | • ***For all study types:*** Exposure variables were not well defined, and sources of data and detailed methods of exposure assessment were not reported [STROBE Checklist 7 and 8 (Von Elm et al., 2008)].<br>**OR**<br>• Exposure was assessed using methods known or suspected to have poor validity (Source: OHAT).<br>**OR**<br>• There is evidence of substantial exposure misclassification that would significantly alter results. | |
| Not rated/applicable | • Do not select for this metric. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 5. Exposure levels (Detection/measurement/information biases)** | | |
| High (score = 1) | • ***For all study types:*** The levels of exposure are sufficient* or adequate to detect an effect of exposure {Cooper, 2016, 3121908}.<br><br>* Sufficient or adequate for cohort and cross-sectional studies includes the reporting of at least 2 levels of exposure (referent group + 1 or more exposure groups) (Cooper) that capture exposure spatial and temporal variability within the study population (Source: IRIS). | |
| Medium (score = 2) | • Do not select for this metric. | |
| Low (score = 3) | • Do not select for this metric. | |
| Unacceptable (score = 4) | • ***For all study types:*** The levels of exposure are not sufficient or adequate (as defined above) to detect an effect of exposure (Cooper et al., 2016).<br>**OR**<br>• No description is provided on the levels or range of exposure. | |
| Not rated/applicable | • Do not select for this metric. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | | |
| **Metric 6. Temporality (Detection/measurement/information biases)** | | |
| High (score = 1) | • ***For all study types:*** The study presents an established time order between exposure and outcome.<br>**AND**<br>• The interval between the exposure (or reconstructed exposure) and the outcome has an appropriate consideration of relevant exposure windows (Lakind et al., 2014). | |
| Medium (score = 2) | • ***For all study types:*** Temporality is established, but it is unclear whether exposures fall within relevant exposure windows for the outcome of interest (Lakind et al., 2014). | |
| Low (score = 3) | • ***For all study types:*** The temporality of exposure and outcome is uncertain. | |
| Unacceptable (score = 4) | • ***For all study types:*** Study lacks an established time order, such that exposure is not likely to have occurred prior to outcome (Lakind et al., 2014).<br>**OR**<br>• Exposures clearly fell outside of relevant exposure window for the outcome of interest.<br>**OR**<br>• For each variable of interest (outcome and predictor), sources of data and details of methods of assessment were not reported (e.g. periods of exposure, dates of outcome ascertainment, etc.) [STROBE Checklist 8 (Von Elm et al., 2008)]. | |
| Not rated/applicable | • Do not select for this metric. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 3. Outcome Assessment** | | |
| **Metric 7. Outcome measurement or characterization (detection/measurement/information, performance, reporting biases)** | | |
| High (score = 1) | • ***For cohort studies:*** The outcome was assessed using well-established methods (e.g., the "gold standard").<br>**AND**<br>• Subjects had been followed for the same length of time in all study groups.<br>• ***For case-control studies:*** The outcome was assessed in cases (i.e., case definition) and controls using well-established methods (the gold standard).<br>**AND**<br>• Subjects had been followed for the same length of time in all study groups (NTP, 2015a).<br>***For cross-sectional studies***: There is direct evidence that the outcome was assessed using well-established methods (the gold standard) (NTP, 2015a).<br><br>Note: Acceptable assessment methods will depend on the outcome, but examples of such methods may include: objectively measured with diagnostic methods, measured by trained interviewers, obtained from registries (NTP, 2015a; Shamliyan et al., 2010). | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| Medium (score = 2) | • ***For all study types:*** A less-established method was used and no method validation was conducted against well-established methods, but there was little to no evidence that that the method had poor validity and little to no evidence of outcome misclassification (e.g., differential reporting of outcome by exposure status). | |
| Low (score = 3) | • ***For cohort studies:*** The outcome assessment method is an insensitive instrument or measure.<br>**OR**<br>• The length of follow up differed by study group (NTP, 2015a).<br>• ***For case-control studies:*** The outcome was assessed in cases (i.e., case definition) using an insensitive instrument or measure (NTP, 2015a).<br>• ***For cross-sectional studies:*** The outcome assessment method is an insensitive instrument or measure (NTP, 2015a). | |
| Unacceptable (score = 4) | • ***For all study types:*** Numbers of outcome events or summary measures, or diagnostic criteria were not defined or reported [STROBE Checklist 15 (Von Elm et al., 2008)]. | |
| Not rated/applicable | • Do not select for this metric. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 8. Reporting Bias** | | |
| High (score = 1) | • ***For all study types:*** All of the study's measured outcomes (primary and secondary) outlined in the protocol, methods, abstract, and/or introduction (that are relevant for the evaluation) are reported. This would include outcomes reported with sufficient detail to be included in meta-analysis or fully tabulated during data extraction and analyses had been planned in advance (NTP, 2015a). | |
