

**MEDICAL DEVICES: PROTECTING PATIENTS
AND PROMOTING INNOVATION**

HEARING
OF THE
**COMMITTEE ON HEALTH, EDUCATION,
LABOR, AND PENSIONS**
UNITED STATES SENATE
ONE HUNDRED TWELFTH CONGRESS
FIRST SESSION
ON
EXAMINING MEDICAL DEVICES, FOCUSING ON PROTECTING PATIENTS
AND PROMOTING INNOVATION

NOVEMBER 15, 2011

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MEDICAL DEVICES: PROTECTING PATIENTS AND PROMOTING INNOVATION

TUESDAY, NOVEMBER 15, 2011

U.S. SENATE,
COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS,
Washington, DC.

The committee met, pursuant to notice, at 2:34 p.m. in Room SD-G50, Dirksen Senate Office Building, Hon. Tom Harkin, chairman of the committee, presiding.

Present: Senators Harkin, Franken, Merkley, Casey, Bennet, Mikulski, Blumenthal, Hagan, Hatch, and Burr.

OPENING STATEMENT OF SENATOR HARKIN

The CHAIRMAN. Good afternoon. The Senate Committee on Health, Education, Labor, and Pensions will come to order. This is the third hearing we have convened as part of our ongoing process to authorize the FDA user fee legislation. Today we examine the FDA's regulation of medical devices.

As the sponsor of the American's Disabilities Act, now 21 years old, I recognize that these devices often enable individuals to live their lives to the fullest. It's hard to imagine modern medicine functioning without them, and countless patients who have had their lives changed for the better by medical devices. Accordingly, it is essential that we encourage the continued development and improvement of medical devices, and that efficient regulatory processes get these innovative devices to patients as quickly as possible. However, there is no virtue in getting devices to patients quickly if the devices don't work or, worse, if they cause injury or death.

I think most Americans would be alarmed if they understood the current process we use to approve most medical devices. People probably imagine that for every moderate or high-risk device—certainly anything that's implantable in the human body—that experts at FDA examine clinical data, and conclude that the device has been demonstrated to be safe and effective. But that's not what happens. Most devices are cleared by FDA through a process in which a device must merely show to be "substantially equivalent" to another device that's already on the market, even if that device was substantially equivalent to a previous device, and that previous device was substantially equivalent to a previous device—and on and on and on and on.

This process gets devices to patients more quickly, but sometimes with catastrophic consequences for patients. Recently, for example,

all-metal hip implants were cleared through the 510(k) process, in many cases without clinical data. As it turns out, when the metal ball rubs against the metal socket, tiny metal particles can wear off, cause damage to the bone and tissues surrounding the implant, and the metal ions can get into the bloodstream and cause problems in the heart, nervous system and thyroid gland. Today, there are around a half a million Americans walking around with a dangerous hip implant, and no great options. Do they have surgery to have implant removed, or keep it and risk becoming another victim of the rush to get these products to market?

There's been a great deal of talk lately about promoting innovation, and I'm all for that, especially when innovation leads to the creation of jobs and even entirely new industries. But promoting innovation doesn't just mean, willy nilly, getting products to market so that device companies can make a profit. In a recent article, one of our witnesses today, Dr. Gregory Curfman, made the point that true innovation is not just the matter of getting products to market quickly, but also of ensuring that they are safe and effective. A device is only a worthy innovation if it works, and it doesn't hurt people. Speeding medical devices to market without adequate data and testing might be good for business in the short-term. It might even create some jobs in the short-term. But if the device is faulty, patients will pay the price, business will be hurt, and those jobs will disappear. As Dr. Curfman noted in his article, and I quote: "Our regulators should not be in the business of creating jobs in the manufacture of dangerous devices." That is not a good business model at all. I want to do everything possible to help U.S. manufacturers to create innovative and safe devices, and get them to market as expeditiously as possible. To that end, the FDA must strike the appropriate regulatory balance.

At a minimum, FDA should reserve its streamlined 510(k) process for devices that are truly of moderate risk. Any high-risk device should be required to submit a premarket approval application. Over 20 years ago, in the Safe Medical Devices Act of 1990, Congress made it clear that FDA should use its premarket approval process for high-risk class III devices, or it should reclassify them to a lower-risk category. Despite this direction from Congress, high-risk devices continue to slip by this requirement.

If we're going to retain a system in which devices can be cleared based on substantial equivalence to predicate devices, we need to create assurance that the predicate device is safe, and works. We need to follow cleared devices throughout their lifecycle so that we know how they perform in the real world. That way, when a follow-on device seeks approval based on a predicate, we know something about how that predicate worked, and we will be more confident that "substantial equivalence" tells us something about safety and effectiveness. Certainly, if a device turns out to be dangerous, if it's withdrawn or recalled for safety reasons, it is absurd to continue to allow that dangerous device to be used as a predicate for later products.

So, I intend to work with FDA and my colleagues on this committee to strengthen and improve FDA's postmarket authorities, so that we all can have more confidence in the 510(k) system's ability to ensure patient safety.

This afternoon, we'll hear from several expert witnesses who approach this important issue from a variety of perspectives. I thank you all for being here, and I look forward to your remarks.

We have two panels. On panel one we have just one witness, Dr. Jeffrey Shuren, who is the Director of the FDA Center for Devices and Radiological Health.

Dr. Shuren became the Director in January 2010. He previously served as Acting Center Director beginning in September 2009. Dr. Shuren is both a medical doctor and a lawyer, having earned his medical degree at Northwestern University, and his law degree at the University of Michigan.

He has had a long and distinguished career at FDA. He's held a variety of policy positions at the agency, including Acting Deputy Commissioner for Policy Planning and Budget, Associate Commissioner for Policy and Planning, Special Counsel to the Principal Deputy Commissioner, Assistant Commissioner for Policy, and a Medical Officer in the Office of Policy.

In the last 18 months, he's led FDA's effort to improve both the performance of the Center for Devices for Radiological Health, and the 510(k) review system. We're pleased to have him here today. We welcome you here, Dr. Shuren. And without objection, your full statement will be made a part of the record. And if you could sum it up in, oh, 5, 7 minutes, or so—we'd certainly appreciate it.

Dr. Shuren, please proceed.

STATEMENT OF JEFFREY SHUREN, M.D., J.D., DIRECTOR OF THE CENTER FOR DEVICES AND RADIOLOGICAL HEALTH, FOOD AND DRUG ADMINISTRATION, SILVER SPRING, MD

Dr. SHUREN. Thank you, Mr. Chairman and members of the committee.

As mentioned, I am Dr. Jeff Shuren, Director of the Center for Devices and Radiological Health at the Food and Drug Administration. Thank you for the opportunity to testify today.

In late 2009, and soon after I came to CDRH, The Center for Devices and Radiological Health, we initiated a review of our medical device premarket programs in response to concerns expressed by industry and others. We conducted an honest and frank self-assessment to these processes, including the 510(k) program.

As part of that process, CDRH has begun to undertake a new, more systematic approach to device regulation—one that continues to focus on protecting public health by assuring that devices are safe and effective, but also focuses on promoting public health by facilitating device innovation. In fact, last year, innovation became one of our top four strategic priorities.

This new approach required that we move away from the traditional misperception that safety, effectiveness and innovation are incompatible. Rather than focus on more regulation or less regulation, we began to focus on smart regulation—how to most effectively achieve both aspects of our mission as both a regulator and a facilitator.

We realized that FDA should help to create a regulatory environment that allows innovation to thrive by eliminating undue regulatory obstacles, while also ensuring consumer confidence that our medical technologies are safe and effective.

In 2010, we released two reports that concluded we at FDA had not done as good a job managing our premarket programs as we could have. The No. 1 problem we found was insufficient predictability which can lead to inefficiencies, increased cost for industry and the FDA, and sometimes in delays in bringing safe and effective products to market.

These circumstances may also create challenges for smaller start-up companies in securing venture capital funding for new early stage technologies.

We identified several root causes of these problems, and they include very high reviewer and manager turnover at CDRH—which is almost double that of our Center for Drugs and our Center for Biologics, insufficient reviewer training, extremely high ratios of front-line supervisors to reviewers, insufficient oversight by managers, a rapidly growing workload caused by increase in complexity of devices, and the rapidly increasing overall number of submissions we receive, sometimes unnecessary or inconsistent data requirements imposed on device companies, insufficient guidance for industry and FDA staff, and poor quality of submissions from industry.

We identified proposed solutions to these problems, and after extensive public input last January, we announced a plan of action detailing 25 specific actions that CDRH would take in 2011 to improve the predictability, consistency and transparency of our premarket programs, and since then, we've announced additional efforts.

The actions we are taking fall into three main areas of emphasis: first, we must create a culture change toward greater transparency, interaction, collaboration and the appropriate balancing of benefits and risks; second, we need to focus on ensuring predictable and consistent recommendations, decisionmaking and application of the least burdensome principal; and third, we need to take steps to implement more efficient regulatory processes, and user resources.

Last month, we reviewed the progress we've made thus far, and issued a 26-page report summarizing many of the concrete actions that have already been implemented or will be implemented, at least in part, in the first half of 2012.

We believe that these actions will have a visible positive impact within the coming year by providing greater predictability about data requirements through guidance, reducing unnecessary or inconsistent data requests through training, and policy and process changes, implementing policies that lead to appropriately balanced benefit-risk determinations using external experts more extensively and effectively, creating incentives to create clinical studies first in the United States, speeding up clinical trial approval decisions, and implementing the innovation pathway.

We understand that in order to best serve patients, both the medical device industry and FDA must have the flexibility to be innovative, to be entrepreneurial, and ultimately successful.

For this to happen, three things must occur. We must continue to make the critical improvements to our device program that we described in last month's report. Just as important, CDRH and industry must work together to assure that the Center receives high quality premarket submissions. And finally, CDRH must have ade-

quate and stable resources to get the job done right, and as quickly as possible. This is the subject of the upcoming user fee reauthorization.

We at CDRH believe that if these three things are accomplished, we will provide the kind of value that patients deserve and come to expect from FDA. Timely access to safe and effective devices that address their healthcare needs, and the medical device industry will have the kind of predictable, consistent, transparent and efficient pathways to market that spur continued innovation and success.

Mr. Chairman, I commend the committee's efforts, and I'm pleased to answer any questions the committee may have.

[The prepared statement of Dr. Shuren follows:]

PREPARED STATEMENT OF JEFFREY SHUREN, M.D., J.D.

INTRODUCTION

Mr. Chairman and members of the committee, I am Dr. Jeffrey Shuren, director of the Center for Devices and Radiological Health (CDRH) at the Food and Drug Administration (FDA or the Agency). I am pleased to be here today to discuss CDRH's premarket review process and the activities that we are undertaking to improve the predictability, consistency, and transparency of our regulatory processes.

The Impact of Regulation on Device Innovation

FDA is charged with a significant task: to protect and promote the health of the American public. To succeed in that mission, we must ensure the safety and effectiveness of the medical products that Americans rely on every day, and also facilitate the scientific innovations that have the potential to save patients' lives. Our ability to work with innovators to translate discoveries into safe and effective products that can be cleared or approved in a timely way is essential to public health, as well as the growth of the medical products industry and the jobs it creates. Importantly, FDA's premarket review of medical devices gives manufacturers a worldwide base of consumer confidence, both domestically and internationally.

U.S.-based companies dominate the roughly \$350 billion global medical device industry. The U.S.-medical device industry is one of the few sectors, in these challenging economic times, with a positive trade balance.¹ In 2000, the U.S.-medical device industry ranked 13th in venture capital investment—now, a decade later, it's our country's fourth largest sector for venture capital investment.² In fact, more than 62 percent of the \$631.4 million that venture capital invested in the life sciences in the third quarter of 2011 went to medical device companies.³ And, the medical device industry has produced a net gain in jobs since 2005, even while overall manufacturing employment has suffered.

As noted in a January 2011 report on medical technology innovation by PwC (formerly PriceWaterhouseCoopers), the U.S.-regulatory system and U.S.-regulatory standard have served American industry and patients well. As that report states,

“U.S. success in medical technology during recent decades stems partially from global leadership of the U.S. Food and Drug Administration. FDA's standards and guidelines to ensure safety and efficacy have instilled confidence worldwide in the industry's products. Other countries' regulators often wait to see FDA's position before acting on medical technology applications and often model their own regulatory approach on FDA's.”⁴

¹PwC (formerly PriceWaterhouseCoopers), “Medical Technology Innovation Scorecard” (January 2011) at page 8, available at <http://pwchealth.com/cgi-local/hregister.cgi?link=reg/innovation-scorecard.pdf>.

²PriceWaterhouseCoopers/National Venture Capital Association, MoneyTree™ Report, Data: Thomson Reuters, Investments by Industry Q1 1995–Q4 2010, available at <http://www.nvca.org>.

³“Medical Device Developers Attract Cash: Venture Capital Increases Its Funding of Medical Technology,” The Burrill Report (Oct. 14, 2011), available at http://www.burrillreport.com/article-medical_device_developers_attract_cash.html.

⁴PwC (formerly PriceWaterhouseCoopers), “Medical Technology Innovation Scorecard” (January 2011), available at <http://pwchealth.com/cgi-local/hregister.cgi?link=reg/innovation-scorecard.pdf>.

In terms of time to market, an industry-sponsored analysis⁵ shows that low-risk 510(k) devices without clinical data (80 percent of all devices reviewed each year) came on the market first in the United States as often as, or more often than, in the European Union (EU). The EU typically approves higher-risk devices faster than the United States because in the EU, manufacturers must demonstrate safety and performance, while in the United States the standard for approval is safety and effectiveness.⁶

FDA has been meeting or exceeding goals agreed to by FDA and industry under the Medical Device User Fee Amendments (MDUFA) for approximately 95 percent of the submissions we review each year. FDA completes at least 90 percent of 510(k) reviews within 90 days or less. In the few areas where FDA is not yet meeting its MDUFA goals, the Agency's performance has generally been improving—despite growing device complexity and an increased workload—without a commensurate increase in user fees.

However, average total days for the review of 510(k)s has been increasing since 2005 (as described later in this testimony), and has been increasing for Premarket Approval (PMA) applications since 2004, with early indicators of longer review times, such as the average number of cycles to review a 510(k), starting to increase since 2002.

FDA recognizes that, if the United States is to maintain its leadership role in this area, we must continue to streamline and modernize our processes and procedures to make device approval not just scientifically rigorous, but clear, consistent, and predictable without compromising safety.

Smart Regulation's Role in Facilitating Medical Device Innovation

Nearly 2 years ago, CDRH recognized that, given the growing complexities of medical product development, we needed to re-evaluate and modernize our regulatory review processes in order to ensure that patients had timely access to safe and effective medical devices. At that time, CDRH began to undertake a new systematic approach to device regulation, moving away from the traditional misperception that safety and effectiveness and innovation are incompatible. Rather than focus on *more* regulation or *less* regulation, we began to focus on “smart regulation.”

Our goal has been to ensure that safety and effectiveness and innovation are complementary, mutually supporting aspects of our mission to promote the public health. As part of our process to improve CDRH's internal systems, we first reached out to stakeholders to hear their concerns and listen to their recommendations about our premarket programs. This is what we heard: industry felt that inadequate predictability, consistency, and transparency were stifling innovation and driving jobs overseas; and consumer groups, third-party payers, and some health care professionals believed that one of our premarket pathways—the 510(k) program—did not provide adequate protection for American patients and did not generate sufficient information for practitioners and patients to make well-informed treatment and diagnostic decisions. In turn, CDRH employees expressed concerns that the 510(k) program had not adapted to the increasing complexity of devices, and that poor-quality 510(k) submissions, poor-quality clinical studies conducted in support of PMA applications, and an ever-growing workload were straining already overburdened premarket programs.

We also began two assessments of our premarket programs to identify issues, their root causes, and the appropriate solutions. One assessment focuses on the 510(k) program. The other looks at how we use science in regulatory decision-making, touching on aspects of several of our premarket review pathways, such as our clinical trials program. In addition, we contracted with the Institute of Medicine (IOM) to conduct an independent evaluation of our 510(k) program.

In August 2010, following extensive public input, we released two reports that identified issues regarding our premarket programs and proposed potential actions for us to take to address the underlying root causes. The No. 1 problem we found was insufficient predictability in our premarket programs, which can create inefficiencies, increase costs for industry and FDA, and delay bringing safe and effective products to market. We identified several root causes of these issues. They include

⁵ California Healthcare Institute and The Boston Consulting Group, “Competitiveness and Regulation: The FDA and the Future of America's Biomedical Industry” (Feb. 2011), available at <http://www.bdg.com/documents/file72060.pdf>.

⁶ See “Recast of the Medical Devices Directives: Public Consultation,” available at http://ec.europa.eu/consumers/sectors/medical-devices/files/recast_docs_2008/public_consultation_en.pdf; European Commission, “Guidelines on Medical Devices: Clinical Evaluation: A Guide for Manufacturers and Notified Bodies” (Dec. 2009), at p. 4, available at http://ec.europa.eu/health/medical-devices/files/meddev/2_7_Irev_3_en.pdf.

very high reviewer and manager turnover at CDRH (almost double that of FDA's drug and biologics centers); insufficient training for staff and industry; extremely high ratios of employees to front-line supervisors; insufficient oversight by managers; CDRH's rapidly growing workload, caused by the increasing complexity of devices and the number of overall submissions we review; unnecessary and/or inconsistent data requirements imposed on device sponsors; insufficient guidance for industry and FDA staff; and poor-quality submissions from industry.

While it is true that providing more user-fee resources alone won't solve the problems with our premarket programs, insufficient funding is at the root of, or a contributing factor to several of these problems. Adequate and stable funding is one key component to our and industry's success in bringing safe and effective devices to market quickly and efficiently.

After considering extensive and varied public input on our recommendations, in January 2011, FDA announced a Plan of Action that included 25 specific actions that we would take this year to improve the predictability, consistency, and transparency of our premarket programs. The following month, we announced our Innovation Initiative, which included several proposals to help maintain the position of the United States as the world's leader in medical device innovation, including the creation of a new approach for important, new technologies called the Innovation Pathway.

Since then, we have announced additional efforts to improve our premarket programs, including actions to improve our program for clinical trials and the Investigational Device Exemption (IDE) program. The actions we are taking can be grouped into three main areas of emphasis. Overall, our actions seek to:

- Create a culture change toward greater transparency, interaction, collaboration, and the appropriate balancing of benefits and risks;
- Ensure more predictable and consistent recommendations, decisionmaking, and application of the least-burdensome principle; and
- Implement more efficient processes and use of resources.

Specific steps that we are taking include:

- Issuing guidance clarifying the criteria used to make benefit-risk determinations a part of device premarket decisions. This will provide greater predictability and consistency and apply a more patient-centric approach by considering patients' tolerance for risk in appropriate cases (draft guidance issued August 15, 2011);
- Creating standard operating procedures for when a reviewer can request additional information regarding a premarket submission and identifying at what management level the decision must be made. These steps are intended to provide greater predictability, consistency, and the appropriate application of the least-burdensome principle by reducing the number of inappropriate information requests (Standard Operating Procedures issued November 10, 2011);
- Developing a range of updated and new guidances to clarify CDRH requirements for predictable, timely, and consistent product review, including device-specific guidance in several areas such as mobile applications (draft guidance released July 19, 2011) and artificial pancreas systems (to be completed by the end of 2011);
- Revamping the guidance development process through a new tracking system, streamlined processes, and, to the greatest extent possible within available resources, core staff to oversee the timely drafting and clearance of documents (to be completed by the end of 2011);
- Improving communication between FDA and industry through enhancements to interactive review (some of these enhancements will be in place by the end of 2011);
- Streamlining the clinical trial (IDE) processes by providing industry with guidance to clarify the criteria for approving clinical trials, and the criteria for when a first-in-human study can be conducted earlier during device development. These actions aim to create incentives to bring new technologies to the United States first (guidances issued November 10, 2011) (IDEs are required before device testing in humans that involve significant risks may begin, and they ensure that the rights of human subjects are protected while gathering data on the safety and efficacy of medical products);
- Implementing internal business process improvements to ensure that decisions are made by the appropriate level of management, that decisions are made consistently and efficiently, and that we appropriately apply the least-burdensome principle. For example, CDRH created the internal Center Science Council to actively monitor the quality and performance of the Center's scientific programs and ensure consistency and predictability in CDRH scientific decisionmaking (Center Science Council established March 31, 2011);

- Creating a network of experts to help the Center resolve complex scientific issues, which will ultimately result in more timely reviews. This network will be especially helpful as FDA confronts new technologies (Standard Operating Procedures issued September 30, 2011);
- Instituting a mandatory Reviewer Certification Program for new reviewers (program launched September 2011);
- Instituting a pilot Experiential Learning Program to provide review staff with real-world training experiences as they participate in visits to manufacturers, research, and health care facilities, and academia (to begin in early 2012);
- Providing industry with specific guidance on how to ensure the quality and performance of clinical trials while applying the least-burdensome principle, so that industry conducts studies that are more likely to support the approval of their products (guidance released August 15, 2011); and
- Streamlining the *de novo* review process, the pathway by which novel, lower-risk devices without a predicate can come to market (draft guidance released October 3, 2011).

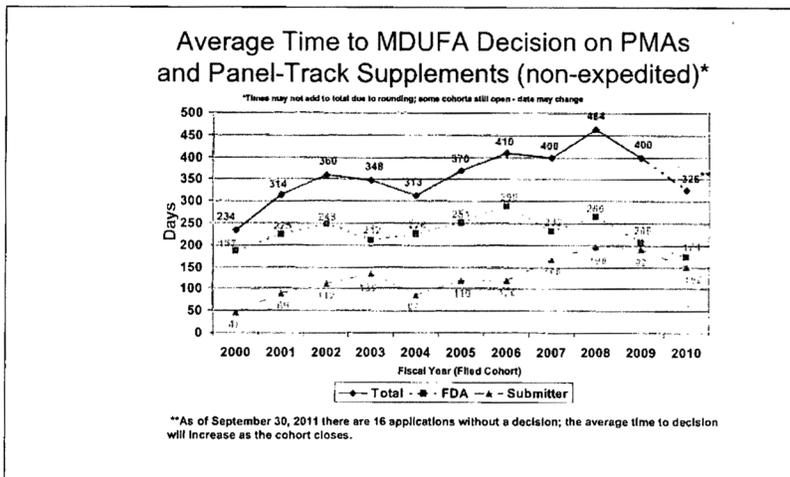
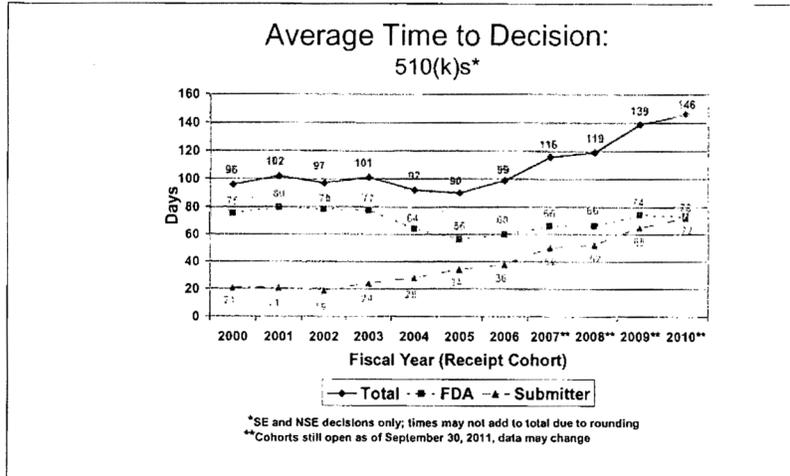
To best serve patients, both the medical device industry and FDA must have the flexibility to be innovative and entrepreneurial. First, CDRH must continue making critical improvements to our device program. Second, the medical device industry and CDRH must work together to ensure that the Center receives high-quality submissions, which contain the information we need to make well-informed and timely decisions. Finally, CDRH must have adequate and stable resources to get the job done right and quickly. The latter is the subject of medical device user-fee legislation reauthorization and congressional appropriations.

