

**REAUTHORIZATION OF MDUFA: WHAT IT MEANS
FOR JOBS, INNOVATION, AND PATIENTS**

HEARING
BEFORE THE
SUBCOMMITTEE ON HEALTH
OF THE
COMMITTEE ON ENERGY AND
COMMERCE
HOUSE OF REPRESENTATIVES
ONE HUNDRED TWELFTH CONGRESS

SECOND SESSION

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REAUTHORIZATION OF MDUFA: WHAT IT MEANS FOR JOBS, INNOVATION, AND PATIENTS

WEDNESDAY, FEBRUARY 15, 2012

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON HEALTH,
COMMITTEE ON ENERGY AND COMMERCE,
Washington, DC.

The subcommittee met, pursuant to call, at 10:17 a.m., in room 2322 of the Rayburn House Office Building, Hon. Joe Pitts (chairman of the subcommittee) presiding.

Members present: Representatives Pitts, Burgess, Shimkus, Rogers, Murphy, Blackburn, Gingrey, Latta, McMorris Rodgers, Lance, Cassidy, Guthrie, Barton, Bilbray, Bass, Pallone, Dingell, Towns, Engel, Capps, Schakowsky, Matheson, Christensen, and Waxman (ex officio).

Staff present: Clay Alspach, Counsel, Health; Nancy Dunlap, Health Fellow; Paul Edattel, Professional Staff Member, Health; Debbie Keller, Press Secretary; Ryan Long, Chief Counsel, Health; Carly McWilliams, Legislative Clerk; Chris Sarley, Policy Coordinator, Environment and Economy; Heidi Stirrup, Health Policy Coordinator; Alli Corr, Democratic Policy Analyst; Eric Flamm, FDA Detailee; Karen Nelson, Democratic Deputy Committee Staff Director for Health; and Rachel Sher, Democratic Senior Counsel.

Mr. PITTS. This subcommittee will come to order.

The Chair recognizes himself for 5 minutes for an opening statement.

OPENING STATEMENT OF HON. JOSEPH R. PITTS, A REPRESENTATIVE IN CONGRESS FROM THE COMMONWEALTH OF PENNSYLVANIA

Congress first authorized a medical device user fee program in 2002, in the Medical Device User Fee and Modernization Act, MDUFMA. We last reauthorized the program in the Medical Device User Fee Amendments of 2007, MDUFA, which expires September 30, 2012.

While I am glad that FDA and industry have reached recently a proposed medical device user fee agreement, the committee did not receive it by the January 15, 2012, deadline, as set in statute. As it is already late, I would encourage FDA and the administration to expedite their review of the agreement so that the committee receives it at the earliest possible date.

The proposed agreement will provide \$595 million in user fees for fiscal year 2013 through fiscal year 2017, a sum that is more than double the current user fee level of \$287 million.

A key goal of the agreement is to increase predictability and transparency. Under the agreement, together with regular Congressional appropriations, FDA should be able to hire 240 full-time review process employees, including 140 reviewers specifically for devices, over 5 years. The increased user fees will pay for additional training for device reviewers and information technology upgrades to improve the review process. With these new resources, FDA has agreed to measure review time in calendar days, not FDA days, which is an important step to providing increased predictability.

Under the proposed agreement, FDA and industry will communicate more often, and earlier in the review process, where FDA will provide the feedback that manufacturers need to go forward.

The United States is the world leader in medical device innovation. This not only benefits patients who need new, innovative treatments, it benefits our economy. In 2008, according to the Lewin Group, the medical device industry employed 422,778 workers nationwide, paid \$24.6 billion in earnings, and shipped \$135.9 billion worth of products.

In 2008, in my home State of Pennsylvania, the medical device industry employed 22,233 people and paid Pennsylvania workers over \$1.1 billion in earnings.

These are good jobs. Nationally, jobs in medical technology pay almost 40 percent higher compared to the national earnings average.

What is best for patients and what is best for jobs is to have a device review process that is clear, transparent, predictable and accountable, and I hope that that is what the proposed agreement accomplishes.

I would like to thank all of our witnesses on today's panels.

[The prepared statement of Mr. Pitts follows:]

Rep. Joseph R. Pitts
Opening Statement
Energy and Commerce Subcommittee on Health
Hearing on “Reauthorization of MDUFA: What It Means for Jobs,
Innovation, and Patients”
February 15, 2012

(As Prepared for Delivery)

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Thank you to all of our witnesses.

Mr. PITTS. I would like to yield the remaining time to Dr. Burgess, the vice chairman of the committee.

OPENING STATEMENT OF HON. MICHAEL C. BURGESS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF TEXAS

Mr. BURGESS. Thank you, Mr. Chairman, and Dr. Shuren, again, thank you for being here. You are going to hear today some concerns from people on the dais and from our subsequent panel, from patients and innovators.

As the chairman points out, funding was increased in fiscal year 2008 and fiscal year 2010 by nearly 35 percent, and during that time the average review time for lower-risk devices increased by 43 percent, higher-risk devices by 75 percent, so we have got an official Washington conundrum. Resources are increasing, performance is decreasing, and you need to be the very best you can but it doesn't look like we are there yet. Delays in reviews through inconsistencies certainly harm public health but they also stifle innovation and cost jobs.