| Medium (score = 2) | • ***For all study types:*** All of the study's measured outcomes (primary and secondary) outlined in the protocol, methods, abstract, and/or introduction (that are relevant for the evaluation) are reported, but not in a way that would allow for detailed extraction (e.g., results were discussed in the text but accompanying data were not shown). | |
| Low (score = 3) | • ***For all study types:*** All of the study's measured outcomes (primary and secondary) outlined in the protocol, methods, abstract, and/or introduction (that are relevant for the evaluation) have not been reported. In addition to not reporting outcomes, this would include reporting outcomes based on composite score without individual outcome components or outcomes reported using measurements, analysis methods or subsets of the data (e.g., subscales) that were not pre-specified or reporting outcomes not pre-specified, or that unplanned analyses were included that would appreciably bias results (NTP, 2015a). | |
| Unacceptable (score = 4) | • Do not select for this metric. | |
| Not rated/applicable | • Do not select for this metric. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | | |
| **Domain 4. Potential Confounding/Variable Control** | | |
| **Metric 9. Covariate Adjustment (confounding)** | | |
| High (score = 1) | • ***For all study types:*** Appropriate adjustments or explicit considerations were made for primary covariates (excluding co-exposures) and confounders in the final analyses through the use of statistical models to reduce research-specific bias, including standardization, matching, adjustment in multivariate models, stratification, or other methods that were appropriately justified (NTP, 2015a). | |
| Medium (score = 2) | • ***For all study types:*** There is indirect evidence that appropriate adjustments were made (i.e., considerations were made for primary covariates (excluding co-exposures) and confounders adjustments) without providing a description of methods.<br>**OR**<br>• The distribution of primary covariates (excluding co-exposures) and known confounders did not differ significantly between exposure groups or between cases and controls.<br>**OR**<br>• The majority of the primary covariates (excluding co-exposures) and any known confounders were appropriately adjusted and any not adjusted for are considered not to appreciably bias the results. | |
| Low (score = 3) | • ***For all study types:*** There is indirect evidence (i.e., no description is provided in the study) that considerations were not made for primary covariates (excluding co-exposures) and confounders adjustments in the final analyses (NTP, 2015a).<br>**AND**<br>• The distribution of primary covariates (excluding co-exposures) and known confounders was not reported between the exposure groups or between cases and controls (NTP, 2015a). | |
| Unacceptable (score = 4) | • ***For cohort and cross-sectional studies:*** The distribution of primary covariates (excluding co-exposures) and known confounders differed significantly between the exposure groups<br>**OR**<br>• Confounding was demonstrated and was not appropriately adjusted for in the final analyses (NTP, 2015a).<br>• ***For case-control studies:*** The distribution of primary covariates (excluding co-exposures) and known confounders differed significantly between cases and controls.<br>**OR**<br>• Confounding was demonstrated and was not appropriately adjusted for in the final analyses (NTP, 2015a). | |
| Not rated/applicable | • Do not select for this metric. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Metric 10. Covariate Characterization (measurement/information, confounding biases)** | | |
| High (score = 1) | • ***For all study types:*** Primary covariates (excluding co-exposures) and confounders were assessed using valid and reliable methodology (e.g., validated questionnaires, biomarker). | |
| Medium (score = 2) | • ***For all study types:*** A less-established method was used and no method validation was conducted against well-established methods, but there was little to no evidence that that the method had poor validity and little to no evidence of confounding. | |
| Low (score = 3) | • ***For all study types:*** The primary covariate (excluding co-exposures) and confounder assessment method is an insensitive instrument or measure or a method of unknown validity. | |
| Unacceptable (score = 4) | • ***For all study types:*** Primary covariates (excluding co-exposures) and confounders were not assessed. | |
| Not rated/applicable | • Do not select for this metric. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 11. Co-exposure Confounding/Moderation/Mediation (measurement/information, confounding biases)** | | |
| High (score = 1) | • ***For all study types:*** Any co-exposures to pollutants that are not the target exposure that would likely bias the results were not present.<br>**OR**<br>• Co-exposures to pollutants were appropriately measured and adjusted for. | |
| Medium (score = 2) | • Do not select for this metric. | |
| Low (score = 3) | • Do not select for this metric. | |
| Unacceptable (score = 4) | • ***For cohort and cross-sectional studies:*** There is direct evidence that there was an unbalanced provision of additional co-exposures across the primary study groups, which were not appropriately adjusted for.<br>• ***For case-control studies:*** There is direct evidence that there was an unbalanced provision of additional co-exposures across cases and controls, which were not appropriately adjusted for, and significant indication a biased exposure-outcome association. | |
| Not rated/applicable | • Enter 'NA' and do not score this metric. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 5. Analysis** | | |