We believe that the actions we are taking now will have a positive impact within the coming year by providing greater predictability of data requirements through guidance, reducing unnecessary data requests through training and policy and process changes, implementing policies to appropriately balance benefit-risk determinations, using external experts more extensively, creating incentives to conduct clinical studies first in the United States, speeding up IDE approval decisions, implementing the Innovation Pathway 2.0 (a priority review program to expedite development, assessment, and review of important technologies), and instituting efficiencies in the premarket review process.

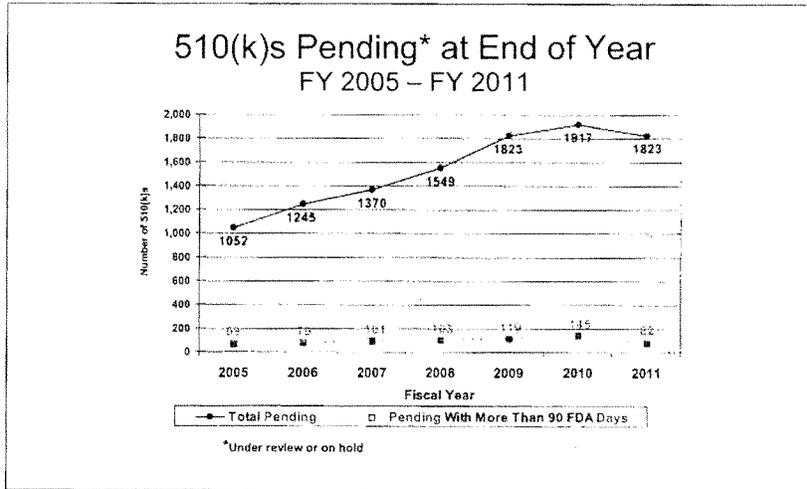
Performance Issues in the Premarket Review Process

As noted above, FDA has been meeting or exceeding goals agreed to by FDA and industry under MDUFA for approximately 95 percent of the submissions we review each year. FDA completes at least 90 percent of 510(k) reviews within 90 days or less. In the few areas where FDA is not yet meeting its MDUFA goals, the Agency's performance has generally been improving—despite growing device complexity and an increased workload—without a commensurate increase in user fees.

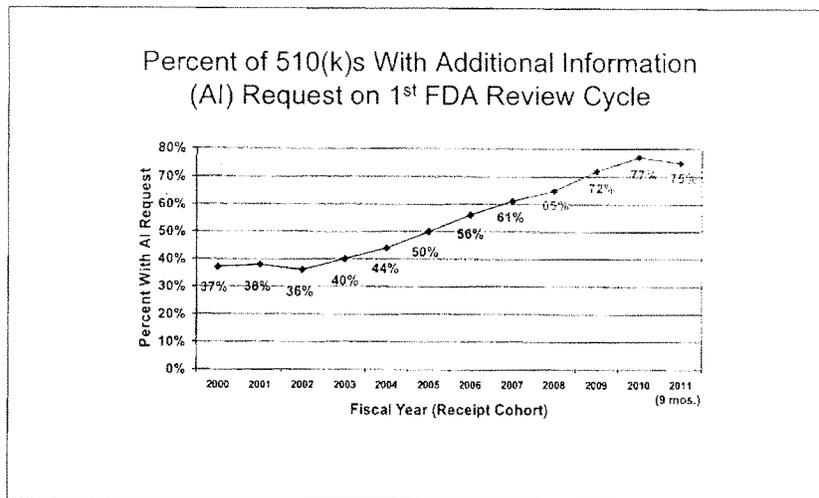
However, MDUFA metrics reflect FDA time only; they do not reflect the time taken by device sponsors to respond to requests for additional information. As the graphs below illustrate, while the time FDA spends reviewing an application has improved (for both low- and high-risk devices), *overall* time to decision—the time that FDA has the application, *plus* the time the manufacturer spends answering any questions FDA may have—has increased steadily since 2001.



FDA bears some responsibility for the increase in total time to decision, and we have been instituting management, policy, and process changes to address this issue. As a result, in 2011, CDRH for the first time began reducing what previously was an increasing backlog of unresolved 510(k) submissions.



There has also been a prolonged increase, since fiscal year 2002, in the percentage of 510(k) submissions requiring an Additional Information (AI) letter after the first review cycle. The increasing number of AI letters has contributed to the increasing total time from submission to decision.



Submission quality problems are a driving force in this increase and we are pleased that, in response to FDA calls for improving the quality of premarket submissions, the medical device industry trade association, AdvaMed, is improving and making available more training courses for its companies to help them develop 510(k) and PMA submissions that meet FDA standards.

We believe that the actions we are taking now will have a positive impact within the coming year by providing greater predictability of data requirements through guidance, reducing unnecessary data requests through training and policy and process changes, implementing policies to appropriately balance benefit-risk determinations, using external experts more extensively, creating incentives to conduct clinical studies first in the United States, speeding up IDE approval decisions, implementing the Innovation Pathway 2.0 (a priority review program to expedite develop-

ment, assessment, and review of important technologies), and instituting efficiencies in the premarket review process.

Moving Forward: Reauthorization of MDUFA

When MDUFA was last reauthorized in 2007, Congress directed FDA to take additional steps to ensure that public stakeholders would have adequate opportunity to provide input to any program enhancements. In addition to FDA receiving input from stakeholders during an initial public meeting in September 2010, Congress directed the Agency to meet with public stakeholders every month while conducting negotiations with regulated industry to hold discussions on their views about the reauthorization and hear their suggestions for changes to the MDUFA performance goals. We have been meeting with stakeholders, including representatives of patient and consumer groups, since January 2011.

Since last January, we also have been holding discussions with regulated industry in an effort to develop a package of proposed recommendations for MDUFA reauthorization. Upon completion of these negotiations and discussions, the public will have an opportunity to comment on these proposals prior to our submission of final MDUFA recommendations to Congress.

As the MDUFA reauthorization process moves forward, it is important to understand and keep in mind the significant differences between FDA's medical device premarket review programs—the 510(k) and PMA programs—and the Agency's program for review of drugs under the Prescription Drug User Fee Act (PDUFA). PDUFA fees account for about two-thirds of the drug review program's budget—nearly \$568 million in fiscal year 2010—while user fees under MDUFA fund only about 20 percent of the device review program.

The structures of the user fee programs also differ in very significant ways. The fee for fiscal year 2012 associated with review of a New Drug Application (NDA) requiring clinical data is \$1,841,500⁷—much greater than the \$220,500 fee⁸ charged for review in fiscal year 2012 of a PMA for high-risk medical devices (a business with gross receipts under \$30 million qualifies for the “small business” PMA fee of about \$55,000—75 percent less than the full fee). For lower-risk devices cleared under the 510(k) review program, the fees are even lower: \$4,049 per 510(k) application review (\$2,024 for small businesses).

While we work with industry toward a reauthorization of medical device user fees in order to provide adequate and stable funding for the program, we also continue to move forward on CDRH program improvements, with a focus on smart regulation. As these new policies and processes continue to be implemented, we expect to see notable improvements in the consistency, transparency, and predictability of our premarket review programs.

Smart Regulation's Role in Assuring Patient Safety

As we continue to look for ways to improve our ability to facilitate innovation and to speed safe and effective products to patients, we must not lose sight of the benefits of smart regulation to the medical device industry, to patients, and to society. Smart regulation of medical devices results in better, safer, more effective treatments as well as worldwide confidence in, and adoption of, the devices that industry produces.

We at FDA see daily the kinds of problems that occur with medical devices that are poorly designed or manufactured, difficult to use, and/or insufficiently tested. We appreciate the concern that some devices come on the market in the EU before they do in the United States. While we want devices to be available to American patients as soon as possible, we believe that, consistent with U.S. law, they need to be both safe and effective. The U.S. system has served patients well by preventing devices from entering the U.S. market that were later shown to be unsafe or ineffective.⁹

Some have suggested that the United States adopt the medical device regulatory system of the EU. Yet, outside the United States, pressure is growing toward *greater* premarket scrutiny of medical devices. A recent report concluded that “[f]or innovative high-risk devices the future EU Device Directive should move away from requiring clinical safety and “performance” data only to also require pre-market data

⁷ See U.S. FDA, “Prescription Drug User Fee Rates for Fiscal Year 2012,” 76 Fed. Reg. 45,831-45,838 (Aug. 1, 2011), available at <http://www.gpo.gov/fdsys/pkg/FR-2011-08-01/pdf/2011-19332.pdf>.

⁸ See U.S. FDA, “Medical Device User Fee Rates for Fiscal Year 2012,” 76 Fed. Reg. 45,826-45,831 (Aug. 11, 2011), available at <http://www.gpo.gov/fdsys/pkg/FR-2011-08-01/html/2011-19335.htm>.

⁹ See, e.g., D. Cohen and M. Billingsley, “Europeans Are Left to Their Own Devices,” *British Medical Journal*, 342:d2748 (2011), available at <http://www.bmj.com/content/342/bmj.d2748>.

that demonstrate “clinical efficacy,” and “[t]he device industry should be made aware of the growing importance of generating clinical evidence and the specific expertise this requires.¹⁰

There are significant differences between the EU and U.S. medical device review systems. In the EU, manufacturers must demonstrate safety and performance, while in the United States the standard for approval is safety and effectiveness.¹¹ In the EU, more than 70 private, nongovernmental entities called “Notified Bodies” review and approve devices by giving them a “CE mark.” These decisions are kept confidential and not released to the public or to EU regulatory bodies. In fact, the EU does not have one centralized regulatory body. Instead, each country can designate an entity as a “Notified Body,” yet the decision of one Notified Body applies to all EU countries.

Because of these factors, it is impossible to track medical device approvals, adverse events, or recalls in the EU, since there are few to no publicly accessible, centralized systems for collecting and monitoring information about medical device approvals or safety problems. The use of Notified Bodies has been criticized as encouraging “forum shopping” by sponsors to identify those Notified Bodies with the most lax operating standards, and the varying levels of expertise among Notified Bodies has been critiqued.

In May 2011, the European Society of Cardiology (ESC) issued a “case for reform” of the European medical device regulatory system: that body’s recommendations included creating a unified regulatory system, imposing stronger clinical data requirements, and requiring more accountability for notified bodies.¹² The ESC cited examples of several different cardiovascular technologies that were implanted in patients in the EU that were later proven to be unsafe and/or ineffective through clinical trials required under the U.S. system, and were subsequently removed from the European market.

Also in May 2011, a series of feature articles was published in the *British Medical Journal*, criticizing the opacity of the European medical device regulatory system, and raising concerns about the regulation of high-risk devices and how well they are tested before coming on to the European market.¹³ Several of the featured articles cited the FDA system’s transparency as helping physicians to make informed decisions about which devices to use and providing patients with access to information about the devices that will be used on them.

FDA continues exploring ways to get medical products to patients with serious and life-threatening diseases or conditions faster, but lowering U.S.-approval standards isn’t in the best interest of American patients, our health care system, or U.S. companies whose success relies on the American public’s confidence in their products. According to the IOM, “FDA should be clear that its role in facilitating innovation in medical devices is to develop regulatory thresholds that are rigorous enough to satisfy the agency’s primary objective of ensuring that marketed devices will be safe and effective throughout their life cycles but realistic enough to permit timely entry of new devices into the market.”¹⁴

We are pleased that a U.S.-medical device industry trade association, AdvaMed, has stated that it supports maintaining our current rigorous standards of safety and effectiveness for marketing medical devices: “The medical technology industry has

¹⁰ Belgian Health Care Knowledge Centre, “The Pre-market Clinical Evaluation of Innovative High-risk Medical Devices,” KCE Reports 158 (2011) at p. vii, available at http://www.kce.fgov.be/index_en.aspx?SGREF=202677.

¹¹ See “Recast of the Medical Devices Directives: Public Consultation,” available at http://ec.europa.eu/consumers/sectors/medical-devices/files/recast_docs_2008/public_consultation_en.pdf; European Commission, “Guidelines on Medical Devices: Clinical Evaluation: A Guide for Manufacturers and Notified Bodies” (Dec. 2009), at p. 4, available at http://ec.europa.eu/health/medical-devices/files/meddev/2_7_Irev_3_en.pdf.

¹² See “Clinical evaluation of cardiovascular devices: principles, problems, and proposals for European regulatory reform” Fraser, et al., *European Heart Journal*, May 2011.

¹³ “The Truth About Medical Devices,” *British Medical Journal*, vol. 342. at pp. 1115–30 (May 21, 2011), available at <http://www.bmj.com/content/342/7807/Feature.full.pdf> (Deborah Cohen, “Out of Joint: The Story of the ASR,” *British Medical Journal* 2011; 342:d2905; Deborah Cohen and Matthew Billingsley, “Medical Devices: European Patients Are Left to Their Own Devices,” *British Medical Journal* 2011; 342:d2748); see also Fiona Godlee, “Editorial: The Trouble With Medical Devices,” *British Medical Journal* 2011; 342:d3123, available at <http://www.bmj.com/content/342/bmj.d3123.full>; Carl Heneghan et al., “Medical-Device Recalls in the UK and the Device-Regulation Process: Retrospective Review of Safety Notices and Alerts,” *BMJ Open* (May 2011), available at <http://bmjopen.bmj.com/content/early/2011/05/12/bmjopen-2011-000155.full.pdf>.

¹⁴ Institute of Medicine, “Medical Devices and the Public’s Health: The FDA 510(k) Clearance Process at 35 Years” (2011), at p. 197, available at http://books.nap.edu/openbook.php?record_id=13150.

long recognized that a strong and well-functioning FDA is vital to maintaining America's pre-eminence in medical technology innovation, and we support the current regulatory framework in the United States."¹⁵

CONCLUSION

Over the course of the last 2 years, CDRH has been working, with extensive stakeholder input, to take concrete actions toward creating a culture change toward greater transparency, interaction, collaboration, and the appropriate balancing of benefits and risks; ensuring predictable and consistent recommendations, decision-making, and application of the least-burdensome principle; and implementing efficient processes and use of resources. These actions—geared toward a system of smart regulation—have already started to have a measurable, positive impact on our premarket programs, and we fully expect that positive trend to continue as we proceed to implement the improvements we have committed to make.

MDUFA II is scheduled to expire on September 30, 2012, and FDA is ready to work with you to ensure timely reauthorization of this critical program. If we are to sustain and build on our record of accomplishment, it is critical that the MDUFA reauthorization occurs seamlessly, without any gap between the expiration of the old law and the enactment of MDUFA III.

Mr. Chairman and members of the committee, I share your goal of smart, streamlined regulatory programs. Thank you for your commitment to the mission of FDA, and the continued success of our medical device program, which helps to ensure that patients and practitioners have access to safe and effective innovative medical technologies on a daily basis. I am happy to answer questions you may have.

The CHAIRMAN. Thank you very much, Dr. Shuren.

I had reserved some time for the Ranking Member to make an opening statement, but, we'll hold that. I will begin a round of 5 minute questions, in the order of appearance.

Dr. Shuren, I've heard a lot of comparisons between FDA's review times for devices here to those in Europe. Some are touting the EU's system as one we should emulate; others express concern about the fact that in the EU, unlike in the United States, manufacturers do not have to demonstrate that their products are effective. Can you talk about the implication of that difference in our approval standards?

Dr. SHUREN. It's a very critical difference in our approval standards. As you mentioned in Europe, unlike in the United States, you don't have to show that your device is effective—that, in fact, it really has benefit to patients.

And, on top of it, that it is a system that is not transparent. The public does not know the basis for approvals, they don't even know about adverse events, unlike in the United States where we make that information available to the public, and the decisions to approve are made by private companies that are paid for by industry. In fact, there are over 70 of them, and concerns have been raised about inconsistent oversight, non-uniform expertise amongst those over 70 different companies, and form shopping from the manufacturers to those particular companies. In fact, the same kind of device could be reviewed by two different notified bodies, and they could ask for different kinds of information in both cases.

We think the implications are huge—that we should not be exposing patients to devices that we don't know if they're effective. We think the U.S. standard is the right standard, but what we need to do is to assure that there is timely access to devices that are, in fact, safe and effective, and the steps we're taking are trying to get there.

¹⁵ Advanced Medical Technology Association (AdvaMed), "AdvaMed Statement on the House Energy and Commerce Subcommittee Hearing on FDA Device Regulation" (July 20, 2011).

In fact, there have been a number of devices that have come on the market in Europe that later have been shown to be unsafe or ineffective. Many times when they are doing studies in support of approval in the United States, we're talking about heart valves, drug alluding stents, breast implants, device to detect breast cancer, device to monitor glucose, implanted wireless heart monitor, elbow implants, abdominal aortic stents.

In fact, if you have ballooning enlargement of the large blood vessel in your abdomen, what you want to do is you put in a stent, a tube, so that the blood goes through that tube rather against the weakened walls of the artery which puts you at risk for rupture.

In the EU, those devices have come on the market first, since at least the late 1990s. And yet, nine of those devices which didn't come to the United States, came on the market in the EU, and subsequently came off the market because they were found to be unsafe, and we don't think that's in the best interest of patients. We don't think that's ultimately in the best interest of industry.

The CHAIRMAN. What are the weaknesses in your current postmarket authority? What, if any, additional authorities do you need to better track the safety of marketed devices? I sort of referred to that in my opening statement.

Dr. SHUREN. This is a question that was also put to us by the Institute of Medicine which recommended that we take a look back at our postmarket authorities. We are due to put out a response to their recommendations and that's currently going through administration clearance. So, it is an answer that we hope to get back to the committee very shortly.

One of the issues we, ourselves, put on the table is about predicates, and are there circumstances where a device that's currently on the market should no longer be available for use as a predicate. That is a recommendation that we also plan to respond to as part of our answer to the IOM report.

The CHAIRMAN. Actually, why—this is something I don't think very many people know—why aren't all implantable devices, things that go in your body, why aren't they considered high-risk and regulated as class III devices for which premarket approvals are required? How is it that implants like the metal hip implants, and I have a whole number of others over the last several years that have been done here—bladder sling, surgical mesh, that type of thing—how is it they get evaluated through the 510(k) process, I mean things that are implanted in your body?

Dr. SHUREN. In some cases, it does make sense for an implantable device to be considered under 510(k), if it truly is moderate risk. And sometimes, we know that upfront. Sometimes we learn over time about that risk and we realize that, in fact, what was previously a high-risk device, we make a low-risk device, and we change that. Our law is based upon taking risk into consideration in terms of applying what our requirements are, and we take that very seriously.

But you raise a very good case with the metal-on-metal hips. Those are devices, right now, that we have brought to an advisory panel to look at whether or not we should actually keep them in a class III, and we should put them on a premarket approval.

In fact, in our efforts to not only apply risk, we also look to apply the least burdensome principle. I will tell you, we have done that inconsistently, and we're taking a number of steps to address that.

But, in one of those cases, for the metal-on-metal hips, and this was the Depuy device, we, under the least burdensome principle, decided—you know what—we're not going to ask for clinical data in this case. And it turns out these are always tradeoffs and judgment calls as we try to figure out what the least justified burden is to impose on the company—that's a scientific decision—and sometimes we slide to a place, and it turns out not to have been the right call, and in the case of that particular hip, there were failures that we might have detected if we had asked for other kinds of information.

The CHAIRMAN. I have a couple of followups. My time has run out. I'll do that in the next round.

Senator Burr.

STATEMENT OF SENATOR BURR

Senator BURR. Thank you, Mr. Chairman. Dr. Shuren, thank you for being here. I'm sorry I missed part of your testimony, but I read the written part.

Let me ask you, why did it take 2½ years to put all these new proposals on the table that you highlight will speed up the process?

Dr. SHUREN. Actually, it didn't take us 2½ years to put them on the table. I will tell you, when I came in late 2009, and having heard concerns about the program, the very first thing I said, the best way to address this is let's assess it because we had industry saying that the program was not sufficiently predictable, consistent, transparent. It was stifling innovation and driving jobs overseas. But we were hearing from some of the consumer groups, third party payors, some of the healthcare professionals, that, in particular, the 510(k) program was letting unsafe devices on the market and not providing good enough information to make well informed treatment and diagnostic decisions.

My own staff had concerns that the current instantiations of those programs were not well-suited to some of the new technologies.

Senator BURR. We're 2½ years down the road since then, and now, I don't want to cut you short, now your testimony is—we have all these things that we're just putting in place, and they're going to solve a lot of the questions that have been raised.

Let me read you your quote, tell me if it's accurate.

“Ninety-five percent of more than the 4,000 medical device applications subject to user fees that FDA reviews every year are reviewed within the goals that were agreed to by the medical device industry under medical device user fees amendment 2007.”

Is that an accurate statement?

Dr. SHUREN. Yes, for the user fee goals. But I will tell you, in spite of that, no one's happy with the program because quite frankly, we're seeing that the total times are going up; so, while our times have gotten better since the start of that program, the total times aren't there, and so industry's unhappy, we're unhappy.

Senator BURR. Let me tell you why some of the unhappiness exists because that statement, one, is misleading. It's misleading, first, because the FDA has not reported 510(k) performance data beyond 2009, second, the device center has failed to achieve 55 percent of its user fee performance goals, and third, user fee performance goals are based on a metric called FDA days. FDA days accrue when FDA, not the manufacturers working on an application to reduce FDA days, FDA can offload the work onto manufacturers.

Let me just ask you simply, would you be in favor of going to calendar days? I think this would bring transparency and clarity, and better understanding of communications.

Dr. SHUREN. Sir, in terms of days, let me say for the FDA days, that's what we agreed to with industry, and actually was the deal then supported by Congress, and we've been following that and reporting on what we agreed to. But as part of our user fee reauthorization discussions now, let me premise by saying we've got ground rules in place, so please understand when there are limited things I can say about it, but I can talk about what's out there publicly.

We've been talking about changing those goals to total time. Now that means that there are things you're going to have to expect from FDA—we're responsible for part of that time, industry is responsible for the other part of the times. Part of those discussions—

Senator BURR. Maybe I was unclear in my question. My question was simply this, would you be in favor of switching to calendar days from FDA days?

Dr. SHUREN. If we're talking about total time? By calendar days, you mean calendar days where it's just with FDA?

Senator BURR. Clock starts—doesn't get restarted, it continues to tick.

Dr. SHUREN. Oh, we're talking about the same thing, total days.

Senator BURR. OK.

Dr. SHUREN. So, that's what we're talking about as a part of user fee reauthorization.

Senator BURR. How do you explain the fact that since 2007, the original PMAs—the length of time that it takes to get processed has gone up 75 percent, to 27.1 months? The average number of months for clearance of a 510(k) since the 2003–7 period has gone up 43 percent, to 4½ months' clearance. Tell me where the companies, based upon their user fees, were benefited in this process?

Dr. SHUREN. Yes, so first, in terms of—I'm not going to quibble over times, we may have disagreements. But, first of all, the problems—

Senator BURR. Tell me where I'm wrong.

Dr. SHUREN. The problem started—

Senator BURR. No, tell me where I'm wrong, don't just say I disagree, show me where my information is inaccurate.

Dr. SHUREN. Oh, for the timeframes? Yes, some of the timeframes are off in terms of the increases. But I would say, so what? So what? We all agree that times are going up, that's the important thing. And if you look at what's been going on, it started in 2002.

