This is a selection of responses the U.S. Food and Drug Administration provided the International Consortium of Investigative Journalists and its partners in November 2018.

ICIJ Q3: The 21st Century Cures Act includes provisions that require FDA regulators to use the “least burdensome” approach to demonstrating safety and effectiveness to approve new products and to train its staff in this concept. What was the industry’s role in influencing this language? Should the public be concerned by a law that ties the FDA’s hands by legally binding regulators to the “least burdensome” approach to regulation?

FDA RESPONSE TO Q3: The “least burdensome” approach has long been misunderstood. It is a balanced method that is intended to allow the FDA to focus its resources on issues of highest public health concern. Timely patient access to high-quality, safe and effective medical devices requires that the FDA reduce or remove outdated, unnecessary burdens in our regulatory approaches that can otherwise add to development costs or forestall beneficial innovation without also enhancing device safety and effectiveness. Gathering and reviewing unneeded information is not beneficial to giving patients that timely access and hinders the FDA’s ability to optimally protect patients by misapplying our limited resources. In the case of mobile medical apps for general wellness, for instance, many consumers count on low risk apps to help plan their diet and exercise. Patients don’t benefit from FDA premarket review of such apps, which Congress recognized when, in the 21st Century Cures Act, they removed such apps from FDA oversight. Patients are better served when the FDA’s resources are spent on higher-risk, and novel products.

In our 2017 draft guidance, the FDA defined least burdensome to be “the minimum amount of information necessary to adequately address a regulatory question or issue through the most efficient manner at the right time (e.g., need to know versus nice to know). Our least burdensome principles do not change the applicable regulatory standards, such as the device approval or clearance standards, nor the applicable requirements, including premarket submission content requirements and the requirement for valid scientific evidence. In fact, the least burdensome approach enables the FDA to establish a modern framework for making sure the agency continues to strengthen and secure its high standard for medical product review.

In the past few years, we’ve seen notable results of our application of the least burdensome principles on medical device review, including improved quality of applications.
The genesis of the “least burdensome” approach dates back to 1997, when Congress directed the FDA to take a least burdensome approach to premarket evaluation. Congress enacted additional least burdensome provisions in 2012 and in the 2016 21st Century Cures Act. During the legislative process for the 21st Century Cures Act, we worked with congressional members, their staff and industry to ensure that the enacted provisions would best serve the interests of patients. Congress also proactively solicited feedback from the stakeholder community on the provisions in the 21st Century Cures Act and, there was an opportunity for anyone impacted by the proposed legislation to provide their perspectives.\(^1\)

Given the benefits of this approach, the FDA made it agency policy in a 2002 guidance to apply the least burdensome approach to the postmarket evaluation of devices, as well. In the 2017 draft guidance, we have proposed to apply it across the total product lifecycle – beyond what Congress has required – including all device-related regulatory decisions.

As we work to encourage innovation and advancement in the market, patient safety is and will remain a cornerstone of our regulatory commitment. The application of the least burdensome approach is important for meeting this commitment.

**ICIJ Q6: Do adverse event reports filed with the FDA reflect an accurate view of problems with medical devices? If so, why, and if not, why not?**

**FDA RESPONSE TO Q6:** Medical Device Reports or MDRs submitted to the FDA are only one source we use to monitor marketed medical devices. These reports may contribute to the detection of potential device-related safety issues as well as to the benefit-risk assessments of these devices. While such reports are a valuable source of information, this type of reporting system has limitations, including the potential submission of incomplete, inaccurate, untimely, unverified, or biased data. Confirming whether a device actually caused a specific event can be difficult based solely on information provided in a given report. Complaints or adverse event reports do not necessarily directly indicate a faulty or defective medical device, and adverse event reports alone cannot be used to establish or compare rates of event occurrence. Additionally, we may receive multiple reports related to the same event making it difficult to determine actual numbers of events.

FDA has long stated that the current system of post-market surveillance has limitations in promptly and consistently identifying safety risks, a challenge that is not unique to the U.S. The FDA discussed these limitations and proposed the steps necessary to address them, including the creation of a national system, in a 2012 document titled, Strengthening our National System for Medical Device Postmarket Surveillance and, over the past six years, the FDA, in collaboration with other stakeholders, has led the effort to establish the National Evaluation System for health Technology (NEST). In our 2012 document, we proposed that the national system – NEST – have active surveillance capabilities to complement our adverse event reporting (passive surveillance) system. Active surveillance involves actively and continuously generating, accessing, and evaluating large data sets on device performance and clinical outcomes associated with device use in routine clinical practice. Active surveillance has the potential to empower stakeholders to make timelier, evidence-based decisions. Here’s a link to more details on our NEST goals:

https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHReports/ucm301912.htm

In addition, the FDA established the unique device identification (UDI) system, which allows for more accurate reporting and analyzing of adverse events so that new and increased known safety issues can be identified and corrected more quickly. The UDI system will also help in the effort to drive change toward an active surveillance system and contribute to our work helping to create new real-world data sources. The continuing implementation of

the UDI system will improve the quality of information in medical device adverse event reports, help the FDA identify device problems more quickly, and better target recalls to improve patient safety. And, the agency continues working with the International Medical Device Regulators Forum on adoption of the UDI globally. This is another example of how the FDA has been at the forefront of developing innovative frameworks for collecting real world data, particularly in the field of device safety. Establishment of the UDI system has been a tremendous milestone in building a stronger, more modernized medical device safety net. The UDI provides a standard and clear way to document device use, including in electronic health records, clinical information systems, claims data sources, and registries.

In addition, UDI provides a mechanism to reduce medical errors by enabling health care professionals and others to more rapidly and precisely identify a device and obtain important information concerning the device’s characteristics, which also prevents confusion between similar devices that can lead to device misuse. UDI provides a mechanism to help device manufacturers, distributors, and health care facilities manage device recalls more effectively. UDI also provides a foundation for a global, secure distribution chain, helping to address counterfeiting and diversion and prepare for medical emergencies.

In our April 2018 Medical Device Safety Action Plan, we proposed next steps for creating these active surveillance capabilities, which we believe is now possible in light of the steps we have already taken.

ICIJ Q9: How does the FDA ensure recall notices reach doctors, hospitals, distributors and patients? At what point is a recall, or a series of recalls, serious enough that a product must be removed from the market altogether?

FDA RESPONSE TO Q9: The FDA takes problems with medical devices very seriously, and recalls are one method the agency uses to alert the public of potential safety issues, ensure manufacturers make key improvements to devices that are on the market and, when necessary, facilitate removal of a device from the market to protect the public health. Typically, a product must be removed from the market when a correction – i.e. a repair, modification, adjustment, relabeling, destruction or inspection (including patient monitoring) -- cannot fix the problem and/or reduce the risk to health (see 21 CFR 7.3(h)).Recalls occur when a medical device violates the Food, Drug & Cosmetic Act (e.g. adulterated or misbranded), when it could be a risk to health, or when it is both violative of the Act and a risk to health. Addressing a recall can involve a broad range of actions depending on the severity of the problem they are meant to correct – from changing the device’s labeling, providing training, or implementing a software patch, to removing the device from the market altogether. Therefore, a medical device recall can take many forms, and does not always mean that one must stop using the product or return it to the company. A recall sometimes means that the medical device needs to be checked, adjusted or fixed.