| **Metric 12. Study Design and Methods (reporting bias)** | | |
| High (score = 1) | • ***For all study types:*** The study design chosen was appropriate for the research question (e.g. assess the association between exposure levels and common chronic diseases over time with cohort studies, assess the association between exposure and rare diseases with case-control studies, and assess the association between exposure levels and acute disease with a cross-sectional study design). | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | **AND**<br>• The study uses an appropriate statistical method to address the research question(s) (e.g., repeated measures analysis for longitudinal studies, logistic regression analysis for case-control studies). | |
| Medium (score = 2) | • Do not select for this metric. | |
| Low (score = 3) | • Do not select for this metric. | |
| Unacceptable (score = 4) | ***For all study types:*** The study design chosen was not appropriate for the research question.<br>**OR**<br>• Inappropriate statistical analyses were applied to assess the research questions. | |
| Not rated/applicable | • Do not select for this metric. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 13. Statistical power (sensitivity, reporting bias)** | | |
| High (score = 1) | • ***For cohort and cross-sectional studies:*** The number of participants are adequate to detect an effect in the exposed population and/or subgroups of the total population.<br>**OR**<br>• The paper reported statistical power high enough (≥ 80%) to detect an effect in the exposure population and/or subgroups of the total population.<br>• ***For case-control studies:*** The number of cases and controls are adequate to detect an effect in the exposed population and/or subgroups of the total population.<br>**OR**<br>• The paper reported statistical power was high (≥ 80%) to detect an effect in the exposure population and/or subgroups of the total population. | |
| Medium (score = 2) | • Do not select for this metric. | |
| Low (score = 3) | • Do not select for this metric. | |
| Unacceptable (score = 4) | • ***For cohort and cross-sectional studies:*** The number of participants are inadequate to detect an effect in the exposed population and/or subgroups of the total population.<br>• ***For case-control studies:*** The number of cases and controls are inadequate to detect an effect in the exposed population and/or subgroups of the total population. | |
| Not rated/applicable | • Do not select for this metric. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| **Metric 14. Reproducibility of analyses [adapted from Blettner et al. (2001)]** | | |
| High (score = 1) | • ***For all study types:*** The description of the analysis is sufficient to understand precisely what has been done and to be reproducible. | |
| Medium (score = 2) | • Do not select for this metric. | |
| Low (score = 3) | • ***For all study types:*** The description of the analysis is insufficient to understand what has been done and to be reproducible OR a description of analyses are not present (e.g., statistical tests and estimation procedures were not described, variables used in the analysis were not listed, transformations of continuous variables (such as logarithm) were not explained, rules for categorization of continuous variables were not presented, deleting of outliers were not elucidated and how missing values are dealt with was not mentioned). | |
| Unacceptable (score = 4) | • Do not select for this metric. | |
| Not rated/applicable | • Do not select for this metric. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 15. Statistical Models (confounding bias)** | | |
| High (score = 1) | • ***For all study types:*** The statistical model building process is transparent (it is stated how/why variables were included or excluded from the multivariate model) AND model assumptions were met. | |
| Medium (score = 2) | • Do not select for this metric. | |
| Low (score = 3) | • ***For all study types:*** The statistical model building process is not transparent OR it is not stated how/why variables were included or excluded from the multivariate model OR model assumptions were not met OR a description of analyses are not present OR no sensitivity analyses are described OR model assumptions were not discussed [STROBE Checklist 12e (Von Elm et al., 2008)]. | |
| Unacceptable (score = 4) | • Do not select for this metric. | |
| Not rated/applicable | • Enter 'NA' if the study did not use a statistical model. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Domain 6. Other (if applicable) Considerations for Biomarker Selection and Measurement Lakind et al. (2014)** | | |
| **Metric 16. Use of Biomarker of Exposure (detection/measurement/information biases)** | | |
| High (score = 1) | • Biomarker in a specified matrix has accurate and precise quantitative relationship with external exposure, internal dose, or target dose.<br>**AND**<br>• Biomarker is derived from exposure to one parent chemical. | |
| Medium (score = 2) | • Biomarker in a specified matrix has accurate and precise quantitative relationship with external exposure, internal dose, or target dose.<br>**AND**<br>• Biomarker is derived from multiple parent chemicals. | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| Low (score = 3) | • Evidence exists for a relationship between biomarker in a specified matrix and external exposure, internal dose or target dose, but there has been no assessment of accuracy and precision or none was reported. | |
| Unacceptable (score = 4) | • Biomarker in a specified matrix is a poor surrogate (low accuracy and precision) for exposure/dose. | |