Senator BURR. So, what's the answer to it, user fees? Increased user fees would eliminate this?

Dr. SHUREN. What's that? If you just throw money at it, you won't solve it. You need to do three things. We need to make improvements to the program—that's what we've been doing over the course of 2011. We do need to work with industry, and we're doing that right now with their representatives on assuring we're getting quality submissions.

We're working on criteria for when we would not accept an application. It's exactly what the drug program does right now, and in fact, in a report we just put out on performance in the drug program, where we're now getting new tech, new device, new drugs, rather, on the market fairly quickly, one of the driving forces was the fact that companies are submitting higher quality submissions. We get it done faster.

And the third part to it is we need to have the adequate resources to get the job done. If you just throw money at this, you won't solve it. But, if we don't have the adequate resources to get it done, we will fail, and ultimately, industry will fail, and that's why we moved forward on these assessments, which we wrapped up in 2010. It involved lots of input from the outside. In fact, not only did industry ask, but many Members of Congress came back to us and said, please don't rush to judgment—make sure you get lots of input.

We tried to push forward quickly because we knew changes needed to be made. But we got from the Hill and from industry, don't do anything until everyone's had enough opportunity to weigh in. Then, we start in 2011 actually implementing, and now people are upset we're not moving fast enough.

And, as it is, as a Federal agency, quite frankly, we get public comment on our policies. Now, that's good because we get lots of input, but it takes time. I mean, we live in a fishbowl. If a company were to try to make changes, and do it in a public process, they'd never get anything done. This adds time to what we're doing, and already, though, we're starting to see some things change.

Let me show you something on 510(k), because you asked about it, if I could actually get chart six. I'd mentioned the problems here actually started in 2002. It's when we started seeing the first indicators where there was going to be reduced performance, and 510(k) started to actually increase in total time around 2004.

This shows the number of 510(k)'s that are still outstanding at the end of the year. You can think about it as a backlog. We're looking from 2005—steady increase, year after year after year. But, now, finally, in 2011, as we're starting to make some changes, that backlog is coming down.

If I can take the slide seven, what you'll see here is the percent of 510(k)'s that we make the decision to allow on the market. We call that clearing the device, and you'll see, again, back up, this is now with 2004, look at the top line, the percents in clearances is 88, it's just steadily coming down—year after year, 2011—the first time that number is starting to go up.

Now, these are early indicators. We still have a long way to go. But much of the actions we're taking are still out there, draft policies for comment or draft process changes that are out for comment—that, in the coming months will be finalized and implemented, and yes, I do think, that we'll have a positive impact.

Senator BURR. Chairman, you've been very accommodating, and I'll look forward to the next round.

The CHAIRMAN. Thank you very much, Senator Burr.

Senator Franken.

Senator FRANKEN. Thank you, Mr. Chairman.

The CHAIRMAN. I just want to say in order—Senator Franken, Senator Casey, Senator Merkley, Senator Bennet.

STATEMENT OF SENATOR FRANKEN

Senator FRANKEN. Thank you, and thank you, Dr. Shuren, for being here, and I appreciate the conversations that we've had, and I appreciate your going out to Minnesota. I understand you're going out again soon.

Dr. SHUREN. Yes, that's correct.

Senator FRANKEN. I think we'd all agree that patient safety is a priority of Congress and the priority of the FDA, and it's my job, and the job of the HELP Committee, to help you to protect patient safety to the best of our ability. As the Chairman said, there are different perspectives on all of this.

I've spent many hours talking with patients across Minnesota, and they tell me that they want access to the newest treatments for their conditions, but too often, these devices haven't been approved. When I talk to medical device manufacturers in Minnesota, they tell me they're frustrated that they are developing innovative devices, but they can't get them to patients because the FDA hasn't approved them.

That's why earlier today, I introduced the Patient Access to Medical Innovation Act with my colleague, Senator Alexander. This legislation will get devices to the market faster and more safely, I believe, by allowing the FDA to consult with experts. It will also reward companies for developing devices for patients with rare conditions.

I believe this bill is a step toward making the process more efficient, and part of this is talking about what some consider—a lot of groups consider—the overly restrictive conflict of interest rules that exist in terms of the experts who have been in the industry—and you've talked in your testimony about the attrition that you've had at the top of experts, and so, that's what my legislation addresses, in part.

When Commissioner Hamburg testified here in July, she expressed an openness to working with us on this issue in committee, would you be willing to work with us as well?

Dr. SHUREN. Yes, absolutely. We consider having access to the right experts to be critical, and so, I'm very happy to explore the issue with you. I'll add it's one of the reasons why we're setting up a network of experts.

Just a few weeks ago, we put out standard operating procedures for working with healthcare professional societies, scientific organizations, to be able to tap into their networks that when we are dealing with challenging scientific questions, that we can rapidly identify who are the experts in the field, kind of supplement who the industry may be bringing in with experts and experts we may already have, so that we get a full discussion, we get the right people at the table to help us address those tough questions.

Senator FRANKEN. I really appreciate your working with Dale Wahlstrom in Minnesota, in talking about creating a center for studying regulatory science because that's really what we're talking about here.

Dr. SHUREN. That is very fair to say.

Senator FRANKEN. OK. I just want to get into the 510(k) proposals that the IOM made, and I think you and I are in basic agreement on things that we didn't like about it. Can you talk a little bit, though, about the things you did, like including postmarket surveillance and that kind of thing, and what you didn't.

Dr. SHUREN. I'm a little ham-strung at the moment.

Senator FRANKEN. OK.

Dr. SHUREN. As our response to the report is currently in administration clearance. But what I can say is, the IOM engaged in a thoughtful report. There's a lot of things in there, and to their credit, they also tried to look at a number of issues beyond just 510(k) at things that might affect the program like postmarket. They looked at software, and I think in the debate, while there was one key recommendation on 510(k) program where we felt, no, we shouldn't get rid of the program in its entirety. There are many parts to that report that really merit a good and thorough conversation, and in our response, we'll kind of come back with what our perspective is on all of the recommendations that the Institute of Medicine made.

Senator FRANKEN. I look forward to seeing that, and, in fact, you said, "FDA believes that 510(k) process should not be eliminated." That's pretty, pretty clear.

Dr. SHUREN. And I stand behind that.

Senator FRANKEN. Thank you, Mr. Chairman.

The CHAIRMAN. We'll have another round. Thank you very much, Senator Franken.

Senator Casey.

STATEMENT OF SENATOR CASEY

Senator CASEY. Doctor, thanks so much for your testimony and for your public service. These are hard issues.

I wanted to ask you about, a kind of basic workforce issue. I'll start with a kind of a fundamental question about what some of the data has shown. Isn't it true that the data shows that the turnover rate is much higher for medical device reviewers than drug reviewers—is that correct?

Dr. SHUREN. That's correct. It's about double, and in fact, our drug and biological centers had this same problem many years ago, and same reasons—too much workload for the staff, not enough management oversight. In fact, for our premarket approval offices, the ratio of front-line managers to staff in some cases, are as high as 1:27, which is untenable, and they finally solved that through user fee discussions, and the drug industry, who, 10 years ago was not happy with the program rolling into PDUFA III, much like we're rolling into MDUFA III, and they finally said, "You know what, we're not happy with performance, but we recognize if we're going to address a lot of these problems, we have to make sure that you are sufficiently funded to get it done," and with us, some of

these problems with high turnover, we're not going to solve if we don't have enough people to do the work, and enough managers to assure that we have good adult supervision.

Senator CASEY. That leads me to a question—I would like to know what direction you are heading in, and what FDA is doing to make an investment in its reviewers? How do you deal with this basic problem of high turnover?

Dr. SHUREN. One step is to make sure we provide them with good training opportunities, and to make the processes as streamlined as possible.

Let me tell you about training. One of the things I encountered when I came to CDRH is that we had no standardized training program for our new reviewers. So we have now instituted and just launched in September a reviewer certification program where all new reviewers will go through standardized courses, and they go through oversight of the applications that they're reviewing. We're going to audit that, see if it works, and from there, think about expanding it, if appropriate, to some of the other reviewers as well.

We're also getting ready to launch what we call an experiential learning program. We think one of the ways to help keep us on top of new technologies is to get us out of the FDA to actually get our reviewers, get our managers to go out to manufacture facilities, see the new technologies that are being developed, go out to healthcare facilities, see the technologies in real world use.

Right now, we've tried it on more of a pilot basis and we've gotten very good feedback. It is my hope as we mentioned with resources, that we'll also have not only enough people to get, do the work in a timely manner, but also that our people can also take time off to go get this training. Because one of the challenges my staff face everyday is a gallon workload and they're getting judged on the workload and they're moving the workload at the same time. We'd like them to leave the workload for a little bit of time, and get out of the office, and get that training, and that means we need enough people to both move the freight, if you will, and to let people take the time off to get such critical training.

Senator CASEY. I have a related question. In some fields such as healthcare, there is a lot of turnover and often it's a burnout factor. Along those same lines you just described, what are you doing about recruiting and staff retaining? Because sometimes you're going to have a problem with both. Your recruiting can go well, they get in the door, but you can't retain them. In other cases, it's the opposite or sometimes a combination of both. What are you doing about that? Have you already answered that or is there something additional you'd like to add to that?

Dr. SHUREN. The critical issue here comes down to funding. I will tell you right now for one of my offices, premarket office, it takes about three people to bring on board to actually get a net gain of one person because of the turnover rate, and in some cases, I can't really pay for people, for some of the top-notch people to come out from the private sector, to come to the FDA and stay at the FDA. It's one of the issues they also addressed in the drugs program.

Right now, it's on the table that we're talking about as a part of user fee reauthorization. But, I really would like that ability to be able to pay some of these very highly talented people to stay in

their jobs rather than leaving. In fact, right now, almost half of my reviewers have 4 years or less of experience, and from my front-line managers, more than half, a little over half, have only 3 years or less experience, and that turnover—oh, I was saying that almost half of my reviewers have 4 years or less experience because they wind up leaving. And from my front-line managers, little over half have about 3 years of experience or less. And we know even from industry that these disruptions and new people coming through disrupts the review that's going on.

At the same token, I can do all the training in the world, but if these people are leaving, I've lost that, if you will, that investment. It's one of the challenges I have on least burdensome principle, which, by the way, I'm very committed to. I mean, to me, I consider that good government, that you're looking at what is the least justified burden that you impose. But, if I'm constantly dealing with new people, it's much harder to get them up to speed on what the expectations are when we apply that principle, and I think if we can break this cycle, we'll win.

It's one of the reasons why, and I empathize with industry, by the way—they are paying more money, they're not seeing the kind of performance they want to see. But quite frankly, what we never tackled is making sure we have enough resources, not only to handle the workload, but to actually get over this hump of too much workload for the individual people, and not having enough managers. And if we can break that cycle, then we will have a program where people stay, they get trained up, they stay. We have enough people to do the work. We make the other program improvements in policies and processes, then we have a top-notch medical device program.

And last, and let me say, I am not trying to put down my staff. They are amazing. I have very talented people, but I don't think we've quite served them well in making sure they have the tools available, the oversight available, and the opportunities available where they can really thrive and have a good work place.

Senator CASEY. We've heard a lot about this in Pennsylvania, so I appreciate your answers. Thank you.

The CHAIRMAN. Thank you, Senator Casey.
Senator Bennet.

STATEMENT OF SENATOR BENNET

Senator BENNET. Thank you. And just to pick up where Senator Casey left off, we've heard a lot about this in Colorado, too, and my understanding, Dr. Shuren, is that, actually, you even lose people to other parts of the agency where people are able to compensate better than the device section.

Dr. SHUREN. That's correct.

Senator BENNET. I want to thank you for all the time you've spent with me, and in Colorado as well. I deeply appreciate it, and as you know, Senator Burr and I on the committee introduced medical device legislation, along with Senator Klobuchar. And we hope to make headway here on the HELP Committee, Mr. Chairman, on this legislation.

A lot of the bill stem from the idea that FDA should not make approval longer or more costly than is necessary to meet the statu-

tory standard of reasonable assurance of safety and effectiveness. I certainly think a pragmatic approach like this makes sense. And it seems the FDA has acknowledged this need for pragmatism as well. I'm referring to the least burdensome guidance document from 1997, and you just raised that concept in the context of training. So, I'd like to hear you a little bit more on this least burdensome concept. How important is it to the agency. Is it a priority for you? And in addition to the training that you just talked about, because I don't want you to have to repeat yourself, how can FDA better apply this concept?

Dr. SHUREN. So, it is important for me, and it's something that I, personally, am committed to. In fact, over this summer, I sent out a central-wide email reaffirming our commitment to the least burdensome principle.

In fact, for folks who may be interested, that report I mentioned from about a month ago—and there's no new activities in here—it's encapsulating things that we talked about beforehand, but what we put on our Web site is an attempt to link all the different actions together that we're taking while we're taking them. And you will see in there, in our top three objectives, one of them actually pertains to least burdensome principle. And along with it, even a chart that lays out everything we're doing. If we put something out, we actually provide the link to that information. If not, we give a timeframe for when we think it's going to come out.

For least burdensome, one of the things we've been doing as a change is, first of all, in our guidance documents—try to more and more, in the guidance documents, themselves, apply the least burdensome principle as opposed to just say something in front as a boilerplate. It's really critical we put that in the guidance themselves, and we've done several of those over the past year, so it's very clear for our staff, and it's also very clear for industry.

The other is assuring that when we're making decisions, and we're going to, if you will, ask for something more, or something different, that that decision is being made at the right level of management. Too often, that decision was being made at the reviewer level. So, we have now put out a change in our standard operating procedures saying for these kinds of decisions, they've got to be made at this level. And, again, another check is to make sure that we are applying the least burdensome principle.

In fact, a few months ago, we created a center science council comprised of our senior leadership. It includes myself and experienced scientists who now oversee those programs, again, for science programs for ensuring consistency, predictability and application of the least burdensome principle. Some of the most important scientific questions are coming up there. And I will tell you that in some cases, we've actually come back to say, we're going to do something different than what was recommended. In part, it's an application of the least burdensome principle.

Senator BENNET. I want to thank Senator Burr for his help on this, and also say how much I'm looking forward to working with the agency to try to get this done.

In your testimony, you cited some statistics about venture capital investing, and seemed to be suggesting U.S.-venture capital investment medical devices is healthy. I want to call your attention to

a recent survey of life sciences, VC investors by MVCA, which found that our venture capital companies are deciding to use their dollars to invest overseas in places like Europe and China rather than here because of their lack of confidence in our regulatory system.

I want to mention the importance of first-time funding statistics. It's the measure of how many new technologies are being taken directly from the lab and to development, that first-time funding is down. That means in the future, there will be fewer technologies advancing toward the market at all stages of the pipeline. According to the Pricewaterhouse MoneyTree Report, first-time fundings of medical device companies fell more than 60 percent from 2008 to 2010, and total medical device VC investment fell by more than \$1 billion during that same time period. So, in light of that data, I'd be interested to know whether you think we ought to be worried about those trends.

I'll say that I'm worried about it for two reasons. One is that, I actually don't think there's a place where it's about balancing safety and innovation. Actually, we need the innovation for the sake of our patients, which is my principal concern. The other is in States all across the country, Minnesota's one, Colorado's one; we really see much of our economic future in the development of these innovations. And so, that's why you're hearing from the two of us and others about this. And I want to make sure that we've got an ecosystem in this country where venture capital is being invested here, and not going to Asia instead out of frustration. Do you want to respond to any of that?

Dr. SHUREN. Yes, I want to see the venture capital dollars flowing here in the United States as well. I'll tell you, one of the things I heard from the VC community, and quite frankly, I've been spending a lot of time traveling around the country. Rather than expecting people to come to Washington, DC, I've been going out there, and I've been out to Colorado—

Senator BENNET. And I can vouch for that.

Dr. SHUREN [continuing]. Minnesota. Many times, been to North Carolina, and all of this is to really hear from people directly. We've held town hall meetings where anyone from the public can come.

One of the things the venture capitalists have said is, where they'd like to have the ability to start clinical trials in the United States earlier. And the reason is, a company will bring their device to a group of doctors. They'll do some testing, and when they come back to do more testing, they go back to the same group of doctors because those are the doctors who have experience with the device.

So, these early tests, they're called early feasibility tests—are so important. That's why just last week, we put out a new policy on these early feasibility, and in some cases, first in-human studies, that would allow them to start in the United States earlier in the device development pathway than has occurred previously. And to allow companies to make changes to that device without necessarily first having to come back to FDA. Because as you know, with a device, the early prototype is not the one that's going to eventually be sold on the market. They test it, they learn from it, they make changes. We're trying to create a more rapid innovation

cycle here in the United States. And we think if we do that, that becomes a greater incentive for the VC community to invest here, and I think that is good for small companies who are really putting up and developing these new technologies.

Senator BENNET. Thank you, and thank you, Mr. Chairman, for your indulgence.

The CHAIRMAN. Senator Mikulski.

STATEMENT OF SENATOR MIKULSKI

Senator MIKULSKI. Good afternoon, Dr. Shuren. I'm glad to see you and to welcome you to the committee. I want you and the people who work at the FDA—the several thousand, almost 7,000, who work at FDA in food, prescription drugs, and medical devices—to know how proud we are of the job they do every day. The fact that we are as safe as we are in regard to our food, drugs and medical devices says something must be working. But I think we all agree it must work better.

I want to go to the personnel issues and rapid turnover raised by Senator Casey. What is the reason for the rapid turnover? Is it all money? Or is it also the fact that Federal employees—in particular, FDA employees—have often been the subject of a sustained, relentless, and persistent demonization as “pointed-headed PhDs” “Pointed-headed bureaucrats—technocrats?” Maybe I'm wrong.

People come to FDA because they want to make a difference. Why then, don't those same people stay in their jobs when every day FDA is actually making a difference?

Dr. SHUREN. You're spot on. First off, we did an organizational assessment of CDRH in 2010, and found that the commitment to the mission is actually off the charts. Over 90 percent of my staff, committed to the mission, were willing to put in extra time, which is beyond what you see in most industries.

But at the same time, morale is hurting. And the No. 1 thing I hear—I just had one of my office directors back in my office again a few days ago—was this issue of demonizing. That, for so long, all they have heard from the device industry, all they've heard, and I really do not mean this as a negative comment, but from many colleagues here on Capitol Hill, much has been focused on what's wrong. And my people everyday are working hard, and if all they hear is, “you're doing a bad job, there's something wrong with you,” that kills morale.

In fact, it is really hurting my ability to try to drive change at the FDA. It's one of the reasons, as Senator Franken mentioned, Dale Wahlstrom at LifeScience Alley, he and I have been talking about—how do we change that dialog? Because if we don't do that, if we don't change the atmosphere, if our people actually don't hear about when they're doing things right—if the things we're doing I'm talking about today makes sense, my folks need to hear that. Because, otherwise, we won't be able to make those changes, we won't change the morale issue, and we'll continue to lose people. I've got to fix the morale, and we will have to have the people to reduce that workload, and also make sure I've got the managers.

Senator MIKULSKI. Well, first of all, I am also deeply troubled by the demonization. It has shifted focus away from the regulatory

process and the IOM report. In other words, the focus is on demonization rather than acquisition of valid information from either industry or learned societies through debate, discussion, and ultimately problem-solving.

But let's also talk about the issue of money. Does the talk about 2-year pay freezes and other monetary proposals being directed at Federal employees also exacerbate the discontent?

Dr. SHUREN. I think it's a contributor. I mean, on the flip side, though, quite frankly, everyone knows the tough straits we're in as a country. There are people without jobs today, there are people who can't find work. And my people get that, they really get that.

Senator MIKULSKI. We're facing a joint committee report. If the joint committee fails to act, or we fail to adopt the joint committee recommendation, we will go to a sequester. The sequester, though not until next July, would mandate what I believe is an 8.5 percent across the board cut.

What would the impact be on your operation in light of such a cut—the literal functionality of it—regardless of how well, able and bi-partisan our MDUFA reauthorization is? What would the impact be on you? I'm not asking about which three jobs you'd need to lay off. But, instead I'm asking what you think the impact would be on your ability to recruit and retain during this year, facing both a sequester and the current demonizing?

Because first, there's the specter of demonization, which I think is just wrong. I just think it's wrong. Quite frankly, it's unbecoming for an American democracy to not recognize that we need an independent civil service. One of the hallmarks of great democracies is that they all have an independent civil service. Regardless of who is in charge, independent civil service serves the Nation.

Then, there's also the fact that there's the sequester. What would the impact of both of these concerns be on morale and recruitment and retention?

Dr. SHUREN. It would have significant adverse impact. I mean, our program, first off, unlike the drug program, is predominantly dependent upon congressional appropriations, that is where we get most of our money. And a big cut means that, not only are we at risk of losing people, but people know that the workload goes up, so the work environment deteriorates. We won't be able to, then, bring in people to handle that workload. I won't be able to keep my good people there, the first people who leave, and, ultimately, the program spirals downward.

Senator MIKULSKI. I know my time is up. Let me just say this. First of all, I'm so glad to hear you want to go out and meet with those who are working on innovations in technology and manufacturing. The reason so many of us are here today is that those types of industries create great jobs in our States. People working in my medical device community are so excited that they're actually building a product that saves or improves lives.

And their work creates an export product, so they're excited about that too. We've got to work together on this issue. This is really, truly an opportunity for jobs, innovation, and exports. I think what we need is to value our civil servants, and let them know they can count on us. If we do that, then we can count on them as we go through this process.

On behalf of myself and Senator Cardin, I would like to thank our employees at FDA. We're really proud of you. We've got a lot of reform ahead and a lot of self-reflection to do. But I think self-reflection starts up here in the Senate as well.

The CHAIRMAN. Thank you, Senator Mikulski.
Senator Blumenthal.

STATEMENT OF SENATOR BLUMENTHAL

Senator BLUMENTHAL. Thank you, Mr. Chairman. I want to join Senator Mikulski in two points that she made so well. The first is that the folks at the FDA, the people who work so hard and well are really doing an enormous public service for the American people. And probably, their only fault, and it's not their fault, is there should be more of them to do the work that's required.

And second, that demonization never makes sense in a democracy, by definition, it makes no sense because to demonize is, essentially, to shift the blame and focus it unfairly.

But, I want to raise a more philosophical question which comes to me from my work at the State level where we have agencies that are funded in whole or in part by the industries that they are supposed to regulate. And, in terms of public credibility, and long-range outlook, I realize it may not be an issue for this reauthorization. Aren't we doing a disservice to the FDA by making it as dependent as it is on funding from the industries, not just device industry but pharmaceutical and others, that it is supposed to regulate?

Dr. SHUREN. It's an important philosophical question. I also look at it, though, as a pragmatist. I know the near impossible task that faces this Congress, about figuring out where the dollars go. You have to make tough decisions all the time. We know there's less money available than before, so, realistically, for us to look at the U.S. Congress as, we're going to continue to see the kind of increases we may need to support the program. I don't know if you're in a position to do that.

So, on its alternative, there are user fee dollars to support us and to make sure we can get the job done. What's critical when we set up these programs is that those dollars support the overall program. There's not like a cut check to individual people, so we kind of keep it separate from, if you will, the dollars coming in, and the decisions being made.

And the second thing is that, on the flip side for industry, I know for them, though, it kind of changes the expectations that they have on the program. What I would like at the end of the day is to have an adequately funded program. I'm almost, I will tell you, personally, agnostic on the source. As long as we have the people we need—

Senator BLUMENTHAL. Oh, you're agnostic on the source. I don't mean to interrupt you unfairly, but, the answer you've given is sort of the second part of an answer that you haven't given, which is, in the best of all worlds, you'd be funded independently, but given the fiscal constraints of the moment, pragmatically and realistically, as you've put it, probably, this source of funding is the one that we need to rely on.