In each case, the FDA thoroughly reviews the recall strategy the company proposes to address the problem, carefully assesses the health hazard presented by the product, works to quickly determine if the problem violates FDA law, potential violations of FDA requirements, and if appropriate, assigns the recall a classification (I, II, or III) to indicate the relative degree of risk (Class I recalls being the highest risk).

A recalling firm is responsible for promptly notifying each of its affected direct accounts (e.g. a distributor) about the recall. Depending on the severity of the problem and extent of the device’s distribution, the recall strategy will specify how far in the distribution chain notification must be provided (e.g. consumer or user level, retail level or wholesale level). The FDA also conducts effectiveness checks for higher risk recalls (e.g., Class I) to verify that all identified persons or entities specified by the strategy have received notification about the recall and have taken appropriate action. In addition, depending on the product and reason for recall, the FDA often works with professional medical societies and hospital organizations directly to distribute and amplify the recall message.

Once classified, the FDA closely monitors the recall to ensure that the recall strategy has been effective. Only after
the FDA is assured that a product no longer violates the law and no longer presents a health hazard, does the FDA terminate the recall.

When a company initiates a correction or removal action, the FDA posts information online about the action in the Medical Device Recall Database and updates the database after it classifies the recall and again after it terminates the recall. In addition, the FDA may post company press releases or other public notices about recalls, market withdrawals and safety alerts that may potentially present significant risks to patients and other users of the product. After a recall has been classified, the FDA notifies the public in the agency’s weekly Enforcement Report. In addition, the FDA posts consumer information about Class I and some Class II and III recalls in order to ensure that patients are aware of the seriousness of the potential health hazard posed by exposure to the product. Other efforts include public notifications via the FDA’s MedWatch alert system, general and targeted emails to the health care and patient community and distribution via various FDA social media channels targeted at health care providers, patients and consumers. These actions are complementary to the notifications provided by the recalling firm.

ICIJ Q11: Annual FDA warning letters to device companies have fallen nearly 90 percent since 2010, reaching a record low of just 25 letters issued in the last fiscal year. Are companies more compliant with FDA rules and regulations than in the past or is there some other reason for the decline?

FDA RESPONSE TO Q11: Our most fundamental obligation to the American public is providing patients with access to safe and effective medical products to meet their health care needs while also protecting them from harmful products and deceptive medical claims. When a manufacturer, its facility or its product is not compliant with FDA requirements, the agency has several options to assure appropriate actions are taken to correct the problem and prevent future recurrence, including issuing a warning letter, issuing an Untitled Letter and conducting a regulatory meeting. The FDA determines which action to take based on a variety of factors.

Rather than decrease its oversight, the FDA has increased the annual number of device inspections it conducts by 57 percent since 2007. Through implementation of a risk-based inspection approach that focuses on “high-risk” firms and/or products, the annual number of Official Action Indicated (OAI) inspections has increased 59 percent. In total, efforts to increase the number of inspections and to focus on firms/products most likely to be violative, has increased the number of firms identified as needing corrective actions.

The agency took a more aggressive approach to the issuance of warning letters beginning in 2008 and reaching a peak in 2012, when 189 warning letters were issued, representing a more than seven-fold increase in the annual number of warning letters in 2012 compared to 2007. The agency has routinely conducted follow-up inspections of violative firms, and in general, more than 75 percent of firms have corrected their violations on follow-up inspection. The annual increase in warning letters during this time period did not impact the rate of firms that corrected their violations on follow-up inspection.

More recently, the agency has been more interactive with violative firms. In particular, agency staff review firm responses to the Form 483 (which notifies the company of objectionable conditions), provide feedback on firm’s proposed corrective action plans, and monitor progress toward remediation. Issuance of warning letters has focused on firms who have more severe violations or who fail to implement or follow-through on their corrective action plan in a timely fashion. This more interactive approach has resulted in a decrease in the annual number of warning letters while maintaining a 75 percent rate of firms that demonstrate correction of their violations on follow-up inspection.

In short, one cannot get a full picture of the FDA’s oversight and industry compliance by looking at warning letters alone.

Further, in 2011, the FDA launched the Case for Quality, an initiative undertaken in collaboration with
other members of the device ecosystem, to identify those practices that can promote a culture of quality and the implementation of a quality management approach that fosters continuous product improvement.

ICIJ Q18: In the history of the FDA, only two devices have been banned. Why so few, given acknowledged major safety issues with many more than that? What does it take for FDA to ban a medical device?

FDA RESPONSE TO Q18: The FDA has used this authority twice and has proposed to use it once more (the latter of which was announced in a proposed rule that is still pending). (More information on bans is available here: https://www.fda.gov/medicaldevices/safety/medicaldevicebans/default.htm.) We are bound by federal law to follow certain criteria that must be met in order to ban a device: the FDA must determine, on the basis of all available data and information, that a device presents substantial deception or an unreasonable and substantial risk of illness or injury that cannot be corrected or eliminated by changes in labeling or advertising. The FDA may consult with the appropriate classification panel before initiating a proceeding to ban a device. To implement a ban, the FDA must issue a proposed rule, consider public comments, and issue a final rule. For additional information, see section 516 of the Federal Food, Drug & Cosmetic Act, 21 CFR 895.20, and 21 CFR 895.21.

In cases where safety issues are present that warrant a device being removed from the market, the FDA typically works directly with companies. Voluntary recalls are used in the vast majority of these cases and generally result in a faster action to remove than the mandatory recall process or going through rulemaking to ban the device. More commonly, identified safety issues can be effectively addressed through other measures rather than simply removal from the market, including changes in labeling or in the design of the device. The FDA’s experience is overwhelmingly that companies will voluntarily correct the problems—either on their own or at the FDA’s request—so that the device can remain on the market.

ICIJ Q20: What share of medical devices approved by the FDA in 2017 were cleared via the 510k pathway? How many class III product types were cleared through 510k?

FDA RESPONSE TO Q20: 82 percent of medical devices approved/cleared by CDRH in calendar year 2017 were cleared via the 510(k) pathway.

During calendar year 2017, no class III product types (classification regulations or product codes) were cleared through the 510(k) process.

ICIJ Q28: The FDA has said “the benefits and risks of breast implants are sufficiently well understood for women to make informed decisions about their use.” How did the agency reach that conclusion? The FDA’s own data show that failure rates are high. Why is the agency confident that women understand the risks?