| Not rated/applicable | • Enter 'NA' and do not score the metric if no biomarker of exposure was measured. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 17. Effect biomarker (detection/measurement/information biases)** | | |
| High (score = 1) | • Bioindicator of a key event in an AOP. | |
| Medium (score = 2) | • Biomarkers of effect shown to have a relationship to health outcomes using well validated methods, but the mechanism of action is not understood. | |
| Low (score = 3) | • Biomarkers of effect shown to have a relationship to health outcomes, but the method is not well validated and mechanism of action is not understood. | |
| Unacceptable (score = 4) | • Biomarker has undetermined consequences (e.g., biomarker is not specific to a health outcome). | |
| Not rated/applicable | • Enter 'NA' and do not score the metric if no biomarker of effect was measured. | |
| Reviewer's comments | | |
| **Metric 18. Method sensitivity (detection/measurement/information biases)** | | |
| High (score = 1) | • Limits of detection are low enough to detect chemicals in a sufficient percentage of the samples to address the research question. | |
| Medium (score = 2) | • Do not select for this metric. | |
| Low (score = 3) | • Do not select for this metric. | |
| Unacceptable (score = 4) | • Frequency of detection too low to address the research hypothesis.<br>**OR**<br>• LOD/LOQ (value or %) are not stated. | |
| Not rated/applicable | • Enter 'NA' and do not score the metric. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 19. Biomarker stability (detection/measurement/information biases)** | | |
| High (score = 1) | • Samples with a known history and documented stability data or those using real-time measurements. | |
| Medium (score = 2) | • Do not select for this metric. | |
| Low (score = 3) | • Samples have known losses during storage, but the difference between low and high exposures can be qualitatively assessed. | |
| Unacceptable (score = 4) | • Samples with either unknown storage history and/or no stability data for target analytes and high likelihood of instability for the biomarker under consideration.<br>• | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| Not rated/applicable | • Enter 'NA' and do not score the metric if no biomarkers were assessed. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 20. Sample contamination (detection/measurement/information biases)** | | |
| High (score = 1) | • Samples are contamination-free from the time of collection to the time of measurement (e.g., by use of certified analyte free collection supplies and reference materials, and appropriate use of blanks both in the field and lab).<br>**AND**<br>• Documentation of the steps taken to provide the necessary assurance that the study data are reliable is included. | |
| Medium (score = 2) | • Samples are stated to be contamination-free from the time of collection to the time of measurement.<br>**AND**<br>• There is incomplete documentation of the steps taken to provide the necessary assurance that the study data are reliable. | |
| Low (score = 3) | • Samples are known to have contamination issues, but steps have been taken to address and correct contamination issues.<br>**OR**<br>• Samples are stated to be contamination-free from the time of collection to the time of measurement, but there is no use or documentation of the steps taken to provide the necessary assurance that the study data are reliable. | |
| Unacceptable (4) | • There are known contamination issues and no documentation that the issues were addressed. | |
| Not rated/applicable | • Enter 'NA' and do not score the metric if no samples were collected. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 21. Method requirements (detection/measurement/information biases)** | | |
| High (score = 1) | • Instrumentation that provides unambiguous identification and quantitation of the biomarker at the required sensitivity (e.g., GC–HRMS, GC–MS/MS, LC–MS/MS). | |
| Medium (score = 2) | • Do not select for this metric. | |
| Low (score = 3) | • Instrumentation that allows for identification of the biomarker with a high degree of confidence and the required sensitivity (e.g., GC–MS, GC–ECD). | |
| Unacceptable (score = 4) | • Instrumentation that only allows for possible quantification of the biomarker, but the method has known interferants (e.g., GC–FID, spectroscopy). | |
| Not rated/applicable | • Enter 'NA' and do not score the metric if biomarkers were not measured. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |
| **Metric 22. Matrix adjustment (detection/measurement/information biases)** | | |
| High (score = 1) | • If applicable for the biomarker under consideration, study provides results, either in the main publication or as a supplement, for adjusted and unadjusted | |

| Confidence Level (Score) | Description | Selected Score |
|---|---|---|
| | matrix concentrations (e.g., creatinine-adjusted or SG-adjusted and non-adjusted urine concentrations) and reasons are given for adjustment approach. | |
| Medium (score = 2) | • Do not select for this metric. | |
| Low (score = 3) | • If applicable for the biomarker under consideration, study only provides results using one method (matrix-adjusted or not). | |
| Unacceptable (score = 4) | • If applicable for the biomarker under consideration, no established method for matrix adjustment was conducted. | |
| Not rated/applicable | • Enter 'NA' and do not score the metric if not applicable for the biomarker or no biomarker was assessed. | |
| Reviewer's comments | *[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]* | |

## H.6 References


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