But, in terms of public credibility, I just wonder whether we aren't doing the agency a disservice by making it so dependent on the industry's funding. Certainly, it is raised, commonly, and the public is increasingly aware of it—that it depends on the industry. And frankly, at the State level, we have it happen, and the same reaction is prevalent—whether it's the utility industry or the banking industry, or the insurance industry—as happens at the State level.

Dr. SHUREN. Yes. And I recognize, also, perception can just as much be a reality as facts are. And I know that there are many who feel that, because we receive user fees, that that may taint the decisions that we get.

All I can tell you is, I don't believe it does taint our decisions. And, however, that funding is provided, as long as we are free to make our independent scientific determinations, and we have the funding to get the job done, and done right and quickly, then I think we're in a good place.

Senator BLUMENTHAL. You may not have the time, I'm guessing, almost certain that you don't have the time, but what I would like you to give me, perhaps in writing, is your analysis of the three instances of FDA failure. And what you think we should learn from them going forward. In other words, case studies—I'm not asking you for a full case study, but what you would point to as what we should regard as failures—and the three success stories. And if you want, you can make them five, you can make them seven on each side.

You can, but what I would like is an analysis of where you regard the failures as having occurred, and what we should learn from them. Because I think that will be useful as an exercise for us, for me, as new to the committee and new to this area compared to other members of this committee.

Unfortunately, my time has expired, so it's a question that, for better or worse, you won't be asked to answer. But if you could provide it in writing or in some other form, I'd be grateful for it.

Thank you, Mr. Chairman.

The CHAIRMAN. Thank you. We'll begin just a short second round.

Dr. Shuren, FDA acted very quickly to reject the core conclusions of the IOM report on the 510(k) process. I'm going to ask why, but I'm going to preface that question by saying, we put a lot of faith in the Institute of Medicine and the National Academy of Sciences. And I can tell you there are times in the past when they have come out with findings that I probably didn't like for a certain, political reason, or that might have gone against a, perhaps a, constituent of mine. But, we recognize the soundness of the process of the National Academy of Sciences and the Institute of Medicine.

So, their request to do this, they said here in their conclusion, they said that the FDA asked the Institute of Medicine to review the 510(k) clearance process, answer two questions. Does the current 510(k) clearance process optimally protect patients and promote innovation in support of public health? Answer: No. Second, if not, what legislative, regulatory or administrative changes are recommended to optimally achieve the goals of the 510(k) clearance process. Their answer was probably, ought to get rid of it and come

up with a new regime. Why did you reject the core conclusion of the IOM?

Dr. SHUREN. Because we think that the 510(k) program, in most cases, has actually worked well. If we're going to be thinking about changing it, putting something else in place, I'd first ask, what are we putting in place instead of it, which is a question the Institute of Medicine felt they were not in a place to actually say?

And the second is to just, at the outset, get rid of the program, which would be highly disruptive, and before anyone would think to do it is, then what are we gaining in return? Do we have an alternative program we're actually turning to that can ensure safety and effectiveness? Is it going to do a better job than what we have right now? And what about a transition to a new program? What will the impact be?

So, for us, we thought that getting rid of the program in its entirety was going too far. That said, much of what we are doing in this past year is about improving the programs that we have. And we still welcome additional thoughts, if there are other actions that we need to take. And if so, we'd be very happy to consider them.

But, it's more focused on making the programs we have work. And some of those products have, kind of, fallen, I'll say a little bit on the wayside.

The CHAIRMAN. I understand that. Thank you very much.

Senator Burr.

Senator BURR. Thank you, and Dr. Shuren, I, for one, commend the FDA on their decision on the 510(k) because I think that it does embrace what it set out to, and it establishes a pathway for devices that have an equivalence that's established, and I think it was the right thing.

The industry says delays in reviews are because FDA keeps moving the goal post, causing regulatory uncertainty and lack of predictability in the review and approval process. In contrast, the FDA has repeatedly said that the problems at the device centers are the industry's fault.

Now, you highlighted earlier that there are improvements in approval times. And I think you said that companies are improving in the quality of their applications. Did I hear that accurately?

Dr. SHUREN. No. First off, I would say we have not been out there saying the problems are all due to industry. I've been saying for a long time, now, that actually the problems are multi-factorial, and a good part of it is due to the FDA. And that's what I tried to make clear in my opening statement, and I've said this to Congress on the House side several times before, and in other forums.

One piece of it is we do get from a number of companies submissions that are of poor quality. And unlike the drug center, which will send them back, we'll let them in. We'll work with companies, we'll take it and we'll go many rounds to try to get it right. But, as a result, it's making us increasingly more inefficient. That is just one piece.

Senator BURR. You would agree that quality applications are an incentive for a company to move through the process as quickly as possible?

Dr. SHUREN. Here's been the challenge. When we take in a submission that may not be of sufficient quality, and we're going to

work with them, we actually end up doing some of the work for the company. We've had companies who come in; they don't even identify the predicate device.

Senator BURR. Let me, I'm trying to make this easy for you. You would agree that a quality application enhances the timeline, and there's an incentive there for the manufacturer to have a quality app, is that an accurate statement?

Dr. SHUREN. Yes.

Senator BURR. OK, great, you made a statement that you haven't been out there bashing the industry. In fact, in a response to the perception that FDA's to blame for the increase in 510(k)'s, you were quoted in February as saying, "Those 510(k) times are all on the industry."

Dr. SHUREN. I would be interested to see the quote and it's context. If we're talking about the times, the increase in times or the increase in the industry times, that is correct. But the factors that led to the increase in times are due to things on our end, and some things that are on industry's end. So, hopefully, I will go back and see that quote in context.

Senator BURR. This was reported in the Medical Device Daily. It was in an ENC Subcommittee hearing in February, and your quote was, "Those 510(k) times are all on the industry."

Dr. SHUREN. So, if it's ENC Committee happy to go back, and we'll pull the testimony to go ahead and look at it.

Senator BURR. I've learned that press is accurate, no matter what they say.

Dr. SHUREN. You must be dealing with a different press than I'm used to. No offense to the press who are here.

Senator BURR. Bottom line, the average total times is getting worse instead of better. While the agency may not be held responsible for every single submission, doesn't the fact that the average total time getting worse clearly shows the FDA is contributing to the problem? I think you admitted to it earlier.

Dr. SHUREN. I agree, we're part of the problem. And I've said we've not managed the programs as well as we should have, and that's why you're seeing a number of the actions we're taking are improvements on the FDA programs, the things we need to do better.

Senator BURR. I looked at the official meetings that were published by the FDA, on the medical device user fee agreement. Those negotiations suggest that the agency is requesting more than a 250 percent increase in user fees from current levels.

Let me ask you, would you agree to pay somebody any money at all, much less a 250 percent increase above what they are currently paying, when the terms of what you're paying for aren't being met?

Dr. SHUREN. Yes, in some cases, I actually would. I know this for research and development. Quite frankly, if you put a little bit in research and development, you may not get enough out of it. You just have to put enough into it, you get enough of a return.

To sing for our program, and it's why I empathize with industry, I actually do because they haven't seen that return on investment, at least in numbers that they would like to see, and to make the argument that in the absence of the funding, things would have

been worse, that is true, but a hard case to actually show somebody.

But at the same token, those fundamental problems that we showed in the program, some of them are due to not having enough people, having that high reviewer turnover, not having enough managers, and I can't solve with some missive that I send out to my people. I can't solve that with a pep talk.

Senator BURR. Do you acknowledge that an increase in the user fee is eventually passed on to the consumer? In other words, an increase in the user fee raises the cost of healthcare in this country? Do you agree?

Dr. SHUREN. Actually I don't know. And if you're saying, then, the companies are passing it on to consumers, then on the flip side, you're saying that the companies never actually absorb the increase. In which case, they're not really paying any more money. And that's not what the companies are telling me. The companies are telling me, if they have to pay more, it's coming out of their hides. So, I'm assuming they're not passing it on to the consumers, in which case——

Senator BURR. I'm not going to get into negotiations that you're having with the companies. But I think, throughout healthcare, any place that we exercise an increase in the cost, that finds its way to the consumer. It finds its way to healthcare at a time that we've got to take \$4 trillion out of healthcare. I think you've got to weigh in this equation. How much are we increasing the cost of devices? It troubles me, and I think, I would hope that it would trouble you, that most companies across this country tell horrific stories about going through the approval process at the FDA.

You talked about the venture capital earlier. I won't get into it, but the majority of the companies that come in to file, are publicly traded companies. They've got a market capitalization that they've got to be worried about. The uncertainty of the process will dictate whether, in fact, they decide to go for FDA approval. But, I will assure you at the end of the day, if it negatively impacts their market capital, they'll make a decision not to get involved. Not unlike the VC community's decision as to whether they're going to get in with a company pre-going public.

So, capitalization, whether it's on the VC side or whether it's in market capital, is affected greatly by the decisions that these companies make. And I think, need to be considered, from a standpoint of how it's affected by the process that we set up. I hope that's something that's food for thought for you.

Mr. Chairman, I apologize, you gave me a tremendous amount of time, and I have cheated my good friend and colleague, Senator Hatch.

The CHAIRMAN. Does anyone have any further questions for Dr. Shuren before I dismiss him and bring up the next panel?

Senator HATCH. Could I ask a few, Mr. Chairman?

The CHAIRMAN. Senator Hatch.

STATEMENT OF SENATOR HATCH

Senator HATCH. Thank you so much. Dr. Shuren, I appreciate the work you're doing, and I appreciate the FDA, in general. Mul-

tiple reports that examined FDA's databases, found that FDA has an extraordinary safety record over the past decade.

Furthermore, the IOM stated that there was no evidence to suggest patients are being exposed to unsafe or ineffective products. Based upon these findings, why has CDRH seemingly diverted precious financial and strategic resources away from the premarket review process, and focused on overhauling a program that really seemed to be working, pretty doggone well, and for which you were complimented?

Dr. SHUREN. Actually, a lot of the actions we are taking are to improve the predictability, consistency, and transparency of that program, and industry has complained about that program not being sufficiently predictable or consistent and transparent.

In fact, many of the actions we're taking are based upon feedback that we had received as we've gone across the country to get input.

Senator HATCH. Some of the things I'm asking may have been asked already. But, sorry, I missed the early part of this. I was at the Judiciary Committee.

Dr. Shuren, FDA performance data shows that the 510(k) review times have increased 43 percent in just 4 years, and PMA review times have increased 75 percent. When American industry is losing its competitive edge and when patients are waiting longer and longer for new treatments and cures, that's a matter of great concern to me.

Now, you've said that the agency has implemented reforms and announced initiatives to reduce these approval times, but I have yet to hear from you any specific actions you will take that will require a guarantee that these approval times will be reduced. And, let me just ask this question, what metrics are you using to measure the success of these initiatives and reforms?

Dr. SHUREN. We're looking at some right now, indicators on performance, and I apologize. I showed one a little bit earlier regarding our backlog on 510(k)'s, which in 2011, for the first time was coming down. We've looked at, kind of, the percent of 510(k)'s that we're now clearing, going on the market. We've got to be a little bit careful on that number because we should only clear a device that, in fact, is substantially equivalent. But that number has actually been going up.

Some of the measures we're looking at are showing early signs we're going to be looking at our performance in terms of the times on the review clock for products coming to market. But, I'll tell you for success, it's going to require that we continue to make the improvements we'd laid out. If there are things that we missed, we still want to hear about it because I keep going around asking people, and people saying, "well, that sounds like the list."

We talked a little bit about what we need to do with companies, making sure we do get quality submissions. And also said that we won't be successful if we don't have the adequate and stable resources. And I'll say right now in terms of the fees being paid, like I said, I empathize with industry, but in the one case of 510(k) right now, the full fee is \$4,000. And if you're a small business, which is \$100 million in annual sales or receipts, it's \$2,000 for a 510(k). And yet, we say, for some more money, if we can reduce the times, and it's not just the times on review, if you have greater pre-

dictability, you actually reduce the time on assessing that device, which we're not even measuring.

I mean, you're talking about—you could be looking at important savings. And yet, you could say, "Well, suppose I increase that fee \$3,000?" And yet I save days and people are telling me in the industry, every day lost is thousands of dollars, that, to me says, if I save 1 day, you may have gotten your return on the investment, in that 1 day.

And those are part of the user fee discussions right now. But, so, for success, we need to make sure we've got the resources, we need to work on the submissions coming in. But, I have to say, again and again, FDA has to do a better job. And those are the actions that we're taking now.

Senator HATCH. I appreciate that, and I appreciate your attitude about it. And we've met about it, and we've chatted about these matters, and it's a tough job you have. But, some find it shocking that the average time to clear a 510(k) application has increased 50 percent since 2002. The average to approve a PMA application has doubled since 2000, and the total review times for both 510(k) and PMAs are now, actually, longer than they were before the user fee program was instituted.

Now, these statistics are from FDA's own data, as you know, yet user fees for CDRH have increased by nearly 30 percent. I know you agree that these statistics are somewhat troubling, they are to me, and I'm very appreciative that you're on top of these things, and willing to do something about it. And I hope that you can. Because I think we're falling behind the rest of the world in approvals and yet we have some of the most imaginative and intelligent people working in this country, compared to the rest of the world.

So, you have a very important job, in my opinion, and I'm looking to you to improve the Agency's performance. And I'm counting on you.

Thank you, Mr. Chairman.

The CHAIRMAN. Senator Hagan.

STATEMENT OF SENATOR HAGAN

Senator HAGAN. Thank you, Mr. Chairman.

Dr. Shuren, I appreciate you coming before the committee, but I also appreciate your time in September when you came down to North Carolina to meet with the hard-working innovative medical device companies in my State. In North Carolina, we employ over 8,000 people in the medical technology industry, and it's an industry that really does create thousands of jobs. And I know that it was interesting and invaluable to hear their perspective as well as the FDA's, so, thank you.

I know that you've made efforts already to improve the quality of work among reviewers, and I appreciate your efforts to increase reviewer training, thank you on that. But, one complaint that I continue to hear from constituent companies is that the FDA's medical device review process is unpredictable and inconsistent, and I know you can't change this overnight. But companies have told me that when they request a pre-submission meeting, it may take months before they're able to meet with the FDA, and this may be a discussion point in some of the MDUFA negotiations.

I'm wondering if and how FDA can speed this up now? In other words, can FDA meet with these companies sooner rather than later, to ensure they are complying with FDA's requirements at the beginning of this process, rather than in the middle?

Dr. SHUREN. We've been looking at what we can do to improve the pre-submission meetings. I will tell you that the requests for these meetings have essentially doubled in the past 5 years. So, it's really outstripping our ability to meet the demand, if you will. And yet, we realize how helpful those meetings are. So, you're quite right that as a part of user fee reauthorization, we've been talking about making sure we have the ability to hold more timely meetings, to hold more meetings.

But, the other piece of it is to make sure those meetings provide the maximum value. So, we are finalizing on policy, on expectations that companies can have of these meetings. And what we'll say in that document is, "here are things we'd like to see from you," so we can have a well-informed meeting.

The second is what you can expect from us. That if we're giving advice, then we should write it down, and we should stand behind it. Unless circumstances really change that you can't do so. You bring us a device, and you say it's for indication X, and you change later on what you're going to use the device for. Well, maybe our advice changes.

But, in many other cases, it wouldn't and it shouldn't, and so, we're going to make those improvements. Namely, we're going to make the improvements we can with the resources we have, regardless of what happens. But, hopefully, we will work things out in user fee reauthorization that will have the ability to hold more and more timely pre-submission meetings. And I think that becomes a win for industry, and it becomes a win for us.

Senator HAGAN. When you stated that you wanted to be sure those meetings are valuable, well, in order for them to be valuable, they do have to take place. I certainly do agree, and anything we can do to speed that up. And I do think that industry recognizes that delays costs them money. So, I think for user fees, that they are definitely willing to pay upfront in order to have the availability of the FDA to meet them early on.

I had a question about, and I know we've also spoken about this, but I wanted to reiterate that I've heard concerns with FDA's proposal to regulate the laboratory diagnostic test as medical devices. I'm concerned that duplicative regulation could slow innovation, impeding improvements to patient care as well as the job growth that has come from this innovation around this industry. And I understand that FDA may be close to releasing guidance to regulate the laboratory-developed tests as medical devices. Can you tell me what the status of this guidance is?

Dr. SHUREN. Certainly. That framework is currently under review by the administration.

Senator HAGAN. What's your timeframe?

Dr. SHUREN. That's not going to be my call.

Senator HAGAN. Can you share with us what that is?

Dr. SHUREN. I don't know. Because, it's currently under administration clearance. So, I don't know when they'll wind up making a decision.

I will say, we have been consistent all along in saying that laboratory-developed tests for medical devices, they are tests just like what's made by a traditional manufacturer. And if we're out with a framework, our intent is not to duplicate existing requirements on laboratories.

Senator HAGAN. I think that's critical.

Dr. SHUREN. Yes.

Senator HAGAN. Thank you, Mr. Chairman.

Senator FRANKEN. Just one question. I've heard from large and small companies in my State that your guidance relating to the modifications of the 510(k) process for devices is of concern. Specifically, they are concerned that the new draft guidance that you release does not provide adequate clarity on when a new 510(k) submission is necessary for a modified device. The companies are telling me that the Center of Devices and Radiological Health may have greatly underestimated the increased workload from the proposed changes that could seriously delay the review process.

Given that the stated goal of reforming the 510(k) process was to bring more clarity and efficiency to the processes, these reports are concerning. How would you respond?

Dr. SHUREN. We've heard the same concerns, and our intent in putting out this guidance was not about seeing some big increase in the number of 510(k)'s being submitted to us. We put out the guidance because a manufacturer can make some changes to a device, and they don't have to come back to the FDA. Now, where that line is crossed is not always clear.

We've run into cases where manufacturers make changes. They should've come to us, they didn't. And those circumstances, it's very disruptive for the company, it's not good for patients. So, the more clarity we can provide, the better. And we're seeing new emerging technologies, and we wanted to provide clarity in that space.

We've heard from companies, though, the policy we put out would wind up leading to many more 510(k)'s being submitted. So what we asked industry to do is, and we've got a number of groups working on this, is to go back with individual companies and apply. You know, say, "here's how I interpret it, here's how we view the impact. Give that back to us so we can go through it, because our intent is to get this policy right." It's one of the reasons, too, why we've extended the time for getting feedback on this guidance, because we want to make sure we work with industry, we get the right policy in place.

Senator FRANKEN. Thank you.

The CHAIRMAN. Dr. Shuren, thank you very much. I'll just close this by saying, the committee—again, the IOM report, in which I place a lot of stock, I think we all have to because it is unbiased, and they don't have to answer to anyone except their own, their own guidance as professionals. They said here, "The FDA has procedures for developing, adopting and implementing guidance and standards. The agency, however, is persistently hindered in fully developing these materials by a lack of, or limitations on human, fiscal and technologic resources and capabilities," which is getting to what Senator Mikulski was saying.

More and more is required of FDA in this area as in other areas, and yet we continually cut the budget, cut the resources from the

Federal Government to the FDA. At the same time, the companies that come in, as you said, we've had this huge increase in the applications for 510(k)'s in the last few years, and yet, as we cut the things down, more and more pressures are put on you since you can't do your job, well, then, we must make it easier. Because we want innovation, we want companies to succeed for all those business reasons. I don't think that's adequate. I don't think that suffices.

I think that we need to understand that the first obligation you have is for the safety of patients, not whether or not a company gets the approval in a timely manner, or whether it makes a profit or not—your first is safety, and effectiveness, safety and effectiveness. We'll leave it up to CMS to talk about whether it's cost effective or not, that's not in your realm, that's in a different realm.

And, so, it seems to me that you see the difference here in drugs, because we're also kind of playing the reauthorizing of the Prescription Drug User Fee Act also.

Pharmaceutical companies now pay \$1.8 million for a drug application. Devices pay, what did you say, \$4,000?

Dr. SHUREN. Four thousand for a 510(k), the equivalent of the new drug application. It's a premarket approval application. That is \$220,000, so about 1/9th of what you pay.

The CHAIRMAN. About 1/9th of what that would be.

Dr. SHUREN. Right.

The CHAIRMAN. So, it seems to me, I know that you're undergoing some conversations now, with the industry, on this, on user fees. But, I would just say this as the Chairman of this committee, that if we want better results from the FDA, more timely results and more transparency, and all the things that the IOM suggested we do, and we want to continue the 510(k) process, which they had said we shouldn't, we should come up with a new regime, and perhaps we'll be looking at that—then it seems to me that the industry is going to have to come up with just a little bit more resources to help the FDA do its job.

Thank you very much, Dr. Shuren. We'll move to our second panel.

Dr. SHUREN. Thank you.

The CHAIRMAN. And we have on our second panel—

Senator FRANKEN. Would you like me to—

The CHAIRMAN. Yes. I have the first one will be introduced first by Senator Franken from Minnesota.

Senator FRANKEN. As the witnesses take their places, I'm very pleased to introduce one of them. And that would be Professor Ralph Hall from my home State of Minnesota.

Professor Hall is a member of the faculty at the University of Minnesota Law School, where he teaches courses on food and drug law, as well as corporate compliance and negotiations. As an expert in medical device regulation, Mr. Hall is also the CEO of a small medical device company in Minnesota. And he also serves as counsel to the law firm of Baker and Daniels. With several decades of experience working with the FDA, Professor Hall has an understanding of the strengths of FDA's regulatory processes, as well as a clear view of the areas where it could be improved.

And thank you very much for joining us, Professor Hall.

The CHAIRMAN. Thank you, Senator Franken. Our next witness up is Dr. David Challoner who is vice president emeritus for Health Affairs at the University of Florida. His clinical specialty is in internal medicine with a sub-special interest in endocrinology.

He has previously served as Dean and Professor of Medicine at St. Luke's University School of Medicine. And from 1988 to 1990, following an appointment by President Reagan, he was chair of the President's Committee on the National Medal of Science.

Significantly, for today's discussion, Dr. Challoner chaired the IOM Committee that evaluated FDA's 510(k) review process and issued the report that I mentioned earlier, this past July.

Our third panelist, Dr. Gregory F. Curfman, who is executive editor of the *New England Journal of Medicine* and assistant professor of medicine at Harvard Medical School. Dr. Curfman also practices cardiology and internal medicine at Massachusetts General Hospital. He graduated from Harvard University Medical School in 1972. He's published numerous articles on FDA issues; particularly in the area of medical device regulation.

We thank you all for being here today. All of your statements will be made a part of the record in their entirety. I'm going to ask you to sum it up in about 5 minutes or so, and we'll go from left to right, just as I introduced everyone.

So, Dr. Hall, Professor Hall, I guess I should say. Oh, you have a J.D., that's a Doctor too, what the heck?

Mr. HALL. That's what they tell me.

The CHAIRMAN. You're first up. Please proceed.

STATEMENT OF RALPH F. HALL, B.A., J.D., PROFESSOR OF PRACTICE, UNIVERSITY OF MINNESOTA LAW SCHOOL, MINNEAPOLIS, MN

Mr. HALL. Thank you, Senator Franken, for the kind invitation. Chairman Harkin, members of the committee, I appreciate the option to come and discuss with you the medical device regulatory system. My disclosures are in the written materials. I need to be clear that I'm speaking on my behalf, and I don't speak for any other organization or individual, so these are my personal views.

My comments are going to focus on how the medical device system currently addresses safety and effectiveness. I want to start with three broad points.