FDA RESPONSE TO Q28: As a public health agency, we play an important role in ensuring that patients seeking breast augmentation and breast reconstruction have accurate information regarding the benefits and risks to make informed decisions on whether implants may be right for them. Breast implants are not lifetime devices and over the past 30 years we have public communicated the potential risks with patients and providers that may come from their use. We continue to maintain a detailed website on breast implants, which contains information about breast implant-associated anaplastic large cell lymphoma (BIA-ALCL), risks of breast implants, product labeling and more. We’ve also issued communications when we obtain new information about BIA-ALCL to ensure that patients and providers are updated with information about BIA-ALCL when making choices about breast implants.

In fact, one of the conditions of approval for breast implants put back onto the market in 2006 were focus group studies. All three sponsors have completed these studies to evaluate how easily patients understand the information.
in the informed decision brochure about the risks associated with the use of silicone breast implants. Overall reaction to two versions of brochures tested was positive (Mentor’s PAS#6 posted to PAS website). Allergan and Mentor have also completed studies on the “Informed Decision Process,” which is an annual survey sent to 50 randomly selected physicians that asks questions on the level of understanding a patient has after consultation with a patient planner. In the Allergan study, the majority (85.7%) of respondents were satisfied with the Patient Planner, with 55.9% rating it Very Good and 29.8% rating it Good (Allergan’s PAS#6 posted to PAS website). In the Mentor study, the majority of respondents (94.2%) reported that the Informed Decision Brochure was of value in helping patients understand the risks and benefits of implant surgery. (Mentor’s PAS#3 posted to PAS website).

The FDA regularly updates our post-approval studies webpage on breast implants and has also recently updated the webpage to make the information easier to understand. The FDA has and will continue to communicate any additional updates we have to share about breast implants and any potential links to diseases or conditions.

The FDA also encourages patients and providers to discuss the benefits and risks of breast implants. Choosing to obtain a breast implant is a very personal decision that patients and their providers should make based on individual needs and with the most complete information.

The FDA continually reassesses whether it should take additional actions to protect patients. As noted, in our response to Question 5, we announced in September our plan to hold a public meeting of our Medical Devices Advisory Committee in 2019 related to breast implant safety and effectiveness. The purpose of this meeting is to discuss the evolving science and give patients, health care providers, and other members of the public an opportunity to be heard. This will help the FDA determine if additional actions may be necessary to protect the public health, including to require a black box warning, a patient safety checklist, or other actions to assure patients understand the benefits and risks of breast implants to make informed decisions.

For more information, please see our statement released in September regarding breast implants.

ICIJ Q30: In a meeting on Sept. 5, patient advocates met with the FDA and called for steps to protect patient safety including a black box label warning, a ban on textured implants and a patient safety checklist. Is the FDA considering these or any other measures to further inform and protect the public from possible safety risks associated with breast implants?

FDA RESPONSE TO Q30: Yes, we are considering additional measures with regard to breast implants. The agency relies on patients for important feedback to help us learn more about the benefits and risks of medical products when they’re used outside of clinical trials in the real world. We appreciate their direct feedback and are looking for more ways to incorporate the patient experience so that we focus on the things that matter to them.

In the FDA’s meeting with patient advocates on September 5, the group provided their perspectives as patients and researchers regarding breast implants and identified several opportunities for improved understanding and communication regarding breast implant risks and benefits. The information they shared is valuable and important for us to be aware of to be effective regulators serving the needs of patients. And, in light of the growing science regarding the benefits and risks of breast implants since our last advisory committee meeting in 2011, we announced in September that we plan to hold a public meeting of our Medical Devices Advisory Committee in 2019 to discuss the evolving science and to give patients, health care providers, and other members of the public an opportunity to be heard and promote an open public dialogue. This will help inform FDA as to whether we should take additional actions to protect patient safety including a black box label warning, a ban on textured implants, a patient safety checklist, or other steps.
ICIJ Q7. How does the FDA coordinate with similar government regulators around the world, both in the developed world like the EU as well as in developing and BRICS nations such as India and South Africa?

FDA RESPONSE TO Q7:

FDA is a founding member of the International Medical Device Regulators Forum (IMDRF), which is the primary mechanism through which the agency focuses on international activities with respect to medical devices. IMDRF consists of medical device regulators from around the world that have voluntarily come together to harmonize the regulatory requirements for medical devices. The FDA participates in IMDRF alongside Australia, Brazil, Canada, China, Europe, Japan, Russia, South Korea, and Singapore. The World Health Organization (WHO) is an Official Observer and APEC's Life Sciences Innovation Forum's Regulatory Harmonization Steering Committee, the Asian Harmonization Working Party (AHWP) and the Pan American Health Organization (PAHO) are Regional Harmonization Initiatives with IMDRF.

While the members of IMDRF are developed countries with robust regulatory systems, developing countries participate through the Regional Harmonization Initiatives. The FDA works alongside other IMDRF members in working groups to develop internationally agreed upon guidance documents on specific topics such as adverse event reporting, standards and Unique Device Identification (UDI). Once created, these internationally agreed upon documents are then adapted by IMDRF members to meet the regulatory requirements of their jurisdictions.

One of the main goals of IMDRF is for regulators to work together to confront key challenges, develop approaches for new and emerging technologies, and improve the safety and quality of medical devices around the world. Some of the areas where the FDA is helping to lead the world to enhance the safety of medical devices include work with IMDRF on universal adoption of UDI, and improving cybersecurity of medical devices globally.

Additionally, the FDA has taken the lead to identify and act on safety signals internationally. For example, the agency has worked for years to improve the safety of infusion pumps, first issuing a letter to infusion pump manufacturers back in 2010 to alert them and the public about MDRs, and has since worked to increase user awareness of safety issues on an international level, facilitate improvements to these important devices, and publish guidance to assure the safety of these devices throughout their total product life cycle. Likewise, it was the FDA that led efforts to better understand and address the safety signals related to metal-on-metal hips. In 2010, the FDA launched the International Consortium of Orthopedic Registries (ICOR), an international collaborative effort designed to advance the harmonization, interoperability and quality of hip and joint replacement registries worldwide. A total of 29 registries participate in this collaboration that collectively captures experience of more than 5.2 million patients from 14 nations worldwide. The ICOR developed minimum core data set for hips and knees, harmonized definitions globally, developed methodology to combine the data from multiple countries and conducted combined analyses including those focusing on metal-on-metal hips. The FDA leveraged ICOR capabilities and included ICOR registry presentations in an FDA panel meeting focusing on metal-on-metal hips to help inform the regulatory decision making. The FDA engages heavily with our international counterparts to share information about potential safety concerns with medical devices, and to identify and take action to protect patients and the public health where possible.