The system has changed substantially over the roughly 35 years of its existence, as Congress has continuously worked to improve the system, as has FDA. That means that we need to look at the system as it exists today, not how it existed, perhaps 20 or 30 years ago.

I think it's also important to recognize that drugs and devices present very different regulatory challenges, and what is appropriate for one realm is not necessarily the right answer for others. Drugs, universally, have a potential systemic effect. Most devices do not. Many devices are tools, not the therapy itself, and tools present, then again, different regulatory needs and regulatory challenges. Devices operate and are improved in an iterative process with very short product lifecycles.

Clinical trial issues between drugs and devices are also very different. In the drug world, the gold standard are the double-blind

placebo-controlled studies. In many cases, in the device world, those studies simply are not appropriate. How does one do a double-blind placebo controlled study on a heart valve? You can't really cut somebody open, pretend to put in a heart valve, sew them up and see if it works?

So, we need different mechanisms here. In the device world, there's a greater importance, generally speaking, of engineering, design, material sciences—those types of hard sciences.

And, finally, as everyone has commented, there is a need here to balance safety, preventing risk with the benefits of access, particularly to innovative new products.

Devices present a broad range of risk, from implantable neuro-modulators to crutches, and there, we have three systems to address those. But it's critical to recognize that each of the classifications, are to provide a reasonable assurance of safety and effectiveness. We differ in how that's achieved, not in the fundamental objective.

Class I, simple devices—those are general controls, quality systems; class II, the 510(k), I'll get into this in a bit more detail use a variety of systems, including general controls, special controls, and the 510(k) system; class III products used a PMA. Within the 510(k) system, we actually have three major pathways or approaches to provide the reasonable assurance.

First of all, the 510(k) premarket system is not simply a physical comparison of one device with another. It's much broader than that. We start with a classification process by which, before the first one is reviewed, FDA in conjunction with experts, makes a risk-based safety and efficacy-based decision as to the appropriate classification. Which class best provides a reasonable assurance? That's subject to reclassification, depending upon new information.

Then, there are general controls, I mentioned, and special controls. Special controls are product-type specific. These can include clinical data, registries, performance standards, data testing requirements, design requirements, materials requirements all designed to ensure that there's this reasonable assurance of safe and effectiveness.

There's then the process of comparing the product, the new product, with the predicate, the old product—and that looks at, from other things, the track record of the product. Safety effectiveness data is available to the agency on those products.

If there's any new intended use, or a change in technology, and technology is defined very broadly, new safety and efficacy information has to be provided.

Second, there are quality systems, these include design controls, postmarket surveillance, looking at product trends, iterative designs, etc.

And finally, there are other regulatory systems to ensure the products are safe. For example, here a product is misbranded, if you can't label it for safe and effective use.

Congress did not create, and the agency is not implementing a system by which the agency has no choice but to approve an unsafe product. Data from multiple source indicate that most devices, the vast majority, are safe, and the area of greatest improvement is in

the quality system—that’s work I’ve done, Dr. Maisel, IOM’s conclusions, and also a recent FDA report.

In conclusion, the FDA uses the 510(k) system to provide a reasonable assurance of safety and effectiveness. There are multiple tools that exist within this system to ensure that those standards are reached.

I’ll be pleased to answer questions at the appropriate time. Thank you.

[The prepared statement of Mr. Hall follows:]

PREPARED STATEMENT OF RALPH F. HALL, B.A., J.D.

SUMMARY

A Critical Balance: FDA and the Reform of the Medical Device Approval Process

There are several key points that one should keep in mind in assessing the current medical device regulatory system.

First, drugs and devices present very different regulatory issues. What works well in one system may not be appropriate or effective in the other arena.

Second, the system created by Congress and implemented by FDA is intended to provide a reasonable assurance of safety and effectiveness for all products, regardless of classification. The means or method by which this is accomplished varies between Class I, II and III devices but the objective of safety and effectiveness does not. Class I uses “general controls” to provide this assurance, Class II uses special controls, general controls and the 510(k) system to provide this assurance of safety and effectiveness. Class III uses the PMA process. These are different means to achieve the same safety objective.

Next, the current 510(k) system gives FDA substantial authority to clear only products with a reasonable assurance of safety and effectiveness. FDA has multiple tools within the Class II/510(k) system beginning with initial product classification and extending through special controls and data submission requirements to assess product safety and effectiveness. FDA is not forced to clear a product just because it is physically identical to an older “predicate” product.

Finally, and perhaps most importantly, available data demonstrates that the system is working well from a safety perspective. Overall, products approved or cleared by FDA, including 510(k) products, have very good safety records. Of course, all stakeholders should always be striving to improve on this already good record. Improvements in QSR (quality systems) offer the greatest potential patient benefit.

Good afternoon, my name is Ralph F. Hall. I appreciate this opportunity to speak to this committee on these important medical device matters affecting patients, physicians, innovation and jobs. I am here to provide an overview of the medical device regulatory system, with particular focus on how the medical device regulatory system assesses product safety and effectiveness. In addition, I will discuss research I and others have done into the safety of 510(k) products.

I want to be clear that I am here speaking in my personal capacity and not on behalf of the University of Minnesota or any other entity.

BACKGROUND AND DISCLOSURES

To start, I serve as Professor of Practitioner at the University of Minnesota Law School where I concentrate my teaching, research and writing in the area of FDA law and compliance matters. In addition, I am part time Counsel at the law firm of Baker & Daniels where I work with clients on a variety of FDA matters and also provide counsel to a national 510(k) coalition. Finally, I serve as CEO at MR3 Medical LLC—a four person startup medical device company working on a new technology for cardiac rhythm devices generally regulated under the PMA process.

I. Medical Device Regulatory Overview

a. Medical Devices are Significantly Different Than Drugs

Many commentators simply compare drug regulation and device regulation. When differences between these systems appear, as they do, these commentators assume that there is some problem. It is absolutely critical to understand that there are important differences between drugs and devices that mandate some different regulatory approaches. These differences include:

- Drugs have a systematic effect on the body. A cardiovascular drug, for example, will also circulate throughout the body and potentially impact the liver, kidneys, muscles, lung, brain, etc. The vast majority of all devices do not have any systemic effect. Thus testing issues and needs are fundamentally different between drugs and devices.

- Medical device development is an iterative process with substantially shorter life cycles. That is not the case with drugs. Drug life cycles cover several decades while device life cycles are often measured in months. Also, drugs do not have the iterative development process found in devices. Any molecular change in a drug creates a new molecule and a whole new set of issues and questions. Most iterative changes to a device (making a catheter longer, for example) do not create new therapeutic issues.

- Essentially all drugs are the actual therapy. Many devices are actually a tool by which a physician delivers therapy, not the therapy itself. For example, a scalpel is a tool by which a medical intervention is performed. In such cases, FDA primary focus should be on whether the tool is performing as required, not whether the therapy such as an appendectomy (a physician decision) is effective.

- Engineering, design controls, human factors and material sciences are much more important to devices than to drugs. As detailed below, most postmarket safety issues with medical devices involve engineering, design, materials and manufacturing issues, problems not discoverable through clinical risks. Available data indicates that this is a different pattern from drugs. This difference in risk should impact premarket requirements.

- Devices span a much greater risk profile than drugs. While essentially all drugs pose some systemic questions that is not the case with devices. There is a world of difference between the risk/benefit of an implantable neuromodulator and that of a crutch. This huge risk spectrum mandates phased regulation of medical devices.

- There is incredible product differentiation within medical devices. Medical devices include diagnostic tools that never touch a patient, multimillion dollar pieces of capital equipment such as CT scanners, simple tools like a scalpel or bandaid and complex implantable devices such as an ICD.

- Device regulation includes robust and broad quality system requirements (often referred to as QSR requirements).

The overall impact of these differences is that device regulation needs different premarket requirements, a risk-based approach to regulation and an emphasis on quality systems.

b. Device Regulatory Overview

By statute and regulation, all medical devices, regardless of risk classification, are to have a “reasonable assurance of . . . safety and effectiveness” before they are marketed.¹ What differs is the method by which FDA and other stakeholders assess whether there is such assurance of safety and effectiveness for different classes of device.² These different ways to provide this assurance of safety and effectiveness and the complex language and statutory systems for medical device regulation can lead to inadvertent confusion and misunderstanding. However, all products of whatever risk classification must provide this reasonable assurance of safety and effectiveness.³

Because medical devices differ so much—from a tongue depressor to a multi-million dollar robotic surgical system—one regulatory approach does not fit all. To address this, Congress created a three-tier regulatory structure.

- Class I devices are the simplest, lowest risk devices. These include crutches, tongue depressors and scalpels. These products usually do not go through a premarket review and are generally referred to as Class I exempt.

- Class II devices are medium risk products such as angioplasty catheters. Class II devices generally go through the 510(k) system.

- Class III devices are the highest risk devices and include heart valves and pacemakers. These products reach market through the PMA process.⁴

¹ 21 U.S.C. § 393(b)(2)(C).

² It goes without saying that all therapeutic products have some risks. The objective is to ensure a positive risk/benefit for each product.

³ Ensuring patient access to beneficial products is also critical. As such, FDA is also charged with promoting product innovation. While the focus of my comments is on the safety aspects of the device regulatory system, one cannot forget the importance of making innovative products available to physicians and patients.

⁴ This is a general description. Some higher risk Class I devices must go through the 510(k) system and some higher risk Class II products require a PMA. There are also some other path-

Each device class, with some overlaps, uses a different method to provide assurances of safety and effectiveness.

Class I products are those for which “general controls” are “sufficient to provide reasonable assurance of the safety and effectiveness of the device”.⁵ General controls can include, as appropriate, manufacturing controls, labeling, quality systems, etc.

Class II products are those for which general controls by themselves are not sufficient but for which “special controls” do provide a reasonable assurance of safety and effectiveness. These products use a different, multipronged system to provide the reasonable assurance of safety and effectiveness. Specifically, Congress provided that a Class II device is:

A device which cannot be classified as a Class I device because the general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness of the device, and for which there is sufficient information to establish special controls to provide such assurance [of safety and effectiveness], including the promulgation of performance standards, postmarket surveillance, patient registries, development and dissemination of guidelines (including guidelines for the submission of clinical data in premarket notification submissions in accordance with section 510(k)), recommendations, and other appropriate actions as the Secretary deems necessary to provide such assurance.⁶

As mandated by Congress, Class II devices generally must receive clearance under the 510(k) system described in more detail below and as part of that process must satisfy both special controls and general controls. 510(k) submissions can include clinical data, bench testing, labeling, reports on prior investigations, etc.

The 510(k) system (described in more detail below) generally requires a product to establish that it is “substantially equivalent” to a predicate 510(k) device. Substantial equivalence is more than a physical comparison of one device to another. 510(k) products must also meet all special controls, all applicable standards and QSR requirements. FDA has the authority under the 510(k) system to request a wide variety of data, including clinical data, bench testing, proposed labeling, and material information, as part of its review of a 510(k) submission.⁷ This submission explicitly includes a variety of safety and effectiveness information.⁸

Class III products must go through the PMA process.⁹ This often includes clinical testing and submissions include detailed manufacturing information, labeling, bench test data, etc. FDA reviews this data for safety and effectiveness.

It is important to understand that there are a number of other systems that also impose safety and effectiveness controls on products as part of an integrated system to provide a reasonable assurance of safety and effectiveness. For example, the QSR system¹⁰ requires design controls to help ensure a safe and effective design. There are also product and adverse event trending requirements, reporting requirements, etc. In addition, FDA has the authority to require postmarket testing on higher risk devices (including specifically Class II/510(k) products).¹¹ There are also general labeling requirements including 21 U.S.C. § 352(f) which mandates that a product labeling include “adequate directions” for safe use.

II. The 510(k) System Includes Safety and Effectiveness Considerations

The 510(k) system has been the focus of recent attention. The 510(k) system does consider safety and effectiveness. Stated differently, current FDA authority gives the agency multiple pathways to keep an unsafe 510(k) product off the market, require whatever testing or data is needed to establish safety and effectiveness and remove unsafe products from the market.

From the beginning, Congress intended for the 510(k) system (and the substantial equivalence part of that process) to include safety and effectiveness determinations. As FDA itself explained to the IOM committee in March 2010, Congress intended the 510(k) substantial equivalence standard to be flexible in order to assure safety and effectiveness. The 510(k) legislative history states:

ways to market including the HDE process and the rarely used PDP system. For our purposes these alternative pathways are not relevant.

⁵ 21 U.S.C. § 360c(a)(1)(A)(i).

⁶ 21 U.S.C. § 360c(a)(1)(B).

⁷ 21 CFR §§ 807.87, .90, .92 and .93 set forth more details about the content and format of a 510(k) submission.

⁸ See, for example, 21 CFR § 807.92(c)(3).

⁹ 21 U.S.C. § 360e.

¹⁰ QSR requirements are generally found in 21 CFR § 820.

¹¹ 21 U.S.C. § 360l. 21 U.S.C. § 360l(a)(1)(A) explicitly includes Class II devices within the group of products subject to so-called “522 orders.”

The [congressional] committee believes that the term [substantial equivalence] should be construed narrowly where necessary to assure the safety and effectiveness of a device but not narrowly where differences between a new device and a marketed device do not relate to safety and effectiveness.¹²

Note the specific linkage of the substantial equivalence determination to safety and effectiveness.

In order to see how the Class II/510(k) system ensures an assessment of safety and effectiveness, one must understand the process from the start. The 510(k) process actually begins before the first product is reviewed. By statute, FDA is obligated to classify each product type into Class I, II, or III. This classification process includes expert advisory panels, assessment of data and an opportunity for stakeholder input.¹³ The purpose of the classification process is to determine which oversight system is best positioned to provide assurances of safety and effectiveness. The product classification is based on safety and effectiveness considerations as confirmed by the implementing regulation which states:

(b) *In determining the safety and effectiveness of a device for purposes of classification*, establishment of performance standards for Class II devices, and premarket approval of Class III devices, the Commissioner and the classification panels will consider the following, among other relevant factors:

- (1) The persons for whose use the device is represented or intended;
- (2) The conditions of use for the device, including conditions of use prescribed, recommended, or suggested in the labeling or advertising of the device, and other intended conditions of use;
- (3) The probable benefit to health from the use of the device weighed against any probable injury or illness from such use; and
- (4) The reliability of the device (emphasis added).¹⁴

Further, by statute, if a product is implantable or is used to support or sustain human life, the default classification is Class III/PMA unless the agency and classification panel specifically determine that the Class II/510(k) process is sufficiently robust and that Class III/PMA systems are not necessary to provide reasonable assurance of safety.¹⁵ Thus, before any device is even eligible for 510(k) review, FDA, in concert with expert classification panels, has made a determination that the Class II/510(k) system provides an adequate assurance of safety and effectiveness for that product type.¹⁶ Therefore, every 510(k) product type has been assessed and it has been determined that the 510(k) system provides the adequate assurance of safety and effectiveness.

Once classified, the 510(k) system uses the concept of “substantial equivalence” as a method to assess safety and effectiveness.¹⁷ The policy behind the 510(k) system is that once it has been determined that a product type is safe and effective for its intended use, future products that are “substantially equivalent” to the initial product and which meet all other regulatory requirements are likewise safe and effective. Substantial equivalence is more than a physical comparison of one product to another.

The 510(k) submission provides the information to FDA by which it can determine that the safety profile of the new product meets the established safety profile of the prior (or predicate) device, all special controls or similar requirements have been met and that the product is otherwise safe and effective for its intended use. The submission specifically includes safety information.

For example, 21 CFR § 807.92(c)(3) states that a 510(k) summary must include:

The conclusions drawn from the nonclinical and clinical tests that demonstrate that the device is as safe, as effective, and performs as well as or better than [the predicate device].

21 U.S.C. § 360c(i)(3)(A) requires a 510(k) submission to include adequate information respecting the safety and effectiveness of the device and/or to make that in-

¹² See FDA’s presentation to IOM available at <http://www.iom.edu/Activities/PublicHealth/510KProcess/2010-MAR-01.aspx>.

¹³ 21 U.S.C. § 360c(c) and (d).

¹⁴ 21 CFR § 860.7(b).

¹⁵ 21 U.S.C. § 360c(c)(2)(C).

¹⁶ As GAO and a number of commentators have noted, FDA is delinquent in classifying 26 out of, I believe, approximately 1,800 product types. These products continue to be reviewed under the 510(k) system. FDA is currently in process of rectifying this situation and completing the classification of these remaining products.

¹⁷ In reviewing 21 U.S.C. § 360c—the key statutory section relating to Class II/510(k) devices—one can see that Congress used the term “safety” with regard to Class II/510(k) products more than 17 times by my count. One can only wonder why Congress would discuss safety so many times unless Congress intended for the 510(k) to consider safety and effectiveness.

formation available. Under 21 U.S.C. § 360c(i)(3)(B), this summary shall include detailed information regarding adverse health effects relating to the product and this information shall be made available to the public.¹⁸

In addition to data submission requirements, Congress has given FDA another powerful tool to ensure product safety and effectiveness. The 510(k) system makes explicit use of “special controls” to ensure safety and effectiveness and any 510(k) product must satisfy all special control requirements. Under 21 U.S.C. § 360c(a)(1)(B), special controls are explicitly used to provide a reasonable assurance of safety and effectiveness. Special controls can include clinical data requirements, performance standards, patient registries, guidance documents, etc. Any new product must comply with all applicable special controls. These special controls are used in addition to physical identity to establish safety and effectiveness.

Products can and usually do evolve over time. The “substantial equivalence” process is designed to subject any new product use or technology to an explicit safety and effectiveness review. Congress specifically required FDA to assess new intended uses and new technologies for safety and effectiveness.¹⁹

There is, of course, the concern that changing information or new data may call into question prior classification decisions or special controls. Congress anticipated this concern and explicitly established reclassification processes under 21 U.S.C. § 360c(e) that FDA can use (and any stakeholder can request) in the event of new information. This reclassification process can address any new information and either up classify or down classify a device type as the data directs. Any down classification from Class III to Class II requires a determination that Class II special controls provide a reasonable assurance of safety and effectiveness. Likewise, FDA can create new or enhanced special controls under 21 U.S.C. § 360c(a)(1)(B) to address new safety or effectiveness issues.

Congress has provided FDA with other tools to ensure that an unsafe Class II product does not reach the market. For example, FDA has the authority to ban unsafe devices,²⁰ and ensure that the product labeling permits safe use.²¹ Any product that has been removed from the market “at the imitative” of FDA or has been found to be misbranded or adulterated by a court cannot be used as a predicate to a later product.²² This is one method by which a “bad” predicate cannot be used for future products. Other tools include the ability to develop new or enhanced special controls and to require additional data to be submitted.

While the term “substantial equivalence” can sound like merely a physical comparison of one product to another, an understanding of the overall 510(k) system demonstrates that much more than physical identity is needed to be cleared for marketing. Before a product can be deemed to be “substantially equivalent” and the product legally marketed the system requires, among other requirements:

- Product classification into the 510(k) system based on safety and effectiveness assessments.
- Compliance with special controls explicitly intended to provide assurances of safety and effectiveness.
 - Compliance with all applicable standards and guidances.
 - Assessment of any new intended uses or new technology for safety and effectiveness.
 - Submission of safety and effectiveness data and adverse health information.
 - Compliance with all applicable general controls.
 - Compliance with QSR requirements.

As such, FDA has multiple avenues to assess and address any safety or effectiveness issues.

III. Key Examples

I will now apply the 510(k) system to the three key product situations to demonstrate that, in each case, FDA has the authority to assess safety and effectiveness.

¹⁸One is hard pressed to argue that Congress intended FDA to have this safety and effectiveness information and then mandated that FDA ignore that data in making 510(k) clearance decisions.

¹⁹21 U.S.C. § 360c(i)(1). Note that new technology is broadly defined to ensure that product changes are reviewed for safety and effectiveness. 21 U.S.C. § 360c(i)(1)(B).

²⁰21 U.S.C. § 360f(a).

²¹21 U.S.C. § 352(f). Even if a product is “substantially equivalent” to another, if it cannot be labeled so that it can be used safely, the product is misbranded and distribution of such a product triggers civil and criminal liability.

²²21 U.S.C. § 360c(i)(2).

a. The New Product

There are situations in which a product is developed for which there is no predicate. Normally, these products are automatically, by application of statute, classified as PMA products.²³ Unless there is an actual reclassification, these products go through the PMA process and so there is no question about the robustness of the 510(k) process.

However, such a product may well be a medium risk product and so best regulated as a Class II/510(k) product. In these cases, the product can be classified as a Class II/510(k) product pursuant to the “*de novo*” process under 21 U.S.C. § 360c(f)(2). This classification process explicitly considers whether the product can be safely regulated under Class II systems including special controls.

As such, no “new” product can be regulated under the 510(k) system unless FDA has made an explicit determination that the 510(k) system provides adequate assurances of safety and effectiveness.

b. Changes to an “Old” Product

The next fact pattern involves an existing product, already in the Class II/510(k) system, to which the company is making some change. This can be a new intended use or some change in technology. In each case, the change in the product must be explicitly assessed for safety and effectiveness.²⁴ The product cannot be cleared if the product raises some new issue of safety or effectiveness.²⁵

Remember that one of the core concepts of the 510(k) system is that once safety and effectiveness has been determined, like products can establish safety and effectiveness based on the prior assessment. Of course product changes can challenge this concept and so Congress as decreed and FDA has insisted that any change in the use of the product or the technology (broadly defined) must be assessed to ensure safety and effectiveness. Thus, Congress and FDA have assured that product iterations or changes will be assessed for safety and effectiveness.

c. Continued Marketing of an “Old” Product

The final challenge is the one that seemed to bother the IOM committee and others the most and this is the old product that hasn’t changed.²⁶ Some seem to believe that these “old” products have never been assessed for safety and effectiveness and that FDA is bound to clear any such product without considerations of any safety or effectiveness issues. This is simply not the case.

FDA has multiple authorities to keep an unsafe 510(k) product—even if literally identical to an old product—off the market.

To start, all products have been assessed for safety and effectiveness issues through the classification process.²⁷ Even if the product existed before 1976, it has been specifically assessed and a determination made that products of that type can be regulated under the Class II/510(k) system for safety and effectiveness.²⁸ Just because a product was on the market before 1976 does not mean that it is part of the 510(k) system.

The related question is what happens if new information is developed on an “old” product subsequent to its classification. First, FDA has access to such information through any number of sources. Importantly, Congress has decreed that the company must include adverse health information in its 510(k) submission.²⁹

Once such information comes to FDA’s attention, FDA has any number of approaches to prevent an unsafe product from being cleared via the 510(k) system. Examples of these tools include:

- Creating new or enhanced special controls to mitigate or eliminate the newly discovered risk.³⁰
- Reclassifying the device into Class III.³¹

²³ 21 U.S.C. § 360c(f)(1).

²⁴ 21 U.S.C. § 360c(i) and 21 CFR § 807.

²⁵ FDA’s internal processes and flow charts reinforce the fact that any change in intended use or technology is assessed for safety and effectiveness. There is a “not substantially equivalent” (“NSE”) determination if there is some new question of safety or effectiveness.

²⁶ This includes situations in which the old, unchanged, feature of the product presents some new safety or effectiveness issue.

²⁷ I recognize that a few products (some number less than 26 out of approximately 1,800 product codes) have not completed this process. As many others have previously said, this process must be completed. FDA is currently in the process of doing so.

²⁸ See 21 U.S.C. § 360c(c) and (d) and 21 CFR §§ 807 and 860 for more details.

²⁹ 21 U.S.C. § 360c(i)(3).

³⁰ 21 U.S.C. § 360c(a)(1)(B).