While stakeholders may participate in some IMDRF working groups, the voting membership in the IMDRF management committee is exclusive to regulators, which was one of the preconditions the FDA specified when we first proposed the creation of IMDRF in 2010 and 2011 in contrast to the entity it replaced – the Global Harmonization Task Force – which included device industry representation. This structure allows regulators to share confidential information about their respective programs and capabilities in order to implement several of the IMDRF adopted actions, and ensure regulators themselves are making the decisions for the practices their respective nations will follow. Even in the case of standards development and recognition, where outside stakeholders can
propose standards for the FDA’s recognition – it is the FDA that has the final say and makes the decision. For additional information on IMDRF, including the documents developed by IMDRF, please refer to: www.imdrf.org.

ICIQ5: [ICIJ question regarding devices such as the birth control implant Essure and breast implants that have been associated with patient harm.] What kind of evidence would you require to order either product from the market -- or, in the case of breast implants, require a black box warning?

FDA RESPONSE TO Q5:

A key aspect of the FDA’s mission is to provide patients with timely and sustained access to high-quality, safe, and effective medical devices. In reviewing premarket submissions, the agency balances the benefits and risks to patients from the use of a device based on the totality of the scientific evidence. As with any medical product, some risks may become evident in the postmarket setting after approval, which is why the FDA imposes postmarket requirements and controls, investigates safety signals, and communicates safety concerns to manufacturers, health care providers, and patients. We also believe it’s important to partner with patient groups, medical professional societies, academic institutions, and industry to understand possible risks from medical devices.

When the FDA learns of a safety concern, the agency determines the appropriate course of action based on the specific facts, risks and benefits of the device. The FDA might ask the manufacturer to voluntarily take risk mitigation steps, such as labeling changes or removal of a product from the market. We realize that there might be confusion about why we take this approach instead of invoking a formal regulatory process, such as banning a device. The reason is that this approach of voluntary manufacturer action with FDA oversight is often the most expeditious and efficient way to address a safety problem, which is in the best interests of patients. When the FDA takes formal action, the agency must demonstrate that the statutory criteria for action have been met, and then initiate the regulatory process. For example, to ban a device, the FDA must determine that the device presents “substantial deception or an unreasonable and substantial risk of illness or injury,” and then promulgate a regulation to make the device a banned device, a regulatory process that can take years to complete (FD&C Act section 516).

It is important to note that our approach to regulation for all medical devices is evidence- and science-based, and the decisions we make are grounded in a thorough review of the totality of available evidence, not all of which may be reflected in the public discourse around a particular product.

For example, the FDA has been extremely focused on the safety profile of the Essure permanent birth control device and has taken a series of escalating actions to address concerns based on available evidence of the risks. These actions, which have included adding a boxed warning and patient decision checklist to the device labeling, were intended to implement meaningful safeguards to ensure women are able to make an informed decision when considering this device. The FDA was notified by Bayer that they will no longer sell or distribute the Essure device after Dec. 31, 2018 for business reasons as they had been doing in other countries.

The post-market safety of Essure continues to be a top priority for the FDA, and even when Essure is no longer sold, the FDA will remain vigilant in protecting patients who’ve already had this device implanted. Information about FDA’s actions related to Essure can be found here: https://www.fda.gov/medicaldevices/productsandmedicalprocedures/implantsandprosthetics/essurepermanentbirthcontrol/ucm452254.htm

Our regulation of breast implants is based on decades of work we have done to assess and communicate the benefits and risks of these products. The steps we’ve taken date back to 1988, when, based on emerging safety concerns, the FDA reclassified breast implants from Class II (moderate risk) to Class III (high risk) devices requiring manufacturers to submit a pre-market approval application before the device could be marketed.

In 1992, the FDA expressed concern about the available safety data for silicone implants and announced a voluntary
moratorium on all silicone implant sales in the U.S. pending further review of safety information. This moratorium was lifted in 2006 with the approval of new silicone implants that met the FDA’s standards for safety. As conditions of approval, each manufacturer was required to conduct six post-approval studies to further characterize the safety and effectiveness of their silicone gel-filled breast implants and to answer additional scientific questions about the long-term safety of breast implants that the premarket clinical trials were not designed to answer. As part of these post-approval studies, the FDA collected data from the studies totaling nearly 100,000 patients. We communicated the results of these post-approval studies in our 2011 report, which noted that breast implants are not lifetime devices and have a reasonable assurance of safety and effectiveness when used as labeled.

While the agency continues to believe that the weight of the currently available scientific evidence does not conclusively demonstrate an association between breast implants and connective tissue diseases, we welcome and will thoroughly evaluate new studies on this important topic. These studies, such as the recent publication in Annals of Surgery, contribute to our discourse on this topic, but more evaluation is required as we noted in an accompanying editorial and statement about this study.

To help generate additional data about these devices, the FDA has worked with stakeholders who have launched two breast implant registries, the National Breast Implant Registry (NBIR) and Patient Registry and Outcomes for Breast Implants and Anaplastic Large Cell Lymphoma Etiology and Epidemiology (PROFILE), to help strengthen available real-world data for breast implants in the U.S. Registry data. These registries are being used to evaluate the safety of breast implants in combination with the information from medical device reports, the medical literature, and post-approval studies. At this time, the FDA does not have sufficient evidence of an association between breast implants and illnesses other than BIA-ALCL. Our participation in PROFILE and NBIR demonstrate our commitment to collecting evidence on BIs. Of note, we were one of the first countries to recognize and inform the public about the association between breast implants and anaplastic large cell lymphoma and helped launch these registries to better understand this association and its cause(s).

Patients and health care providers are valuable partners in this effort when they report any problems they observe with breast implants to the FDA through the MedWatch program.

Additionally, in light of the growing science regarding the benefits and risks of breast implants since our last advisory committee meeting in 2011, we announced in September our plans to hold a public meeting of the General and Plastic Surgery Devices Panel of our Medical Devices Advisory Committee in 2019. The purpose of this meeting is to ensure that patients and health care providers continue to have accurate, scientifically sound information about breast implant safety and effectiveness, and to promote public dialogue on the issue. Advisory committees like this one serve to provide the FDA with independent advice from outside experts. This committee will likely include several members from the medical community, academia, industry, and importantly, patient representatives. This meeting will be to encourage discussion of the evolving science, such as any relationship between texturing and BIA-ALCL, and give patients, health care providers, and other members of the public an opportunity to be heard. This meeting will help the FDA determine if additional actions may be necessary to protect the public health in the case of this particular device, including to require a black box warning. The FDA will continue to provide the public with new information as it becomes available.

ICIJ Q12: In 2012, CDRH set a new goal -- Dr. Shuren has called it “our north star” -- of being “first in the world” to introduce new medical devices. When exactly was this goal first publicly announced or posted? To what extent was it a response to industry criticism that the FDA was slower to approve new devices than regulators in Europe? Was the new goal approved prior to implementation by then-FDA Commissioner Hamburg or Health and Human Services Secretary Sebelius? If so, please provide documentation, including the date, of the decision. If not, why was such a significant goal made without input of FDA and HHS
leadership?

FDA RESPONSE TO Q12:

In 2012, the FDA announced a Vision for its medical device program to help achieve its public health mission to both protect and promote public health. This goal was made with the support of FDA and HHS leadership, including then-Secretary Sebelius. The FDA strives to protect public health by assuring that medical devices are safe and effective. It also strives to promote public health by facilitating medical device innovation and timely patient access to safe and effective technologies. CDRH’s Vision is more expansive than “first in the world,” and not considering this Vision in its entirety would be misleading to its intent, particularly as the agency has been taking concurrent actions to implement all of its parts. Our full Vision statement is the following: “Patients in the U.S. have access to high-quality, safe, and effective medical devices of public health importance first in the world. The U.S. is the world’s leader in regulatory science, medical device innovation and manufacturing, and radiation-emitting product safety. U.S. post-market surveillance quickly identifies poorly performing devices, accurately characterizes real-world performance, and facilitates device approval or clearance. Devices are legally marketed in the U.S. and remain safe, effective, and of high-quality. Consumers, patients, their caregivers, and providers have access to understandable science-based information about medical devices and use this information to make health care decisions.”

Then-Secretary Sebelius made her support for this Vision and CDRH’s overall mission clear on April 10, 2012 through a videotaped message to CDRH staff about the public release of our Vision and the availability of the Innovation Pathway 2.0 pilot, the progenitor for the current Breakthrough Devices Program. And, CDRH has included its Vision in each release of the Center’s Strategic Priorities, which are discussed with the Commissioner and reviewed by the Commissioner’s Office prior to public release and posting on the FDA’s website. These Strategic Priorities include the actions the Center commits to take and the goals it commits to achieve to assure public accountability. Over the years, in an effort to promote transparency, CDRH has continued to report to the public on the progress it has made on completing these actions and achieving these objective metrics. The Center includes its Vision in many of the presentations it gives to members of the public throughout the year, as well as in congressional testimony and in material for and responses to the media.

With regard to helping ensure that U.S. patients are first in the world to have access to high-quality, safe and effective medical devices, we have stated over the years that this is not about a competition between countries, but rather a reflection of our mission that we want devices to benefit patients, but only when a device is safe and effective. This objective reflects our concerns about the delay we observed between when pioneering new technologies were reaching U.S. patients as compared to other developed countries, putting U.S. patients at risk.

Our Vision also acknowledges that safe and effective medical devices are of limited benefit to patients if they do not have timely access. Approving a safe and effective device five years later than we otherwise could does not benefit patients. “First in the world” is simply a good metric for timely patient access because it means:

• development of new devices that make less-invasive treatments possible and bring new options to patients whose conditions would have been considered untreatable in the past, or when existing alternatives are unavailable, ineffective, or associated with substantial risks to patient safety

• helping ensure patients have more options to treat or diagnose their disease or condition and potentially improve clinical outcomes, which is an important measure of safety

• fostering innovation that spurs the development of safer, more effective technologies generally

We do all of this while providing the assurances patients depend upon. The FDA’s work in this area has made dramatic differences to the millions of Americans whose lives have been saved or vastly improved by these technologies

The U.S. has one of the highest regulatory standards for marketing authorization in the world – reasonable assurance
of safety and effectiveness – which serves us well in protecting public health. However, because it is one of the highest standards, more evidence is often needed to meet the U.S. standard, which can create, and has created, disincentives for developers of important new devices to seek access to the U.S. market early, if at all. This ultimately has a negative effect on patient health, thereby not promoting public health. Prior to 2010, the time gap continued to grow between when important technologies reached U.S. patients as compared to other developed countries putting U.S. patients at increasing risk. That said, the FDA does not believe, and has long stated publicly, that the solution to this problem is not to change the U.S. standard or to compromise the robust evidence on which we rely to approve devices. Instead, the FDA has been focused on taking steps to reduce the time and cost of the total product life cycle of medical devices, as appropriate, that do not compromise our standard of reasonable assurance of safety and effectiveness. Our goal is that innovators will view the U.S. marketplace more favorably, and bring safe and effective products to U.S. patients earlier than they have been. That would be a win-win for patients.

ICIJ Q17: Does the FDA track the off-label use of devices? Should the FDA have an official reporting system for off-label use?

FDA RESPONSE TO Q17:

The FDA does not typically track off-label use of devices. The FDA may not regulate the practice of medicine as it pertains to the use of legally marketed devices, which includes the off-label use of devices by health care providers. With few exceptions, health care providers generally may choose to prescribe or use a legally marketed medical device for an unapproved or uncleared use when they judge that the unapproved use is medically appropriate for an individual patient. It is also important to note that the FDA, and even manufacturers, may not become aware of adverse events associated with the off-label use of a device because these events may not be reported by physicians and patients.

That said, when the FDA learns of serious adverse events associated with off-label use of a medical device, it can and has alerted health care providers and patients of those concerns and provided clarification on using the device as intended in the label. Two recent examples are safety communications about the improper use of rupture of membranes tests, and deceptive health claims and significant risks related to devices marketed for use in medical procedures for “vaginal rejuvenation.”

ICIJ Q22: What is the FDA doing to ensure that device companies are properly filing adverse event reports? ICIJ has identified thousands of reports in which patients died that were reported as less serious incidents such as injuries and malfunctions.

FDA RESPONSE TO Q22:

The FDA has made it a priority and taken several actions in recent years to assure better and proper reporting of adverse event reports.

The agency has taken several steps to improve the adverse event reporting process, including making it easier to report adverse events, both for industry and for patients, caregivers and consumers who submit voluntary reports. For example, in February 2014, the FDA issued the electronic Medical Device Reporting (eMDR) Final Rule and Guidance, which requires mandatory electronic reporting for manufacturers and importers. While the rule did not change what must be included in an MDR submission to the FDA, it facilitated more expedient and timely reporting by industry. The FDA worked closely with industry through the August 2015 implementation date to help them meet their eMDR reporting obligations. With eMDR reporting, the FDA received reports in a more expedited way when compared to mailing and processing the paper reports. With paper reporting, it took from three days to more than six months before an MDR submitted on a paper copy of the Form FDA 3500A was available for analysis in the FDA’s database. With a standardized electronic format, the majority of medical device reports are available for analysis within a day or two after submission to the FDA electronic submission gateway. Moreover, the option for
high volume reporting supports the batch submission of more than one individual MDR at a time.

The FDA also finalized guidance on medical device reporting for manufacturers in November 2016. The document organizes and makes more transparent our current thinking and recommendations on medical device reporting for manufacturers, which has evolved significantly since guidance on this topic was first issued in 1997.