³¹ 21 U.S.C. § 360c(e).

- Creating or adopting new guidances or standards.
- Requiring new labeling to mitigate or eliminate the issue (or concluding that such improved labeling would not be effective and thus the product is misbranded).³²
- Imposing postmarket obligations.³³
- Banning the device.³⁴
- Utilizing QSR requirements to address the issue.³⁵

Thus, each product type is reviewed for safety and effectiveness issues at the time of initial classification. Post classification, FDA has multiple statutory and regulatory authorities available to prevent an unsafe product from being cleared.

Congress did not create—and FDA is not implementing—a regulatory system under which FDA has no choice but to clear an unsafe device.

IV. FDA in Fact Makes Safety and Effectiveness Determinations in Product Clearances

How the 510(k) system actually works is best demonstrated by looking at actual product clearances. In many cases, FDA specifically indicates in the clearance documents that the product in question is safe and effective for its intended uses.

For example, Via Biomedical, Inc.'s Stent Graft Balloon Catheter has been determined substantially equivalent and cleared for market distribution.³⁶ Included in the 510(k) summary was the following:

The Stent Graft Balloon Catheter underwent mechanical, performance, and Biocompatibility testing to verify that the device functions in a **safe and effective** manner. The results of the tests provide reasonable assurance that the device has been designed and tested to assure conformance to the requirements for its indications for use.³⁷ (emphasis added).

Becton, Dickinson and Company's (Becton) BD Flu+ Syringe was cleared for market on July 2, 2009. As part of its submission, Becton expressly indicated that [d]esign [v]erification tests were performed based on the risk analysis performed, and the results of these tests demonstrate that the BD Flu+ Syringe performed in an equivalent manner to the predicate device and is *safe* and *effective* when used as intended.³⁸

Likewise ArthroCare's Bone Cement Opacifier was cleared under 510(k) after the FDA confirmed that the performance testing and device comparison demonstrated that the subject device [was] substantially equivalent to the predicate device, **and is safe and effective for its intended use**.³⁹ (emphasis added).

There are numerous other examples of 510(k) submissions that have been included in the safety and effectiveness data and have been assessed by FDA for safety and effectiveness. A few examples include the Master Healthcare's Easy Touch Insulin Syringe,⁴⁰ ZOLL Circulation's Central Venous Catheter and Thermal Regulating System⁴¹ and Medtronic's Cardiopulmonary Centrifugal Blood Pump.⁴² All of these submissions included performance data specifically relating to the safety and effectiveness of the device as part of the 510(k) clearance.

As these and other examples demonstrate, FDA in fact considers safety and effectiveness in product decisions.

Furthermore, in numerous presentations, guidance documents and public statements, FDA has said that the 510(k) system includes safety and effectiveness protections.

³² 21 U.S.C. § 352(f).

³³ 21 U.S.C. § 360l.

³⁴ 21 U.S.C. § 360f.

³⁵ 21 CFR § 820.

³⁶ 510K Summary from Via Biomedical, Inc., on the Stent Graft Balloon Catheter (May 29, 2009), http://www.accessdata.fda.gov/cdrh_docs/pdf9/K091624.pdf.

³⁷ *Id.* (emphasis added).

³⁸ 510K Summary of Safety and Effectiveness from Becton, Dickinson and Company on the BD Flu+ Syringe (Jul. 2, 2009), http://www.accessdata.fda.gov/cdrh_docs/pdf9/K091377.pdf.

³⁹ 510K Summary from Becton, Dickinson and Company on BD Flu+ Syringe, http://www.accessdata.fda.gov/cdrh_docs/pdf4/K042947.pdf. The device was not found to be as safe as the predicate, but there was an independent assessment. The device was both substantially equivalent to the predicate as well as safe and effective.

⁴⁰ 510K Summary from Masters Healthcare on the Easy Touch Insulin Syringe (May 14, 2009) http://www.accessdata.fda.gov/cdrh_docs/pdf9/K091474.pdf.

⁴¹ 510K Summary from ZOLL Circulation for Venous Catheter and Thermal Regulating System (Oct. 12, 2010), http://www.accessdata.fda.gov/cdrh_docs/pdf10/K101987.pdf.

⁴² Summary of Safety and Effectiveness from Medtronic for the Cardiopulmonary Centrifugal Blood Pump (Jun. 21, 2010), http://www.accessdata.fda.gov/cdrh_docs/pdf10/K100631.pdf.

In summary, it can be seen that products going through the 510(k) system are assessed for safety and effectiveness beginning with the initial classification process. FDA has a variety of tools including special controls to ensure product safety. Congress did not create a system by which literally thousands of devices have been cleared without protecting patient safety.

V. Medical Device Safety Study Summary

The actual safety of medical devices is, of course, of prime importance to patients, physicians and other stakeholders.

There have been several studies of medical device safety (or reasons for medical device problems) over the past 2 years. These include a study I have done (and presented to the IOM 510(k) committee), a study by Dr. William Maisel (also presented to the IOM 510(k) committee) and a recent report by FDA itself.

In my view, these studies, individually and together, support two key conclusions:

(1) There is no evidence of any overall systemic issue with the safety of 510(k) products; and

(2) The primary cause of medical device safety recalls are quality system issues, not a lack of premarket clinical testing. I will also note that the IOM 510(k) committee itself also found no evidence of a systemic issue with the safety of 510(k) products. The committee has explicitly stated: “The committee is not suggesting that all, many, or even any medical devices cleared through the 510(k) process and currently on the market are unsafe or ineffective.”⁴³

My comments will focus on the study I performed assessing the overall safety profile of medical devices approved or cleared by FDA from 2005–9 by using Class I safety recall data. This research was funded by the Ewing Marion Kauffman Foundation, a private nonpartisan foundation based in Kansas City, MO. Their generous support made this research possible. The Kauffman Foundation has given me complete academic freedom to pursue this research.⁴⁴

This study⁴⁵ evaluated Class I (or high risk) recalls of all medical devices, regardless of whether they were approved through the PMA system, cleared through the 510(k) process or were otherwise exempt.

The key conclusions from my research are as follows:

(1) Overall, 510(k) regulated medical devices have an excellent safety profile. Over 99.5 percent of 510(k) submissions assessed during this study period did not result in a Class I safety recall. Over 99.7 percent of 510(k) submissions did not result in a Class I recall for any reason relevant to the 510(k) premarket system.

(2) Products approved through the PMA system also have an excellent safety record. Again, greater than 99.5 percent of PMA or sPMA submissions do not result in a Class I safety recall during the study period.

(3) Very few (less than 9 percent), Class I recalls during the study period involve possible undiscovered clinical risks. As such, increased preapproval clinical testing would not have any meaningful impact on reducing the number of Class I recalls.

(4) The majority (approximately 55 percent) of all Class I recalls involve problems or issues that arose after market release and could not be affected by premarket approval systems or requirements. For example, a manufacturing mistake made 3 years after FDA approval or clearance may trigger a Class I recall. However, any premarket requirements such as clinical testing are irrelevant to preventing such a recall.

(5) A very significant majority (over 90 percent) of all Class I recalls (including both premarket and postmarket issues) are directly related to quality system issues (so-called QSR systems⁴⁶). Improved QSR systems will have the greatest effect in reducing the number of Class I recalls.

(6) My study did identify a bolus of Class I recalls in two device types—automatic external defibrillators (“AEDs”) and infusion pumps. Any changes to the premarket

⁴³ See IOM report brief available at <http://www.iom.edu/Reports/2011/Medical-Devices-and-the-Publics-Health-The-FDA-510k-Clearance-Process-at-35-Years.aspx>.

⁴⁴ I want to thank Amanda Maccoux, Mark Jones, Chris Walker and Ron Song—the research assistants at the University of Minnesota Law School—who spent long hours doing the detailed data collection and coding required for this study. Their talents, hard work and dedication are vital to this research and I appreciate all that they did.

⁴⁵ An earlier version of this research into the safety of medical devices through an analysis of safety recalls was presented to the Institute of Medicine committee reviewing the 510(k) system and reviewed with FDA.

⁴⁶ QSR requirements are intended to provide “cradle to grave” product quality in a closed loop, learning system. QSRs include design input and processes, design validation, product testing, manufacturing controls, process controls, change controls, management review and postmarket assessments. See, generally, 21 CFR § 820.

review process should be targeted to demonstrate problems rather than applied in some random, shotgun way.

(7) Finally, one should not confuse classification for premarket review processes with recall classification. These are very different things and serve very different purposes.

VI. Study Background

The need for the research that I will describe goes back several years when a number of stakeholders started to question the robustness of the 510(k) system. I was particularly struck by the fact that there was no good, objective data to support or refute the assertion that the 510(k) system needed to be changed because of these presumed safety issues.

Given my concerns over the lack of hard data, I commenced a study (with the able assistance of four research assistants) assessing the safety performance of FDA approval processes. To my knowledge, this was the first study designed to systemically assess the safety performance of the 510(k) system.

VII. Study Methodology

This study assessed the overall safety profile of medical devices approved or cleared by FDA from 2005–9 by using Class I safety recall data.

Class I safety recalls were chosen as the measure of safety as these recalls involve any medical device problem posing any significant risk of serious health consequences to patients and also correctly exclude risks considered as part of the approval or review process. Class II recalls involve generally remote risks to patients and Class III recalls involve minimal or no risk to patients. FDA, not industry, is responsible for assigning the recall classification.

Note that the Class of recall assigned by FDA is independent of the product’s device classification. For example, no one would argue that a tongue depressor is a high-risk device or needs a clinical trial. For premarket purposes it is classified as a low-risk, exempt device. However, if the tongue depressor gets contaminated with deadly bacteria because of product tampering or some manufacturing problem, there is a significant risk to patients. This would be a high-risk or Class I recall even though for premarket review purposes it is a low-risk device.

Using FDA databases, we identified all Class I recalls posted by FDA on public databases during 2005–9. We first combined all duplicate recalls into one data set of unique or stand alone recalls. (FDA may have several recall announcements and thus there may be multiple data entries for the same issue because of different package configurations, brand names or product sizes).

There were 118 unique recalls identified. We then coded each recall for a number of factors including regulatory pathway, medical specialty, whether implantable and three letter product code. We also coded each recall with 1 of 13 reasons for recalls. Generally speaking, these 13 recall reasons can be combined into three broad groupings of premarket issues (*i.e.*, something that could, at least theoretically, have been discovered during a premarket review process), postmarket issues and miscellaneous (counterfeit and “quack” products). We used FDA Web sites and publicly available information for this coding.

This study must be assessed in light of the following factors and limitations:

(1) First, we relied entirely upon publicly available data. We did not identify any meaningful errors in this data but did not conduct any structured assessment of the accuracy of FDA’s data.

(2) Second, while companies are obligated to report recalls, there may be situations in which the company failed to meet this obligation. We believe that any such missing recalls would tend to be small and not common because of the penalties for non-compliance and the variety of information sources that would disclose any such recall. Importantly, there is no reason to believe that the distribution of the causes of such recalls would be different than the data we had.

(3) Third, we reviewed Class I recalls and not Class II recalls. (FDA defines a Class II recall as a situation in which the problem might cause a temporary health problem, or pose only a slight threat of a serious nature.) We believe that Class I recalls represent all recalls with any meaningful risk to patients and so that represents a valid safety picture. Remember that Class II recalls are for remote risks or low impact problems. Class I recalls represent the majority of actual patient risk and tend to err in the direction of higher rather than lower classification. Risks as low as 1/20,000 have been classified as Class I recalls thus demonstrating the breadth of risks captured by Class I recalls.

(4) Anecdotal review of some Class II recalls indicate (but does not establish) the same general pattern of reasons for recalls between Class I and Class II recalls.

(5) Finally we did not assess any effects of various regulatory systems or actions on patient access to new products, innovation or the economy in general.

We also determined the percentage of 510(k) submissions that resulted in a subsequent Class I recall. The numerator for this calculation is the number of recalls. The denominator is the number of submissions. The denominator for this calculation is a close estimate as there is no direct connection between the date of the submission and the subsequent recall. For example, a recall for a design defect might occur within a month after market release while a recall for a manufacturing error or packaging mistake could occur literally years after approval or clearance.

We determined an annualized number of submissions by taking the average number of submissions for a 10-year period (2000–2009) and annualizing that number. We used this number for all percentage calculations. Those percentages, however, are approximations due to this data challenge.

VIII. Study Results and Data

Initially, we looked at the reasons for recalls for these 118 Class I recalls. We determined the reason for the recall by examining FDA's public data bases and also reviewing publicly available information including physician notification letters and SEC filings. I was responsible for all decisions relating to the reason for recall. I blindly recoded 10 percent of the recalls and had a complete match with the initial determination of the reason for the recall.

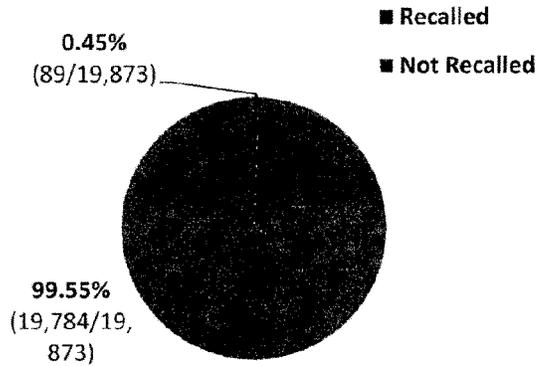
As shown below, the majority of all recalls (approximately 55 percent) are for postmarket issues. For these recalls, no change in the premarket 510(k) or PMA process would affect the recall occurrence or frequency.

	Total recalls	Recalls for premarket issues	Recalled for postmarket issues	Recalled for other issues	Percent of recalls to total recalls
Class I or u/k	7	1 (14.2%)	6 (85.7%)	0 (0%)	5.9
510(k)	95	43 (45.3%)	46 (48.4%)	6 (6.3%)	80.5
PMA	16	7 (43.8%)	9 (56.3%)	0 (0%)	13.56
Total	118	51	61	6	118

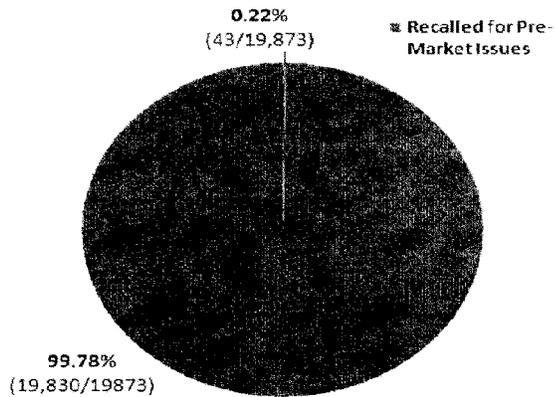
As seen below, a very small percentage of 510(k) submissions led to a Class I recall during our study period. The first chart shows the ratio of 510(k) submissions to all Class I recalls and the second chart shows the ratio of 510(k) submissions to Class I recalls related to any theoretical premarket issue.

Based on this data, approximately 99.55 percent of all 510(k) submissions did not result in a Class I recall for any issue during the study period. More importantly for assessing the 510(k) process, approximately 99.78 percent of all 510(k) submissions did not result in a Class I recall for any reason related to the premarket process. Stated differently, the maximum theoretical impact of any change in the 510(k) system would be on 0.22 percent of all 510(k) submissions. This data also demonstrates that additional premarket clinical testing would be ineffective in reducing Class I safety recalls.

Total 510(k) Recalls for the Last 5 Years - All Causes (2005-2009)



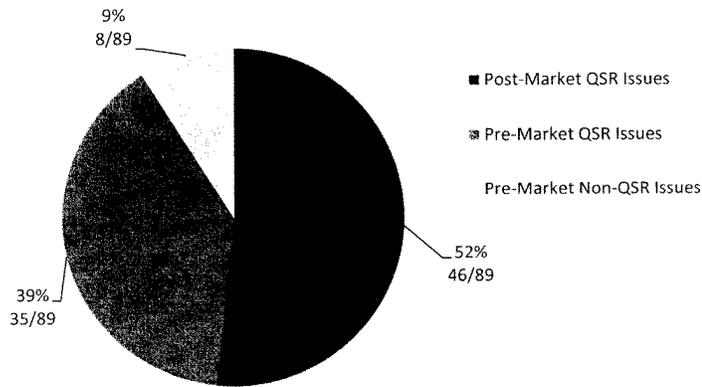
Total 510(k) Recalls for the Last 5 years – Premarket issues



Total 510(k) Submissions in 10 years	39,747
Average Submissions in 5-year time period	19,873
Total 510(k) Recalls for 2005–2009	89
Total 510(k) Recalls for Premarket Issues for 2005–2009	43

The number of recalls related to premarket issues is most relevant in assessing whether the 510(k) system is adequately addressing patient safety during the review process. This data demonstrates that postmarket issues, not premarket processes, should be the focus to improve patient safety.

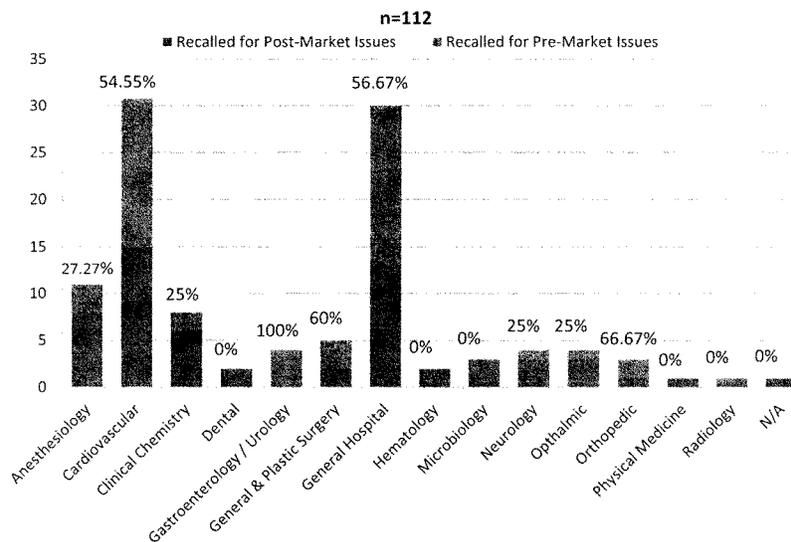
This conclusion is reinforced when we reviewed the role of quality systems in recalls. As shown below, over 90 percent of all Class I safety recalls are related to quality system issues and not to other factors such as a lack of clinical trials.



Clearly, this data demonstrates that all stakeholders should concentrate on QSR systems such as design control and bench testing—not the 510(k) submission system—as the most effective way to provide greater patient safety.

We also did sub-analysis by product type and medical specialty. Such analysis can be used to identify concentrations of issues for further investigation by FDA, industry and other stakeholders. As seen below, Class I recalls are concentrated in several product types.

Recalls by Medical Speciality, Percentage of Recalls for Pre-Market Issues



MEDICAL SPECIALITY

Further analysis indicated that automatic external defibrillators (AEDs) and infusion pumps accounted for 28 percent of all Class I recalls and accounted for a substantial part of the bolus or recalls seen in the cardiovascular and general hospital categories. Within the past 9 months, FDA has triggered new regulatory initiatives for both AEDs and infusion pumps.

Our confidence in our study design and results has been bolstered by subsequent studies by others such as FDA itself, Dr. Maisel and Battelle finding very similar numbers and reasons for Class I recalls.

IX. Study Conclusion

This study demonstrates that very few 510(k) medical device submissions—less than 0.5 percent—become the subject of a Class I safety recall. Even in this small number of Class I recalls, the majority of Class I recalls involve postmarket issues such as manufacturing mistakes, and are focused around two product categories (cardiovascular and general hospital). These recalls involve quality system issues, not premarket issues. Overall, in excess of 90 percent of all recalls appear to involve quality system issues.

Our study shows that FDA has a very positive safety record in its 510(k) clearance decisions.

X. Conclusion

The current 510(k) system gives FDA substantial authority to clear only products with a reasonable assurance of safety and effectiveness. FDA has multiple tools beginning with initial product classification and extending through special controls and data submission requirements to assess product safety and effectiveness.

Overall, products approved or cleared by FDA have very good safety records. Of course, all stakeholders should always be striving to improve on this already good record. Improvements in QSR (quality systems) offer the greatest potential patient benefit.

Again, I appreciate the opportunity to present to the committee and would be happy to answer any questions.

STATEMENT OF DAVID R. CHALLONER, M.D., VICE PRESIDENT FOR HEALTH AFFAIRS, EMERITUS, UNIVERSITY OF FLORIDA AND CHAIR, COMMITTEE ON THE PUBLIC HEALTH EFFECTIVENESS OF THE FDA 510(K) CLEARANCE PROCESS, INSTITUTE OF MEDICINE OF THE NATIONAL ACADEMIES, GAINESVILLE, FL

Dr. CHALLONER. There we go, thank you.

I'm vice president for Health Affairs Emeritus at the University of Florida, and I also served as chair at the Institute of Medicine in this committee on the public health effectiveness of the 510(k) clearance process.

The IOM is the health arm of the National Academy of Sciences—an independent, non-profit organization that provides unbiased and authoritative advice to decisionmakers and the public.

I am accompanied this afternoon by several members of the NRC and IOM staff, and by Mr. William Vodra, who was also a member of my committee.

The IOM was asked by the FDA to review the 510(k) clearance process, and to answer two questions, as has already been pointed out. Does the current 510(k) process optimally protect patients, and promote innovation and support of public health? And if not, what legislative, regulatory or administrative changes are recommended to optimally achieve the goals of the 510(k) process?

The IOM assembled an expert committee of which I was chaired to address this task. The committee met in person 6 times over an 11-month period to gather evidence, deliberate on its findings and recommendations, and write its report. That report, then, underwent a rigorous, independent, external review before being released in July of this year. More detailed information on the committee's findings and recommendations is included with my longer, written statement.

The committee's task was challenging for several reasons—devices regulated within the 510(k) process encompass a broad range of function, benefits, and risks. Also, the 510(k) process is not a standalone process, but is part of a larger regulatory system that is dependent upon all the components functioning optimally to ensure the public health. And finally, the 510(k) process was continuing to evolve as the committee was conducting its work.

The committee evaluated legislative, regulatory and administrative components of the 510(k) process, and other related components of medical device regulation. We came to the conclusion that the 510(k) process, as outlined in law, generally does not evaluate the safety and effectiveness of a device, only the new device's similarity to a predicate.

Furthermore, the 510(k) process cannot be transformed into a premarket evaluation of safety and effectiveness, as long as the standard for clearance is substantial equivalence to any previously cleared device.

I want to emphasize that we believe the FDA has done an admirable job of protecting the public, given the constraints on its regulatory authorities, and limited resources, as we've heard discussed earlier today. The committee recognizes that replacing the 510(k) process will take some time, and that a substantial amount of in-

formation will need to be obtained to inform the design of a new framework.

However, there are steps that FDA can take now to improve regulatory oversight of medical devices. The committee believes, strongly, that it is important that regulatory oversight of devices be conducted throughout their lifecycle.

In its report, the committee makes eight recommendations geared toward using resources wisely to ensure both short-term and long-term benefits. Among the actions recommended by the committee are that the FDA strengthen its postmarketing surveillance program for devices, identify limitations in the use of its postmarket regulatory authorities, and to address them, and implement a program of continuous quality improvement.

We understand that the FDA, on its own initiative, is already moving forward with making improvements to its postmarketing surveillance, and quality assurance programs. Ultimately, these changes will benefit patients, healthcare providers, the industry, and the FDA.

Thank you very much for the opportunity to testify, and I will be happy to answer any questions later.