However, the FDA’s MDR analyses recognizes that some adverse events are not properly reported. In these cases, the FDA takes steps to correct the event type in these analyses. If adverse event reports are repeatedly received referencing the wrong type of event (e.g., references a malfunction when it should be a serious injury or death), the FDA contacts the manufacturer alerting them of the error in the submission and asks that they submit a supplemental report to correct the error. Since the eMDR rule became effective, the electronic supplemental reports received are publicly available soon after receipt. In the event that an FDA analyst becomes aware of an incorrect event type, they may take additional actions, which include correcting the event type in the internal database, or contacting the firm for additional information regarding the report submitted, as appropriate. The corrections made by the analyst are not available in the public database. Please note that the information that is publicly available is a reflection of what the FDA receives, and does not include FDA actions to analyze or correct information. This is why, as noted below, due to limitations of the current MDR system, conclusions about a device’s safety or role in an adverse event cannot be drawn from publicly available MDRs alone. We also note that sometimes an individual or entity may submit an adverse event as a death to the FDA, but upon further evaluation by the firm it is determined that the death was not the result of use of the device although the device may have malfunctioned or caused a less serious harm. In those cases, the report submitted to FDA should not identify the event as a device-related death.

The FDA also conducts inspections to identify mis-reporting or incomplete reporting, and takes enforcement actions against manufacturers when appropriate.

Medical device reporting is a key part of the FDA’s ongoing effort to detect and correct medical device problems in a timely manner, and these reports may contribute to the detection of potential device-related safety issues as well as to the benefit-risk assessments of these devices. While such reports are a valuable source of information, this type of reporting system has notable limitations, including the potential submission of incomplete, inaccurate, untimely, unverified, or biased data. Confirming whether a device actually caused a specific event can be difficult based solely on information provided in a given report. Complaints or adverse event reports do not necessarily directly indicate a faulty or defective medical device, and adverse event reports alone cannot be used to establish or compare rates of event occurrence. Additionally, we may receive multiple reports related to the same event making it difficult to determine actual numbers of events. Therefore, conclusions about a device’s safety or role in an adverse event cannot be drawn from publicly available MDRs alone.

It is important to note that MDRs submitted to the FDA are only one source we use to monitor marketed medical devices. Other sources the FDA uses include, but are not limited to, reports from our MedSun Hospital Network, data from mandated post-market studies (post-approval studies, 522 studies), clinical trials or data published in the scientific literature, epidemiological research including evaluation of administrative databases, health care claims data or registries, patient feedback, and inquiries or investigations from foreign government, federal or state health agencies.

The FDA believes, and has long stated, that the current passive system of post-market surveillance has limitations. We refer you to responses on other questions detailing our work to establish an active surveillance system through NEST.

In addition, if ICIJ and its partners believe that there are adverse event reports submitted to the FDA that have been incorrectly reported we urge the ICIJ and its partners to share that information with us so we can review to determine whether or not any or all of them have in fact been mis-reported, and, if so, follow up accordingly.
ICIJ Q4. In recent years the FDA has used a concept called “acceptable uncertainty,” in which the agency puts devices on the market sooner and collects data about their safety and effectiveness afterwards. Does the FDA believe that its current system of post-market surveillance is capable of promptly and consistently identifying dangerous devices and enables the agency to protect public health? If so, why?

FDA RESPONSE TO Q4

We understand how critical it is for patients to continue to trust that the medical products the FDA reviews are safe and effective before they go on the market. But we can never have absolute certainty about all aspects of how a new product will perform. No reasonably sized premarket trial can ever be expected to reveal everything that could eventually become known about a medical product, particularly as it will not reflect the full spectrum of patients and providers who will use the product. This is reflected in the device regulatory standard enacted by Congress in that it requires a reasonable assurance, rather than absolute assurance, of safety and effectiveness. Therefore, the question is not whether there is uncertainty about the benefits and risks of a medical product but rather how much uncertainty is appropriate in a given case.

In addition, federal statute requires that the FDA consider whether the extent of data that otherwise would be required for approval of a premarket approval application with respect to effectiveness can be reduced through reliance on post-market controls, e.g., post-market data collection.

When we are dealing with a technology that is intended to address a life-threatening disease for which there is currently no treatment – a breakthrough device – it may be appropriate to accept a little more uncertainty in the pre-market context with a requirement to gather additional data in the post-market context, while still meeting the standards for marketing authorization. The breakthrough device provisions were enacted into federal law by Congress as part of the 21st Century Cures Act, and include a provision stating that the FDA may facilitate, when scientifically appropriate, expedited and efficient development and review of the device through utilization of timely post-market data collection with regard to a premarket approval application. However, because of challenges with conducting and completing post-market studies due to the lack of incentives for patients to enroll, we typically do not accept more uncertainty because we do not have adequate assurances the evidence needed to address the greater uncertainty will be generated. The FDA has issued draft guidance designed to make these considerations on uncertainty more transparent, consistent and objectively-defined for the review of medical devices. It provides a more rigorous, methodical and science-based approach for how the FDA considers uncertainty in benefit-risk determinations to support certain medical device premarket decisions that are based on the totality of the scientific evidence available at the time of market entry. More information about the draft guidance and background on the consideration of uncertainty is available here:

https://www.fda.gov/NewsEvents/Newsroom/FDAInBrief/ucm619414.htm

The FDA has long stated that the current system of post-market surveillance has limitations in promptly and consistently identifying safety risks, a challenge that is not unique to the U.S. These limitations include relying on passive surveillance. This type of surveillance relies on certain entities becoming aware of an incident resulting in patient harm or likely to result in harm, determining that the incident was related to the use of a device, and then taking the time to report it to the FDA or the device manufacturer. As a result, many adverse events are not reported and we may not identify a new safety risk until after more patients have been unnecessarily exposed to a potentially harmful device. The FDA discussed these limitations and proposed the steps necessary to address them, including the creation of a national system, in a 2012 document titled, Strengthening our National System for Medical Device Postmarket Surveillance and, since then, in collaboration with other stakeholders, has led the effort to establish the National Evaluation System for health Technology (NEST). In our 2012 document, we proposed that the national system have active surveillance capabilities to complement our adverse event reporting (passive surveillance) system. Active surveillance involves actively and continuously generating, accessing, and evaluating large data sets
on device performance and clinical outcomes associated with device use in routine clinical practice. Active surveillance has the potential to empower stakeholders to make timelier, evidence-based decisions.

To drive change toward an active system, under the statute, the FDA established and continues to implement the unique device identification (UDI) system, which will allow for more accurate reporting and analyzing of adverse events, and we have been helping to create new real-world data sources. In our April 2018 Medical Device Safety Action Plan, we proposed next steps for creating these capabilities, which we believe is now possible in light of the steps we have already taken.