[The prepared statement of Dr. Challoner follows:]

PREPARED STATEMENT OF DAVID R. CHALLONER, M.D.

SUMMARY

The Food and Drug Administration (FDA) asked the Institute of Medicine (IOM) to review the 510(k) clearance process for medical devices and to answer two questions:

1. Does the current 510(k) process optimally protect patients and promote innovation in support of public health?
2. If not, what legislative, regulatory, or administrative changes are recommended to optimally achieve the goals of the 510(k) process?

An expert committee assembled by the IOM addressed that task in its report, *Medical Devices and the Public's Health: The FDA 510(k) Clearance Process at 35 Years*. The report was released in July 2011.

On the basis of its review and evaluation of legislative, regulatory, and administrative components of the 510(k) process and other related components of medical-device regulation, the committee concluded that the 510(k) process in general is not intended to evaluate the safety and effectiveness of medical devices. Furthermore, the 510(k) process cannot be transformed into a premarket evaluation of safety and effectiveness as long as the standard for clearance is substantial equivalence to any previously cleared device.

The committee recognizes that replacing the 510(k) process will take some time and that a substantial amount of information will need to be obtained to inform the design of a new framework. However, there are actions that the FDA can take now to improve regulatory oversight of Class II medical devices. In its report, the committee makes eight recommendations geared toward using resources wisely to ensure both short-term and long-term benefits. Among the recommended actions are that the FDA should strengthen its postmarketing surveillance program for devices, identify limitations in the use of its postmarket regulatory authorities and address them, and develop and implement a program of continuous quality improvement.

The committee believes that there should be an integrated premarket and postmarket regulatory framework that provides a reasonable assurance of device safety and effectiveness throughout the device lifecycle. Implementation of the committee's recommendations will improve regulation of Class II devices in the short term and inform the design of the integrated regulatory framework in the long term. Ultimately, these changes to the way Class II devices are regulated will benefit patients, healthcare providers, the industry, and the FDA.

Mr. Chairman and members of the committee, I am David Challoner, vice president of health affairs, emeritus, at the University of Florida. I also served as chair

of the Institute of Medicine's Committee on the Public Health Effectiveness of the FDA 510(k) Clearance Process. The Institute of Medicine, or IOM, is the health arm of the National Academy of Sciences, an independent, nonprofit organization that provides unbiased and authoritative advice to decisionmakers and the public. Thank you for the opportunity to submit testimony for the record based on the IOM's report, *Medical Devices and the Public's Health: The FDA 510(k) Clearance Process at 35 Years*.

BACKGROUND

The Federal Food, Drug, and Cosmetic Act (FFDCA) requires a "reasonable assurance of safety and effectiveness" before a device can be marketed. The U.S. Food and Drug Administration (FDA) is responsible for enforcing this requirement. Devices that are deemed to have a moderate risk to patients generally cannot go on the market until they are cleared through the 510(k) process, named for Section 510(k) of the FFDCA.

The 510(k) process has become a major component of medical-device regulation in the United States. Thousands of devices are cleared via the 510(k) process each year—about one-third of devices entering the market. The remaining devices are exempt from any premarket review (67 percent) or enter the market by the premarket approval (PMA) pathway (1 percent) or by other means such as the humanitarian-device exemption (1 percent).

In recent years, individuals and organizations have expressed concern that the 510(k) process is neither making safe and effective devices available to patients nor promoting innovation in the medical-device industry. Several high-profile mass-media reports and consumer-protection groups have profiled recognized or potential problems with medical devices cleared through the 510(k) process. The medical-device industry and some patients have asserted that the process has become too burdensome and is delaying or stalling the entry of important new medical devices to the market.

THE CHARGE TO THE IOM COMMITTEE

The FDA asked the IOM to review the 510(k) process for medical devices and to answer two questions:

1. Does the current 510(k) process optimally protect patients and promote innovation in support of public health?
2. If not, what legislative, regulatory, or administrative changes are recommended to optimally achieve the goals of the 510(k) process?

THE IOM COMMITTEE'S CONCLUSION ON SAFETY AND EFFECTIVENESS

On the basis of its review and evaluation of legislative, regulatory, and administrative components of the 510(k) process and other related components of medical-device regulation, the committee came to the conclusion that the 510(k) process is not intended to evaluate the safety and effectiveness of medical devices with some exceptions. Furthermore, the 510(k) process cannot be transformed into a premarket evaluation of safety and effectiveness as long as the standard for clearance is substantial equivalence to any previously cleared device.

THE IOM COMMITTEE'S RECOMMENDATIONS

The committee believes that the FDA should obtain adequate information to inform the design of a new medical-device regulatory framework for Class II devices so that the current 510(k) process, in which the standard for clearance is substantial equivalence to previously cleared devices, can be replaced with an integrated premarket and postmarket regulatory framework that effectively provides a reasonable assurance of safety and effectiveness throughout the device life cycle. Once adequate information is available to design an appropriate medical-device regulatory framework, Congress should enact legislation to do so. The committee believes that a move away from the 510(k) process should occur as soon as reasonably possible but recognizes that it will take time to obtain the information needed to design the new framework.

In its report, the committee outlines several actions that the FDA should take in the short term to improve regulatory oversight of medical devices. These actions also will serve to generate the necessary information to inform the design of the new framework for Class II devices.

The committee believes strongly that it is important that regulatory oversight of devices be conducted throughout their lifecycle. Premarket review, including the 510(k) process, and postmarket oversight—from product labeling regulations to the

reporting of adverse events associated with use of a device—make up a comprehensive medical device regulatory system. All the components of the system need to be functioning well in order to provide a reasonable assurance of the safety and effectiveness of medical devices.

No premarket regulatory system for medical devices can guarantee that all new medical devices will be completely safe and effective when they reach the market. Robust postmarketing surveillance is essential. The FDA should give priority to postmarketing surveillance as an invaluable investment in short-term and long-term oversight of medical-device safety and assessment of device effectiveness. The committee identified substantial problems in the current postmarketing surveillance of devices, and recommends that the FDA develop and implement a comprehensive strategy to collect, analyze, and act on medical device aftermarket performance information. Congress should support the capacity of the FDA's postmarketing surveillance programs by providing stable and adequate funding.

The appropriate use of postmarket regulatory authorities, such as seizing or banning a device, is an essential component of a successful medical-device regulatory program. The FDA has stated that there are limitations to the use of these authorities but has not identified the limitations. The committee recommends that the agency review its postmarket regulatory authorities to identify these limitations and address them. If it is required, Congress should pass legislation to remove unnecessary barriers to the FDA's use of postmarket regulatory authorities.

It is the committee's assessment that the FDA lacks a continuous quality-assurance process for regulation of medical devices. As a result, the FDA cannot effectively address new issues as they arise. The committee recommends that the FDA develop and implement a program of continuous quality improvement to increase predictability, transparency, and consistency in all regulatory decisions for devices and to address emerging issues that affect decisionmaking.

SUMMARY

The IOM committee believes that there should be an integrated premarket and postmarket regulatory framework that provides a reasonable assurance of device safety and effectiveness throughout the device lifecycle. In its report, the committee outlines several actions that should be taken by the FDA that will ensure both short-term and long-term benefits. Among the actions recommended by the committee are that the agency strengthen its postmarketing surveillance program for devices, identify limitations in the use of its postmarket regulatory authorities and mitigate them, and develop and implement a program of continuous quality improvement.

Thank you, again. I would be happy to answer any questions the committee might have.

The CHAIRMAN. Thank you very much, Dr. Challoner.
Dr. Curfman.

STATEMENT OF GREGORY D. CURFMAN, M.D., EXECUTIVE EDITOR, NEW ENGLAND JOURNAL OF MEDICINE, BOSTON, MA

Dr. CURFMAN. Chairman Harkin, and other distinguished members of the committee. My name is Gregory Curfman. I'm a cardiologist and the executive editor of the *New England Journal of Medicine*.

For 200 years, the *New England Journal of Medicine* has published research on novel medical therapies. We're strongly committed to innovation in medical treatments, but experience has taught us that innovation does not come easily.

Now, Senator Blumenthal asked for a case study. And I'm going to give you a case study. Exactly 2 months ago, on September 15, we published an important clinical trial on a novel medical device called Wingspan—a highly innovative blood vessel stent. Wingspan was designed to reopen narrowed blood vessels in the brain, and thus prevent strokes.

According to the American Heart Association, there are 795,000 new strokes each year in the United States. And a novel therapy effective in stroke prevention would be a major advance.

Wingspan looked very promising. In fact, video images of the Wingspan in operation are nothing short of dramatic. Within minutes of insertion, the Wingspan stent system can reopen a blocked artery in the brain.

In 2004, a preliminary study of 45 patients showed that Wingspan successfully reopened blocked arteries in a high percentage. But, the study was very small, it included no randomized controls, and so it was impossible to conclude that Wingspan actually prevented strokes. Nevertheless, in 2005, on the basis of this small study, Wingspan was approved for unrestricted clinical use in Europe. It was also approved by the FDA, under a humanitarian device exemption, which authorizes use in up to 4,000 patients a year, but does not require that the device be shown to be clinically effective.

It was not until November 2008, over 3 years after Wingspan was approved for use, that a pivotal, randomized trial of its clinical effectiveness, was begun. The study was funded, not by the manufacturer of Wingspan, but instead by the taxpayers through the National Institutes of Health.

In the trial, patients at high-risk of stroke were randomized to receive Wingspan's stenting or no stenting. It was expected that Wingspan would reduce the risk of stroke or death. But it did not. In fact, there was a 2½-fold greater risk of stroke or death in the Wingspan group than in the unstented group—2½-fold greater risk.

Contrary to expectations, this innovative medical device actually caused the very clinical problem that it was designed to prevent. It was a disturbing result.

What are the lessons of Wingspan, which, by the way, is still on the market with FDA approval. First, implantable medical devices such as Wingspan are complex, and regardless how innovative they may first appear, their ability to improve human health cannot be known until they have been rigorously tested in controlled clinical trials.

Second, benefit for a surrogate endpoint may not necessarily translate into benefit for human health. In the case of Wingspan, the surrogate endpoint was its success in reopening the narrowed blood vessels in the brain. But this did not prevent strokes, and in some patients, actually caused them. The use of surrogate endpoints for FDA device approval is advocated in Senate bill S. 1700.

Third, the European approach to medical device approval is not an acceptable alternative for the United States. In Europe, Wingspan received unrestricted approval, even though clinical effectiveness had not been established.

Wingspan is but the latest of examples of a failed medical device. Others include, as Senator Harkin already mentioned, metal-on-metal artificial hip implants, and the Sprint Fidelis implantable defibrillator lead, both of which were also high-risk devices that received FDA approval without clinical data, and harmed many patients.

Mr. Chairman, legislation recently introduced in both chambers that would weaken the FDA approval process for complex implantable medical devices, should be viewed skeptically. And

may not be in the best interest of the health of the American people.

Thank you, Mr. Chairman.

[The prepared statement of Dr. Curfman follows:]

PREPARED STATEMENT OF GREGORY D. CURFMAN, M.D.

SUMMARY

Many Americans benefit from the implantation of medical devices; tragically, many also suffer or even die from complications related to medical devices that were never studied in clinical trials before being implanted in a large population of patients. The current device approval process, an outdated system created 35 years ago in an era of much simpler and few devices, has become less capable of assuring safety and effectiveness.

Two recent, but not rare, examples provide a cautionary tale about the challenges of ensuring that complex medical devices are both effective and safe. In 2005, a new metal-on-metal artificial hip implant, the DePuy (Johnson & Johnson) ASR XL Acetabular System, was cleared by the FDA through the 510(k) process by showing that the new device was “substantially equivalent” to an already-marketed hip resurfacing system. Because this was approved through the 510(k) process, clearance was based not on clinical trials or other clinical data but on bench testing in a laboratory. Once approved, it soon became clear that the metal-on-metal hip implant failed at the astonishing rate, requiring thousands of additional surgeries to replace the defective, painful implants.

The second example, the Wingspan endovascular stenting system, was approved through another less stringent humanitarian device exemption, which primarily relied upon data from a small, non-controlled phase I trial. A Phase III clinical trial showed a lack of both safety and efficacy, 6 years later, just 2 months ago. The disturbing experience with the Wingspan stent system, which harmed many patients, serves as a stark reminder that innovative medical devices, regardless of how promising they may first appear on the basis of preliminary studies, do not always prove to be successful when subjected to rigorous controlled clinical trials.

Additionally, I believe that the July 2011 IOM report, which concluded that it was impossible for 510(k) clearance to assure safety and effectiveness, is insightful, judicious, sensible, and long overdue. I support the IOM committee’s recommendation that the 510(k) process be replaced with an evaluation of safety and effectiveness.

As the best long-term improvements are contemplated, there are important steps that the FDA can take now. First, the use of 510(k) clearance for class III devices should stop, as Congress made clear 20 years ago. Second, the tenuous practice of allowing use of multiple predicates in 510(k) clearance should be eliminated. Third, as was recommended by the IOM committee, a formal system of postmarketing surveillance for medical devices should be put in place. Fourth, I strongly endorse the FDA’s Sentinel Initiative and the associated Mini-Sentinel pilot program. Fifth, I believe that the European medical device regulatory system is not a suitable model for the United States and would not be in the best interest of the American people.

I strongly believe that, in the interest of advancing human health, patients must have easy access to innovative medical devices and that the approval process needs to be sensible and efficient. But no one’s interest is served by putting defective medical devices onto the market where they cause harm to patients, waste health care dollars, and may kill jobs when they are withdrawn.

Many Americans benefit from the implantation of medical devices, such as artificial joints and lifesaving defibrillators. Tragically, many also suffer or even die from complications related to the same types of medical devices, some of which have never been studied in clinical trials before being implanted in a large population of patients. As devices have evolved and become more complex, our device-approval system has become less capable of assuring safety and effectiveness. The system we use today was created 35 years ago in an era of much simpler and fewer devices, and it is now inadequate.

A recent, but not rare, example provides a cautionary tale about the challenges of ensuring that complex medical devices are both effective and safe. Osteoarthritis of the hip joint is a common and debilitating disorder. Each year, more than a quarter of a million patients with advanced painful arthritis receive a total hip replacement in the hope that it will restore mobility and improve their quality of life.¹ Conventional artificial hip implants consist of a metal ball inserted into a plastic cup.

In 2005, a new metal-on-metal design was introduced in which both components were made from a metal alloy. The design was touted as a major innovation that would improve durability and reduce the risk of hip dislocation—advantages that were especially appealing to younger patients. However, these design innovations were never tested.

One metal-on-metal design is the DePuy (Johnson & Johnson) ASR XL Acetabular System, which was introduced into the U.S. market in 2005. The ASR was cleared by a Food and Drug Administration (FDA) process known as 510(k), which refers to the section of the 1976 Medical Device Amendments to the Federal Food, Drug, and Cosmetic Act that created it. Under that section, the criterion for clearance of a new medical device is that it be “substantially equivalent” to an already-marketed device (a “predicate”); clinical data are not required nor are data on safety and effectiveness.

The ASR was constructed by borrowing a metal alloy cup from a different hip device known as the ASR Hip Resurfacing System and retrofitting it onto a standard hip implant. The manufacturer successfully made the case that the re-engineered implant was “substantially equivalent” to a predicate device. Its marketing clearance was therefore based not on clinical trials or other clinical data but on bench testing in a laboratory, which was inadequate to simulate the stresses that would be placed on it in patients’ bodies.

It soon became clear that the device failed at the astonishing rate of at least one in eight. According to a recent report presented at the British Hip Society Annual Conference, 21 percent of these hips have had to be replaced (revised) by 4 years after implantation, and the revision rate rises to 49 percent at 6 years, as compared with 12 to 15 percent at 5 years for other devices.² Failure appears to be due to erosion of the metal in the articular surfaces and migration of metallic particles into the surrounding tissues and the bloodstream. Thus, the innovation led to tragedy for many patients.³ Before it was recalled in 2010, the ASR had been implanted in nearly 100,000 patients, and the result was a public health nightmare.

The ASR is a class III device—the FDA’s highest risk classification. As a high-risk device, it should not be cleared (without clinical data) via the 510(k) process, especially as its design is novel and thus there is no predicate for a 510(k) clearance. Congress envisioned that class III devices would be approved through the more stringent premarket approval (PMA) process, which does require clinical testing, and the Safe Medical Devices Act of 1990 requires that the FDA either use the PMA process for class III devices or reclassify them in a lower-risk category. Despite the clear intent of Congress, a recent GAO report noted that most high-risk devices continue to slip by this requirement. In fact, a recently published study found that among high-risk device recalls from 2005 to 2009, nearly three-quarters had been cleared through the 510(k) process.⁴

The Wingspan endovascular stenting system provides yet another cautionary tale about the potential risks to human health of innovative medical devices. The Wingspan stent was designed to be placed into small blood vessels in the brain in patients at high risk of a stroke, in order to re-open narrowed vessels to prevent a subsequent stroke from occurring. The Wingspan system was approved for use in both Europe and the United States in 2005. While in Europe the device received standard approval by a notified body, in the United States the FDA approved the device with a humanitarian device exemption (HDE), which requires a less stringent approval process than standard pre-market approval (PMA) and limits use to no more than 4,000 patients per year. One phase I trial in 45 patients but no controls, which demonstrated angiographic benefit, served as the basis for HDE approval. On the basis of this phase I trial, the company optimistically referred to the device as a “groundbreaking system.”

Just 2 months ago, and 6 years after the Wingspan was approved by the FDA, a phase III clinical trial (SAMMPRIS) comparing the device with intensive stroke-prevention medical therapy was published in the *New England Journal of Medicine*.⁵ The study was investigator-initiated and funded by the National Institute of Neurological Disorders and Stroke (the commercial sponsor, Stryker Neurovascular [formerly Boston Scientific Neurovascular], donated the devices), and thus was paid for principally by taxpayer dollars. The hypothesis tested in the study was that the stenting system would improve patient outcomes, as measured by the primary endpoint of stroke or death within 30 days of enrollment. After just 451 patients had been enrolled, the study was terminated prematurely because of a serious adverse safety signal in the stent-treated group. The incidence of the primary endpoint (stroke or death) in the stent-treated group was 2½ times greater than in the medically treated group (14.7 percent versus 5.8 percent), a worrisome result that was unanticipated by the investigators. The comparable figures at 1 year were 20 per-

cent and 12.2 percent. Despite these worrisome outcomes, the device remains available in the United States.

The disturbing experience with the Wingspan stent system, which harmed many patients, serves as a stark reminder that innovative medical devices, regardless of how promising they may first appear on the basis of preliminary studies, do not always prove to be successful when subjected to rigorous controlled clinical trials. Implantable medical devices are complex pieces of engineering, and bypassing clinical testing to rigorously evaluate their function inside the human body can result in substantial harm to patients.

On July 20, 2011, the U.S. House Energy and Commerce Subcommittee on Oversight and Investigations held a hearing entitled “Medical Device Regulation: Impact on American Patients, Innovation, and Jobs.” The subcommittee’s chairman, Congressman Cliff Stearns (R-FL), argued that FDA regulation of medical devices is too burdensome, stifles innovation, and drives device manufacturers overseas. Since then a number of bills have been introduced in Congress that would diminish FDA’s ability to assure safety and effectiveness of medical devices. But the disastrous outcomes of the use of DePuy ASRs and the Wingspan endovascular stenting system show that rushing untested and potentially dangerous medical devices into the marketplace carries serious risks; our regulators should not be in the business of creating jobs in the manufacture of dangerous devices.

On July 29, 2011, the Institute of Medicine (IOM) released an FDA-commissioned report on the 510(k) clearance process.⁶⁷ The report concluded that it was impossible for 510(k) clearance to assure safety and effectiveness, because it assesses neither, instead establishing only “substantial equivalence” to an existing device. The report therefore recommended that 510(k) clearance be eliminated. In addition, it recommended monitoring medical devices throughout their life cycle, especially during the postmarketing period. Despite its reasonable (and relatively modest) recommendations, the report has been aggressively attacked by the device industry and by politicians from States where device companies are located. In fact, the attacks began even before the report was released, which is highly unusual for an IOM report.

I believe that the IOM report is insightful, judicious, sensible, and long overdue. The 510(k) clearance process was established 35 years ago, and although it may have been a reasonable approach then, it surely is not today. The 510(k) process was never intended for use for clearing Class III medical devices, defined by the Code of Federal Regulations as products used for life-supporting or life-sustaining indications, for preventing impairment of human health, or presenting a potentially unreasonable risk of illness or injury. I support the IOM committee’s recommendation that the 510(k) process be replaced with an evaluation of safety and effectiveness. It is important to maintain and encourage innovation in medical devices. But true innovation requires that safety and effectiveness be proven by scientific study in clinical trials.

Under intense pressure from the device industry, the FDA leadership has already indicated that it does not intend to implement this key recommendation of the report, although it may be open to other changes. As the best long-term improvements are contemplated, there are important steps that the agency can take now.

First, the use of 510(k) clearance for class III devices should stop, as Congress made clear 20 years ago. A substantial equivalence standard for clearance of such complex devices is untenable. This recommendation was made previously in a report from the Government Accountability Office (GAO),⁸ but it has not been fully implemented by the FDA.

Second, the use of multiple predicates in 510(k) clearance should be eliminated. Now a device may be cleared if it is found to be substantially equivalent to an existing device that was cleared, in turn, by being found substantially equivalent to another device, and so on. A device can receive 510(k) clearance by being substantially equivalent to a device that is no longer on the market. This tenuous process should be discontinued.

Third, if a substantial equivalence standard is to be retained for certain devices deemed not of high risk, there must be a clear definition of substantial equivalence including the authority of FDA to require the submission of clinical data to assess whether the new device meets the substantial equivalence definition.

Fourth, as was recommended by the IOM committee, a formal system of post-marketing surveillance for medical devices should be put in place. Strong, mandatory, and transparent postmarketing data, in registries, allow rapid identification of serious problems that may emerge after approval. Careful tracking of every patient with a high-risk device is a crucial step for ensuring patient safety and avoiding nightmare scenarios. To this end, I hope that the FDA will soon finalize its rule about a system of Unique Device Identification (UDI), and then that the Centers

for Medicare & Medicaid Services will require the UDI to be submitted with claims. That would allow safety surveillance for medical devices to be much more tractable.

Fifth, I strongly endorse the FDA's Sentinel Initiative and the associated Mini-Sentinel pilot program.⁹ Through the Mini-Sentinel pilot program, capabilities are being developed for actively monitoring the safety of approved medical products using the electronic health information in claims systems, inpatient and outpatient medical records, and patient registries. Such a system will be an important step forward.

Sixth, I believe that the European medical device regulatory system, in which 82 privately run notified bodies rather than a government agency make decisions on market authorization for medical devices, is not a suitable model for the United States and would not be in the best interest of the American people. Notified bodies do not adhere to uniform standards, and device manufacturers can select the notified body that will put their device through the least stringent assessment of safety and performance. Most surprising, manufacturers do not have to demonstrate a beneficial effect on clinical outcomes.

I strongly believe that, in the interest of advancing human health, patients must have easy access to innovative medical devices and that the approval process needs to be sensible and efficient. But no one's interest is served by putting defective or untested medical devices onto the market where they cause harm to patients, waste health care dollars, and may kill jobs when they are withdrawn. It is essential that the FDA be adequately funded to carry out its mission to ensure the safety and effectiveness of medical devices. The IOM report charts a path that is right for the future, and despite well-financed outside pressures, I urge the FDA to initiate an action plan with congressional support to adopt these important recommendations.

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The CHAIRMAN. Thank you very much, Dr. Curfman. And thank you for that exposition of that one case, and I have a whole list of others to go with it.