Ensuring the safety of medical devices on an ongoing basis is far more complex than having a vigilant post-market surveillance system for quick identification of new or increased safety signals. It requires the ability to conduct and complete post-market studies to determine if those signals represent a true risk to patients or are a false signal and timely public communication when there is a real safety issue. However, quickly identifying and addressing safety risks is only half the story. The FDA also believes it is important to foster innovation that spurs the development of safe and effective technologies that improve patient care or provide treatment where none exists. That’s why timely access is also important for public health. Patients are harmed by their underlying disease or condition. Timely access to safe and effective technology that addresses an unmet medical need or offers significant advantages over existing alternatives means less patient harm. We need both more effective post-market surveillance and device innovation to optimally improve the health and quality of life of patients and enable decision-making based on the best available evidence about medical devices. That is why the FDA has led the effort to establish NEST.

ICIJ Q13: Dr. Shuren has discussed pushing some experimentation with new devices onto certain patient populations that are deemed to need access to experimental devices. Patient advocates warn that this approach could turn the general patient population into test subjects. How confident is the FDA that shifting some data from premarket approvals onto the postmarket will not put some patient populations in harm’s way?

FDA RESPONSE TO Q13:

The FDA generally and Dr. Shuren specifically have not been pushing experimental devices into the marketplace. We only provide marketing authorization for devices that meet the applicable statutory standards. In certain cases—for example, a breakthrough device—it may be appropriate to accept a little more uncertainty in the pre-market context with a requirement to gather additional data in the post-market context, while still meeting the standards for marketing authorization. The reasonable assurance of safety and effectiveness standard provides for this flexibility.

Additionally, the Federal Food, Drug, and Cosmetic Act (FD&C Act) requires the FDA to consider whether the extent of data that otherwise would be required for approval of a premarket approval application with respect to effectiveness can be reduced through reliance on postmarket controls. Companies must still provide the data required in the post-market phase to remain on the market, even when some data is not required at the time of approval. This provision in the law is intended to provide timely patient access while still assuring a device is safe and effective. Because patients often lack an incentive to enroll in clinical trials once a device has been approved, it can be challenging to conduct post-market studies. That has been a limitation with respect to this statutory provision and, when we do consider it appropriate to collect some data post-market rather than premarket, we typically limit what data we will permit for post-market collection. To address these limitations, we proposed a strategy in 2012 and have since taken steps to establish the National Evaluation System for health Technology (NEST). We further describe NEST and the rationale behind it in our response to your Question 4 above.

The FDA has recently issued draft guidance to make these considerations on when it is appropriate to accept greater uncertainty more transparent, consistent and objectively-defined for the review of medical devices. The guidance, released in September 2018, provides a more rigorous, methodical and science-based approach for how the FDA
considers uncertainty in benefit-risk determinations to support certain medical device pre-market decisions that are based on the totality of scientific evidence available at the time of market entry. This provides a more systematic approach to how we evaluate and address uncertainty while still ensuring patients are protected.

Congress and many stakeholders, including patient groups, have long recognized the importance of facilitating access to devices, but still providing reasonable assurance that the device is safe and effective based on the totality of the evidence, when there is a public health need, such as for those patients with life-threatening diseases who have few to no alternatives on the market. Moreover, the approach in the draft guidance is consistent with section 515B(e)(2)(C) of the FD&C Act, which was added by the 21st Century Cures Act, in which Congress required the FDA to “facilitate, when scientifically appropriate, expedited and efficient development and review of the device through utilization of timely post-market data collection with regard to application for approval” -- for breakthrough devices. Organizations such as the National Organization for Rare Disorders (NORD)\(^2\) and the Infectious Disease Society of America\(^3\) supported inclusion of this provision and organizations including the Juvenile Diabetes Research Foundation (JDRF) supports the FDA’s breakthrough devices program in general as, when appropriate, it helps patients have access to safe and effective medical devices earlier when they may not have other options (or existing options are not helpful). Again, see our response to Q4 for more information about “acceptable uncertainty.”

**ICIJ Q8. How are recalls and warnings communicated between the FDA and its counterparts overseas? How does the FDA evaluate warnings or recalls issued first overseas?**

**FDA RESPONSE TO Q8**

Information the FDA obtains regarding overseas warnings and recalls is considered along with all of the information the FDA has available when considering the public health impact. Warnings or recalls issued first overseas may not pertain to devices marketed in the U.S. When they are, the FDA typically follows up to better understand the basis for the action and whether additional action by the FDA is warranted.

The FDA engages heavily with our international counterparts to share information about potential safety concerns with medical devices, and to identify and take action to protect patients and the public health where possible. The FDA has confidentiality commitments with numerous regulators around the world. With those countries that we have confidentiality commitments in place, we often exchange information about potential safety issues, including recalls and warnings initiated either in the U.S. or abroad, and have discussions about those issues. In addition, under a program created through the International Medical Device Regulators Forum, the National Competent Authorities Report exchange program is one mechanism used to exchange information related to reportable events or potential trends that individual regulators have observed in their jurisdictions, but have not yet resulted in recalls or warnings. This program includes a total of 23 countries (including the U.S.) and the EU.

**ICIJ Q1: Most new products allowed on the market by the FDA are cleared through a substantial equivalence pathway, such as the 510(k) process. Some of these devices include new technology not subjected to clinical trials. How do you ensure that patients are protected from unanticipated harms that can result**

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from these devices? Should the FDA require more devices to go through pre-market approval?

FDA RESPONSE TO Q1: Several of the premises included in your question are incorrect. For instance, most 510(k) devices are not truly new products, all 510(k)-cleared devices have been determined to be substantially equivalent to a legally marketed predicate device, 510(k) submissions may require extensive testing, and in some cases 510(k) submissions must include clinical trials when it is necessary to demonstrate the device is at least as safe and effective as the predicate device.

The FDA’s device program is risk-based, which means devices that pose the highest risks to patients have the most rigorous requirements before they can be marketed. This system was set up by Congress to ensure patients are as best protected as possible from risks, while also enabling timely access to safe and effective medical devices, consistent with the FDA’s mission to both protect and promote public health.

Generally, new technology is subject to a pre-market approval application (PMA) when it is high risk and subject to the de novo pathway when it is lower risk. The 510(k) pathway is typically available for lower risk devices for which one or more similar technologies are already on the market, not for truly “new products” as stated in the question above.

The FDA may require extensive testing for devices subject to a 510(k), generally requiring more evidence for more complex technologies. Because most devices, unlike drugs, are hardware and have localized effects on the body, robust non-clinical testing can demonstrate that a device performs similarly to comparable devices already on the market and that its benefits outweigh its risks. And we can often get this information without subjecting patients to clinical trials. For example, for some devices, such as syringes and infusion sets, bench testing – for biocompatibility, and mechanical and physical performance tests – can provide the information the FDA needs to determine that these devices are safe and effective for patients. For others, such as some bone void fillers or substitutes, animal studies provide information in cases where histology and destructive testing cannot be done on humans. And, when appropriate, we do require clinical studies for certain devices subject to a 510(k).