Professor Hall, you assert in your testimony that 510(k) system generally works pretty well. But how do you reconcile a system based on substantial equivalence with the phenomena of, what they call, predicate creep? You know what that means—where device after device is compared with a slightly newer or a different version of an original device, such that the newest models bear little resemblance to the original? You have the original device, you have another iteration of it that's substantially equivalent, then there's another device that is substantially equivalent to that, and there's another device, and on and on to the nth degree. Doesn't

this system really allow firms to compare apples to oranges, once you get out two or three or four or five iterations?

Mr. HALL. Properly implemented, I do not think the system does do that. Let me give you a couple of reasons why.

In each of these iterative steps, if there is either a new indication or a new technology being employed, and again, new technology is very, very broadly defined, the sponsor of that 510(k) submission has to provide data of whatever is the appropriate type—clinical data, bench testing, whatever to establish safety and effectiveness.

The agency reviews that and makes a decision. So, what you see is a constantly increasing bar. That's how the system is designed. So, then my latest generation with another tweak or whatever, is not compared simply to the original one from, let's say, 20 years ago, but rather, then, we have this increasing knowledge.

Second, the agency has a number of tools to take into account new information. We can revise special controls, put in place performance standards, etc., all to address newly discovered information or experience in the clinical setting.

The CHAIRMAN. Dr. Challoner, there was a lengthy discussion in the IOM report about the need to enhance postmarket review of devices. What sort of precise fixes, if any, would you suggest? What are the gaps in the postmarket authorities that you might respond to here?

Dr. CHALLONER. This is a major and important tool as you look forward to where we're going to be in the next decade or so in this industry.

At the moment, usually, except for a few cases in pediatric realm or where you have an interested professional society, there are some device-specific areas in which prospective data on complications is gathered.

But, generally speaking, it's an ad hoc system with multiple responsibilities for reporting up the chain, if you will, to finally come to either public or FDA attention, and there's no consistency or regularization of it.

Now, the opportunity is if you're going to speed up the device process for public health safety and efficacy, to have the opportunity to be not intrusive on the front end, except for manufacturing standards and design issues, and to streamline in those processes, as long as you could rely on a very consistent population-wide reporting system for complications of low incidence and high substance, you would begin to have safety and efficacy over the lifetime of a drug. New information systems—

The CHAIRMAN. Or device.

Dr. CHALLONER [continuing]. Or device. I'm sorry.

New information systems, new healthcare organizations, organizations like Kaiser, and in particularly the VA, give us an opportunity to get an early warning system for devices through their electronic record systems, that will improve the process over time. And I think that needs to be explored by all the interested parties as we go forward.

The CHAIRMAN. My 5 minutes are up. I will turn now to Senator Franken.

Senator FRANKEN. Thank you, Mr. Chairman.

Professor Hall, thank you for coming from Minnesota. You have decades of experience working with the FDA, and as CEO of a medical device company, and also as a professor of food and drug law at the University of Minnesota Law School.

As you know, I introduced a bill earlier today that will get devices to the market faster and more safely, and I know you know about the bill because you endorsed it, and thank you again for your support. Would you explain why it is important to expand the FDA's ability to consult with outside experts while maintaining the requirement that the FDA disclose any conflicts of interest that advisory panel members may have?

Mr. HALL. As we see burgeoning technology and whole new areas of science, the agency cannot and should not be expected to be an expert in anything and everything. And the agency, in my opinion, needs access to experts to provide the scientific, engineering, material science, whatever expertise, to advise the agency so they, then, can make the appropriate risk-benefit decision in a safety efficacy scenario.

I happen to have a personal interest in nanotechnology with my academic hat on. It's incredibly complex, and if we don't give the agency access to expertise, they're going to be making decisions without the benefit of the best science. And we need to make sure they have that, in my opinion.

Senator FRANKEN. We heard from Dr. Shuren that they are losing senior people, and there is attrition, and it would be nice to work out a system where the higher bar of conflict of interest—that exists in, just in this, in the FDA—in this field is looked at again.

Can I, Professor Hall, can I get your take on the IOM's report on the 510(k) process?

Mr. HALL. Let me make a couple of comments—there are aspects of the report with which I do agree. For example, postmarket surveillance, the importance of a quality system within FDA, the need to finalize the classification of post-amendment classification, and several others.

I must say, I do disagree with the fundamental conclusion that the 510(k) system is not capable of providing a reasonable assurance of safety and effectiveness. I think the statute in Congress have provided that. I think FDA has implemented that, and I think that even as the IOM said, the actual experience with the system has been remarkably positive.

Senator FRANKEN. Thank you very much. Thank you, Mr. Chairman.

The CHAIRMAN. Senator Mikulski.

Senator MIKULSKI. Thank you. This is a great panel.

Dr. Challoner, first of all, we so value the Institute of Medicine as Senator Harkin said. But this issue of totally replacing the 510(k) gives us pause, and I think one of the reasons it gives us pause is the looming question of who would design the new system? Would we have to approve the new system given both the political climate and the clock ticking—when we also have to reauthorize MDUFA as we know it?

What prompted a learned society like IOM to say, "Throw out the whole thing," when you know how Congress is working—or not

working. If you're going to criticize FDA for approval, criticize us for bill approval.

So do you, speaking for yourself, believe that there are intermediate steps that we could take that would address the most cogent and compelling of the issues raised in your report?

Dr. CHALLONER. Senator Mikulski, thank you, and the answer is that the more we looked at it, and we had a very diverse committee—I was on the board of directors of a device corporation, a large one, Cortis Corporation, for 6 years. We had two attorneys who spent most of their professional life in the device industry. We had people, an individual, who had taken a device through the process.

We were surprised, ourselves, as a group, that we all came unanimously to the conclusion that the logic of this transition system that was put in place with the 75 amendments, simply to get from nothing to something, had now had 35 years of a life-span, and we felt it was not going to be capable of dealing with the technology and science of devices for the next two decades.

Therefore, our expectation is not that the FDA would take our advice, and dump it next week, and put something in place. But we would begin a conversation such as we're having here, and at other venues, just as it took 5 years to get the 75 amendments in place. It may take 5 years of conversation, probably managed by the FDA, and the Congress, to be able to put in place, that makes use of modern information technology over the life-span of a device.

So, we expect a 5-year transition. In the meantime, there are things that can be done with postmarket authorities that the FDA has, and with improving postmarket surveillance that will immediately improve public health and safety.

Senator MIKULSKI. When I read the report, I thought the message was essentially—these are Barb Mikulski's words—dump it and deal with it.

Dr. CHALLONER. No.

Senator MIKULSKI. And quite frankly, that message gave every one of us a great deal of pause. But what you're saying is—well, let's take a look at what you're saying—Mr. Hall, Mr. Curfman, and Dr. Shuren have talked reforms; we're all talking about reforms and what you are saying in your recommendations is that the postmarketing suggestions would be the most potent reforms right now to include in any reauthorization bill.

Dr. CHALLONER. Yes. Would have immediate effects.

Senator MIKULSKI. I want to thank the IOM for what they did. They certainly started the conversation.

Dr. CHALLONER. Good.

Senator MIKULSKI. And thank you very much. Thank you, Mr. Chairman.

The CHAIRMAN. Senator Blumenthal.

Senator BLUMENTHAL. Thank you, Mr. Chairman.

I think what the panel was hearing and what I've heard over the last months, maybe longer, is a developing consensus that the present system simply isn't working, that it's broken, and, in fact, fatally defective, not just in implementation, but also concept.

And I think Senator Mikulski raised the key question, which is, what do we do to make it better while we try to improve the law?

And perhaps I can ask this question of all the members of the panel. Isn't one of the things we can do is to improve postmarket surveillance? Because that kind of greatly increased scrutiny and oversight, at least, can stop harm that may be developing, and save patients the hip on hip implants, or the Wingspan stent problems, and try to deal with those problems at an earlier stage, and thereby, save people from a lot of suffering, and even death?

Dr. Curfman, you've raised those two case studies, and I suspect that they may be included in Dr. Shuren's response to my question on case studies. But, would increase postmarket surveillance be advisable?

Dr. CHALLONER. Thank you, Senator Blumenthal. I think that's critical, and I know that there are initiatives ongoing in the FDA that are quite interesting. And I think that, as they're implemented, they are going to really strengthen postmarketing surveillance. Dr. Shuren can certainly speak to that in more detail than I.

But, there is a program that is coming to fruition called the Uniform Device Identification Program, which is a way of giving a unique identifying number to each implanted medical device, allowing that device to be tracked throughout its lifetime, and hooked up with an individual patient.

These numerical codes can, then, be linked to outcome data, claims data, so that we can, then, find out exactly what's happening to the patients who have them.

Now, this program is very interesting. It's being headed by a very high-quality individual within the agency, and I think it's going to be a very important step forward when it's actually implemented, and I understand that that will be fairly soon.

That's associated with the larger sentinel initiative that's ongoing within the FDA. That's associated with the larger sentinel initiative that's ongoing within the FDA, and the mini-sentinel pilot program, which is a smaller research program going on to develop new ways of doing postmarketing surveillance. And, here again, there are very high-quality people working on these programs within the agency.

So, I expect that we will be seeing advances in postmarketing surveillance, and I agree with you, Senator Blumenthal, that this is quite critical as we await larger-scale changes in the 510(k) program.

Senator BLUMENTHAL. But, postmarket is really no substitute for fundamental reform of the entire 510(k) system.

Dr. CHALLONER. It's part of a process, but I don't think that it's really going to be enough, in the long run.

Senator BLUMENTHAL. Professor Hall, I wonder if you would comment on those two case studies, for lack of better word, and whether you think they don't indicate faults in the present process.

Mr. HALL. I'll be glad to.

First of all, I only know what's public about those situations, and so, I'm not in a position or qualified to make any conclusions. I have not reviewed the regulatory submissions or anything like that.

So, what I will try to comment on, given on what I do know, publicly, is whether the agency has authority to have addressed those

issues. I believe the agency does. In the case, again, of the metal-on-metal, the agency, submission to the agency is to include safety and effectiveness data. The agency can decide whether it needs clinical data or not to make that assessment, so they have that authority.

Dr. Shuren talked about that briefly in his comments, as to whether they should have. And again, I don't know the details on that. But they have the authority to get clinical data, if that is what is appropriate in that situation. I do agree with the other panelists of the importance of postmarket surveillance, and the need to improve postmarket systems so that they are more effective and more efficient.

Within any product issue, the agency has a number of authorities to impose warnings, recalls, and postmarket studies under section 522—I have to mention at least statutory section, otherwise, I guess I'm not really a lawyer in this.

Senator BLUMENTHAL. So, your point is that, even under existing authority, the FDA has the power to be more vigilant and vigorous in protecting the public, and, I think many of us would agree.

Mr. HALL. Correct.

Senator BLUMENTHAL. Thank you. Thank you, Mr. Chairman.

Senator HAGAN. Thank you, Mr. Chairman. And, I too, echo Senator Mikulski's comments about this panel. Thank you for being here, and it's an excellent group.

Dr. Challoner, you state that the Institute of Medicine Committee believes that there should be an integrated premarket and postmarket regulatory framework that provides a reasonable assurance of device safety and effectiveness throughout the device lifecycle. Can you elaborate on this, and what you think we need to see?

Dr. CHALLONER. We just don't have enough data at the moment, and, our charge, if you will, in making our recommendation to the FDA is that it needs to spend some time with its varied constituencies over the course of the next several years, finding out exactly what kind of data they need about their processes, that will make them more transparent and predictable.

Dr. Shuren has already undertaken, parallel with our report, many of these items. But there are some things in which we just don't have data.

There's a difference between postmarket surveillance and the identifier issue that Dr. Curfman just raised, and postmarket authorities already in place, for instance, that may or may not be used adequately to survey and monitor the postmarket arena. And it may be because the data just isn't coming forth from the clinical environment to the leadership of the FDA.

For instance, there's a seizure authority, and the agency has brought about 13 seizure actions from fiscal year 2001 to 2008. Now, is that adequate? I don't know. The absence of evidence is not evidence of absence; banning, used once since 1976; recall orders, the agency has not formally tracked recall orders, but believes the authority has been used at least three times in the last 20 years.

So, we were unable to get enough data to really understand how to put all of this in place, which is why we suggested that things

need to change, and that a process needs to be put in place to study it, gather the data, and understand it.

Senator HAGAN. Thank you.

Professor Hall, we've heard from the other two panelists that the 510(k) process or program isn't working well; primarily from a safety perspective. However, you've got a different view of this process.

Can you elaborate on the safety findings that you mention in your testimony, and do you think the 510(k) program is, generally, working well. Or should it be replaced, and what do you envision the impact to industry and access to medical devices are if the 510(k) program, was, in fact, scrapped?

Mr. HALL. There are a number of studies—I have done one that has looked at the safety profile of medical devices. I mention mine, Dr. Maisel, now with FDA, has done a study, FDA recently did a study. IOM, itself, said that they find no evidence of a systemic problem with medical devices.

What my study, in particular, did, is that we looked at all class I recalls for a 5-year timeframe, looked at the reason for the recall, etc. What that data indicates is that quality systems are, by far, the most potent tool to use to increase product safety.

This links in directly to your earlier question about integrated postmarket and premarket. Outside of the formal 510(k) system, you have quality systems. So, for example, a company is to have a corrective and preventive action program by which they track information, product trends of problems, then decide using that data—does a correction need to be made? That data is also to be fed into the front end of the design process for the next iteration of devices, so we get into this continuous improvement loop, using data that exist.

Can that be made stronger? Do we need, I think we're all in agreement we can do a better job on postmarket. But, the recent study by FDA also indicated that the primary cause of recalls are quality system challenges, not issues with, for example, lack of clinical trials or other issues.

Senator HAGAN. Thank you, Mr. Chairman.

The CHAIRMAN. Thank you, Senator Hagan.

I want to get on this issue of clinical data. I heard you say, Mr. Hall, that FDA can—of course, we request clinical data, to see if something is equivalent to the predicate.

If I reference the IOM report again here, in the United States, use of clinical data in the regulatory review process is defined by the enabling legislation, regulations and FDA's implementation of the legislation and regulations. The clinical data can be requested by the FDA only if necessary to determine that the new devices are as safe and as effective as a predicate device.

Moreover, the agency may not ask for scientific evidence, greater than the "least burdensome," to answer the question. In practice, clinical data play a very small role in the 510(k) process. The GAO found that from fiscal year 2005 to 2007, about 15 percent of class II and class III 510(k) submissions had new technologic characteristics.

The FDA found that only 8 percent of 510(k) submissions include certain elements, I don't get into all of that. Less than 1 percent of non-in-vitro diagnostic 510(k) submissions reference a clinical

trial. So, again, there's not very much clinical data for the vast majority of the devices that are asked for clearance under the 510(k) process, is that not true?

Mr. HALL. I think you have to look at the reasons the 510(k) was submitted. There are many 510(k)'s that are submitted for changes in the product, for which clinical data is simply irrelevant.

For example, one has to submit a 510(k) if one is adding a warning to a product. Now, you don't need clinical data for that.

Senator Franken asked about the new modifications guidance. If you change suppliers under that, that requires a 510(k). Again, clinical data would seem to be not important to deciding whether it's appropriate to change from supplier A to supplier B.

So, I think you need to look at the subset of submissions, and then ask the question, does the agency have the authority or is that information being submitted.

Senator HARKIN. It would seem to me, Professor Hall—I ask Dr. Curfman for his thoughts on this—that, if you're talking about an implantable device, and a company is going through the 510(k) process, based on a predicate, obviously, that is where postmarket surveillance would be most important.

What happened from the original through the first iteration, the second iteration, the third iteration, the fourth iteration? What happened to people out there? We don't have that. The FDA is not really doing that, now.

Why aren't they doing it? Well, let's see. Let's go back here to the report. The FDA's device postmarketing surveillance programs have been adversely affected by the instability of the agency's congressional financing. Interesting.

Moreover, user fees can be used only for premarket activities. The inadequate postmarketing surveillance systems, both those in the FDA and those which are privately funded, and the resulting lack of useful, consistent, and reliable data make it impossible to draw confident conclusions about the performance of medical devices now in the market.

So, now I can get to the nub of it. If the clinical data is not there because we don't have enough postmarket surveillance, we don't have enough postmarket surveillance because Congress doesn't fund it well enough, and user fees cannot be used for postmarket surveillance, we have a conundrum. We have a conundrum.

Mr. HALL. Let me try to be clear with my comments. There are many circumstances in which clinical data is important. I think you're absolutely—implantable, right.

The CHAIRMAN [continuing]. Implantable, right. I preface it by saying implantable devices.

Mr. HALL. For many of those, it's important. I agree with you completely, about the importance of postmarket surveillance. I think you and I are in absolute agreement on the importance of that, and the need to make sure that the system is effective and efficient.

The CHAIRMAN. Let me ask you this question.

Mr. HALL. Yes.

The CHAIRMAN. You have a device company, or you're CEO of one, or something—let me ask you this—should user fees also be used for postmarket surveillance?

Mr. HALL. I believe in an adequately funded agency.

The CHAIRMAN. Hey, I'm asking you if—

Mr. HALL. I understand. And the reason I hesitate is—I'm on record. I'm Don Quixote occasionally, OK? I'm on record as saying that user fees are bad public policy. That doesn't mean the agency shouldn't be funded. Alright? I just think the source of funding—there are better sources of funding than user fees. I recognize, completely, the current financial situation, which is why I may be Don Quixote in my views on that. But, I do think we need adequate funding.

One of the challenges of using user fees for postmarket surveillance is that we are actually taxing innovation. Because the people paying user fees are the ones with the new ideas, the postmarket surveillance is for old products. They are already out there.

And, so, that's one of the reasons, I think, we need to come up with a better funding mechanism.

The CHAIRMAN. Yes.

Mr. HALL. But, that's me, and I didn't say—

The CHAIRMAN. But, the innovation, the new products is based upon all those predicates that came before it.

Mr. HALL. Most of your user fees, as Dr. Shuren pointed out, come from PMAs, not from 510(k)'s.

The CHAIRMAN. But, a lot still comes through the 510(k) process.

Mr. HALL. Right. I'm in agreement. We need postmarket surveillance, and it needs to be funded. I absolutely agree with that.

The CHAIRMAN. Any observations from you, Dr. Challoner or Dr. Curfman, about this? Dr. Curfman, I will single you out first because you had, sort of, spoken about postmarket surveillance.

Dr. CURFMAN. Mr. Chairman, I think you've focused, very appropriately, on the implantable high-risk class III devices—that's really where a lot of our concern is, and where we most need the clinical information that you've referred to.

The use of the 510(k) clearance for class III devices really needs to stop, and Congress called for that 20 years ago. It still hasn't stopped. That needs to stop.

You've also referred to the use of multiple predicates—this daisy chain of predicates to approve high-risk devices. It's clearly inappropriate—I disagree with Mr. Hall about this. It just doesn't make sense. And that, also, needs to be eliminated.

If 510(k) is going to be retained for some devices of lower risk, then we need to have a very clear definition of what we're talking about for substantial equivalence, and FDA needs to be able to call for clinical data to substantiate that definition of substantial equivalence for a particular device. So, I would agree with you, Mr. Chairman, we need more clinical data in all of these realms.

The CHAIRMAN. Dr. Challoner, any observations on this? I keep quoting from your report.

Dr. CHALLONER. Right. Thanks, you've already spoken for me, Mr. Chairman.

The CHAIRMAN. The more I get into this—as a Chairman, I've peripherally been involved in the past, the more I'm just wondering if—perhaps a simple reauthorization is really not what's needed. Perhaps, we have reached a point in time after 35, 36 years, that we need to take a more intense look at this whole realm of the ap-

proval process, postmarket surveillance, especially for certain higher risk devices. Obviously, some were so low-risk, no big deal. And, perhaps, we need to step back a little bit, and take a look at this.

I agree with the Professor, I fought all my adult life against having user fees when I put on my agriculture hat, against user fees for things like meat inspection. I mean, you're going to have the companies that slaughter the meat do the inspection? It's for the public good that we have the meat inspectors.

I've often said all along that our FDA had to be fully publicly funded. But, in this present climate, that is not going to happen. And, so, the user fee system has been in place for a long time, and it looks like something we're just going to have to live with.

But, nonetheless, we still want to make this system one that, first and foremost focuses on safety and that we have a definable pathway that's transparent, that industry can rely upon, and know, I mean, this is where I agree with the industry. A lot of times, it's sort of opaque, on how the process is going to go. And I think the IOM report pointed that out also. So, we need some more clearly defined pathways.

I also say, just sort of off the top of my head after reading all this, and going through the IOM report, I wonder if there shouldn't be a limit on how many predicates there can be? Maybe there should be the initial device. Maybe it can do one, and maybe, to the second degree after that, they have to go back and start the process over again, so you don't get devices to the nth degree out there, that bear very little resemblance to what was initially approved.

But, thinking about that, you limit the 510(k) process to a certain limited number of predicates. After that, you'd have to go back to the entire process again. And, then, looking at the class III, the devices that are, well, I just call them implantable devices, that really cause a lot of risk, and need to have a lot of postmarket surveillance as we go along. How we fund that, I just don't know. But, I'm thinking that, maybe, user fees also need to be used for postmarket surveillance.

I know what you're saying, Professor Hall, that user fees are to be approved. But a lot of times, the approval is based upon what happened before, so I don't know where the two separate, sometimes.

Those are just my thoughts. It's not an easy subject, and it's not one that lends itself to any real easy answers, I know. But, I think through this process, we might come up with some better suggestions.

I'm concerned that we might be reauthorizing this, and not doing a more adequate job of refining, and redefining the process along some of the lines of the IOM, maybe not all of it, but along some of the lines. And at least putting a spotlight and some focus on, and some support for postmarket surveillance.

Thank you all very much. This has been very healthy, a very good interchange, and I learned a lot here, today.

I request that the record be kept open for 10 days so that statements and questions can be submitted for the record. Did anyone else have anything else they wanted to add?

Thank you all very much. I appreciate it, very much, for being here. Meeting is adjourned.
[Additional material follows.]

ADDITIONAL MATERIAL

RESPONSE TO QUESTION OF SENATOR BENNET BY DAVID R. CHALLONER, M.D.

Question. Professor Hall, you cited that over 90 percent of all Class I recalls are directly related to quality system issues and Dr. Curfman and Dr. Challoner you also cite the need for increased quality assurance from companies as well. What can Congress do to directly address this quality system and quality assurance problem?

Answer. The IOM Committee on the Public Health Effectiveness of the FDA 510(k) Clearance Process focused on how the lack of an effective continuous quality assurance program within the FDA's Center for Devices and Radiological Health (CDRH) has hindered the agency's ability to assess the effectiveness of the 510(k) program. As detailed in the committee's report, without adequate management and information technology infrastructure, the FDA cannot address new problems as they arise or develop a long-term vision of CDRH and its mission. For example, the FDA does not currently have the ability to trace the history of the 120,000 or so 510(k) decisions made during the last 35 years and, therefore, the potential exists for problematic devices to continue to be used as predicates because there is no systematic way to identify them. The committee recommends that the FDA develop and implement a program of continuous quality improvement to track regulatory decisions on devices, identify potential process improvements in the device regulatory framework, and address emerging issues that affect decisionmaking. The committee did not recommend specific actions by Congress with regard to establishing a program of continuous quality assurance for devices within the FDA or the medical device industry. It should be noted, however, that the committee did determine that the FDA does not currently have adequate resources for its multiple responsibilities and implementation of a quality assurance program would require such from Congress.

[Whereupon, at 4:53 p.m., the hearing was adjourned.]