PMA is the most rigorous type of device marketing application required by the FDA, and is appropriate for higher risk devices where general and special controls are not sufficient to provide reasonable assurance of safety and effectiveness of the device. However, the PMA pathway is not appropriate for all medical devices. Requiring a PMA for lower risk devices that are similar to other devices already on the market – those eligible for a 510(k) – would not necessarily provide better patient safeguards, but would result in unnecessary costs and delays while diverting FDA staff resources away from studying and evaluating higher-risk and novel devices.

However, if based on new information, we determine that a device type should no longer be eligible for the 510(k) pathway, such as due to a significant safety concern, we can and have reclassified these devices into class III and required submission of a PMA. In the past few years, the FDA has been more active in using this authority. Since Congress enacted the Medical Device Amendments in 1976, the FDA has eliminated the use of 1,758 devices subject to a 510(k) as predicates through reclassification into class III, 84 percent (1,477/1,761) of which were eliminated between 2009 and the present; we eliminated roughly six times more devices as predicates in the past 10 years than in the prior 30 years of the program (1,477 vs 219). This is not because newer 510(k) devices are less safe. To the contrary, most device types we have reclassified into class III are older technologies.

We also do establish higher thresholds for the data required to market certain 510(k) devices when we believe the 510(k) remains the appropriate pathway but also determine that requiring new or additional testing would best protect patients. For the past few years, the FDA has made a concerted effort to assure we require the appropriate level of testing, including raising the bar when appropriate, such as in the case of infusion pumps. Because of these efforts, since 2009 the average page count of a 510(k) submission more than doubled to more than 1,100 pages. While industry has raised concerns about these increased demands, we believe additional information for certain applications is necessary and in the best interests of patient safety. Where we believe there is insufficient evidence to support the safety and effectiveness of a device type, we will reclassify those devices into Class III, which we have
done on several occasions. For more information, see our response to Question 15.

While 510(k) devices have become more complex given scientific advances, we have not seen the risks from these devices increased. In fact, only 1 percent of 510(k) devices are subject to a recall annually; a recall being any correction made to a device, including labeling changes and user training. That number has remained relatively steady for more than a decade.

Regardless of the type of submission – 510(k), PMA, or de novo – FDA requires a reasonable assurance of safety and effectiveness of the device before it can be marketed. FDA has demonstrated its willingness to require more data or reclassify devices when necessary to protect patients, as further explained in our response to Question 15.

ICIJ Q15: What is the FDA’s legal authority to rescind the 510k of a dangerous, defective or ineffective device? How many 510ks has the FDA rescinded? Relatedly, what is the FDA’s authority to block manufacturers from referencing the 510k of a defective or dangerous device as a predicate in new device applications? How many 510ks has the FDA blocked from serving as a predicate? Please provide specific examples.

FDA RESPONSE TO Q15:

Based on the decision of the United States Court of Appeals for the D.C. Circuit in Ivy Sports Medicine, LLC v. Burwell, 767 F.3d 81 (D.C. Cir. 2014), the FDA’s authority to rescind 510(k) clearances is more narrow than the agency had traditionally interpreted it to be. However, the FDA maintains that it has authority to rescind a clearance decision in certain circumstances such as where there is fraud or misconduct. Within the past 15 years, the FDA has rescinded approximately 40 510(k)s.

The FDA will take action to eliminate the use of a 510(k) cleared device as a predicate when it raises safety concerns. For example, the FDA may pursue reclassification (from Class II to Class III) and issue a call for Premarket Approval Applications (PMA) when the agency has determined that a device type should be regulated as high risk because general and special controls are not sufficient to assure its safety and effectiveness. This process eliminates the use of previously cleared 510(k)s as legal predicates.

Since Congress enacted the Medical Device Amendments in 1976, the FDA has eliminated the use of 1,758 devices as predicates in the 510(k) process. Of these, 1,477 (84 percent) have been eliminated since 2012. We have eliminated roughly six times more devices as predicates in the past 10 years than in the prior 30 years of the program. This is not because newer 510(k) devices are less safe. To the contrary, most device types we have reclassified into class III are older technologies.

Specific examples include the elimination of previously cleared 510(k)s for vaginal mesh for the treatment of pelvic organ prolapse, automated external defibrillators and metal-on-metal hip implants.

Although the FDA must clear devices that are shown to be substantially equivalent to predicates, the FDA will take other actions when a device raises safety concerns. For example, the FDA may determine that the product under review is substantially equivalent but misbranded or adulterated, meaning the company cannot lawfully market the device. Typically, we do not have to issue such a decision because companies generally will fix the product under review to address the safety concern and be able to lawfully market their product. This is an infrequent occurrence for the roughly 3,500 510(k) submissions we receive annually on average. In addition, when a device that could be used as a predicate raises safety concerns, we will take steps to have those concerns satisfactorily addressed or have the device removed from the market. Voluntary recalls are used in the vast majority of these cases and almost always result in a faster action to remove or correct devices than the mandatory recall process. The FDA’s
experience is overwhelmingly that companies will voluntarily correct the problems—either on their own or at the FDA’s request—to ensure that the proposed device can be placed on the market or the predicate device can remain on the market.

ICIJ Q10. What are the rules and processes for medical devices manufactured by US companies and approved for “export only”?

FDA RESPONSE TO Q10

Medical devices designated as “export only” and that do not comply with the Federal Food, Drug, and Cosmetic Act (the Act) cannot be marketed in the U.S. but can be exported if certain requirements are met.

Some devices (generally Class I or II) can be exported as “export only” devices if they meet the criteria outlined in Section 801(e)(1) of the Act: they must be in compliance with the specifications of the foreign purchaser, not in conflict with the laws of the nation to which they are intended for export, labeled that they are intended for export, and not be sold or offered for sale in the U.S.

Other devices must meet additional requirements to be exported, such as Class III devices, investigational devices and banned devices. Such devices could be exported if they qualify under section 802 of the Act. For example, under one of the section 802 pathways, devices may be exported if, among others, they have a valid marketing authorization from one of the listed countries (Australia, Canada, Israel, Japan, New Zealand, Switzerland, South Africa, a member of the European Union, or the European Economic Area), and are in substantial compliance with the FDA’s good manufacturing practices (GMPs). In addition, the device must be in compliance with the specifications of the foreign purchaser, not in conflict with the laws of the nation to which they are intended for export, labeled that they are intended for export, and not be sold or offered for sale in the U.S.

Exporting a class III device under section 802 does not require prior approval from the FDA; instead, the exporter must submit a “simple notification” to the FDA, identifying the product’s trade name, type of device, product’s model number and the country that is to receive the exported article if the export is to one of the countries that is not listed above. Alternatively, such devices qualify for export via a different pathway under section 801(e)(2) if the company provides information to the FDA for a determination that the exportation of the device is not contrary to public health and safety and that the device has the approval of the country to which it is intended to be exported. In addition, the device must be in compliance with the specifications of the foreign purchaser, not in conflict with the laws of the nation to which they are intended for export, labeled that they are intended for export, and not be sold or offered for sale in the U.S.