We don't want the FDA to approve anything that harms patients, and that is your mission, but a little predictability could go a long way. The industry should not have to double user fees in order to get the very basics of customer service. So the question is, have you become more interactive, predictable and innovative? Those should be the goals of the basic agreement but they also are tenets of a well-run organization. We worry about the jurisdictional creep that has been going on where you seek to grab as much regulatory territory as possible, oftentimes through draft guidance, absent legislative direction. Things like mobile apps and laboratory-developed tests are things that you want to do but we are not sure you are doing what you are supposed to do. We shouldn't enable your efforts to duplicate efforts of other Federal agencies.

Mission creep may be a cry for help, and Doctor, this morning we are here to try to provide that help for you. But some days we wonder if you don't need a bigger check but you need a check on what is exactly happening at the level of your agency. We want to help. I think we all admit that there are problems in our device approval regimen that hurt patients and it is just critical that we get it right for them.

I yield back the balance of my time, Mr. Chairman.

Mr. PITTS. The Chair thanks the gentleman and now recognizes the ranking member of the subcommittee, Mr. Pallone, for 5 minutes for opening statement.

OPENING STATEMENT OF HON. FRANK PALLONE, JR., A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW JERSEY

Mr. PALLONE. Thank you, Chairman Pitts. I welcome every here for our third installment of the UFA hearings.

Today we will be discussing the reauthorization of the Medical Device User Fee Agreement, known as MDUFA, and let me say at the outset that we are all very relieved and encouraged by the current circumstances. There was grave concern that the parties would be unable to reach a compromise, and I am happy that things are moving forward.

While there is still no legislative language, there is an agreement in principle that we will be discussing at length. It includes \$595 million in fees over 5 years, specific goals for total review times, additional meetings with sponsors, third-party analysis of the FDA's review process as well as other program improvements. In addition, I understand that the additional funding would allow FDA to hire over 200 new full-time workers by the end of the 5-year program.

Now, we have consistently heard for a long time about the need for FDA to improve the predictability, consistency and transparency of its premarket review program. This agreement will not solve all of those issues overnight but it certainly sets FDA on a good path moving forward with important tools and more resources at their disposal. It also provides the industry with some much-needed insight into the review process and better metrics to measure the FDA's performance, and these are quality enhancements that should allay those concerns.

I know that Congress and the FDA greatly appreciate the industry's investment in this program. This proposal represents a strong compromise, and I commend the hard work of both parties in getting to this place I am confident will help the agencies continue to improve efficiencies.

Let me also say that I have been encouraged by FDA's commitment both over the past year and as part of this user fee agreement to recognize the need for some internal transformations. Change doesn't happen overnight, and regardless, Dr. Shuren, your center has been more than willing to listen and learn from member stakeholders and industry on how to shift and adapt in ways to make these processes better for companies and consumers. You have recognized some of the inadequacies of the agency and maintained an open mind on fixing what is broken. At the same time, you have also maintained the policies are important to patient safety and device effectiveness. You and the Commissioner were kind enough to visit my district and talk one on one with me and New Jersey companies about these processes, so I appreciate that and I look forward to working with you to continue to improve the center.

Today's hearing will also touch upon a number of FDA policy proposals from my Republican colleagues. In general, I have concerns with some of these bills and I look forward to discussing them further. Specifically, I wonder whether these proposals could make it difficult for the agency to meet its negotiated commitments. I also think it is critical we understand at length the intended impact, justification and potential unintended consequences of these proposals before moving forward.

I will just close by stating what I have said a number of times. I agree that MDUFA is of the utmost importance. I agree that FDA should facilitate an environment that doesn't create added unnecessary burdens upon innovating companies, but we must not make FDA policy changes at the expense of patient safety. The public health must be our number one goal above all else. We need to take a long, hard look at any potential policy that could make it more difficult for FDA to protect patient safety, and I know there

are a number of witnesses joining us today that will talk about that important aspect. I look forward to that.

But I wanted to especially welcome Jim Shull—I hope I am pronouncing it right—from Browns Mills, New Jersey, who is here to share his personal story.

Thank you, Mr. Chairman. I yield back.

Mr. PITTS. The Chair thanks the gentleman and now recognizes the chair emeritus of the full committee, Mr. Barton, for 5 minutes for opening statement.

**OPENING STATEMENT OF HON. JOE BARTON, A
REPRESENTATIVE IN CONGRESS FROM THE STATE OF TEXAS**

Mr. BARTON. Thank you, Mr. Chairman. I am not going to take 5 minutes. I believe I am supposed to yield to Dr. Murphy.

I have an opening statement that I will put in the record. I hate to be the skunk at the garden party, but every now and then I am. These user fees are not something that have been on the books for a hundred years. We first put them in place in 2002 and we have reauthorized them once. Currently, it is about \$287 million, I believe. I think it is a lot to ask this committee to swallow a doubling of the user fee budget to almost \$600 million. I checked yesterday, and I understand that it may be the tradition but I couldn't find that any member or any staff member of the majority or the minority had been involved in these negotiations with the FDA and the industry. If we came in and asked to double the income tax receipts, we would be laughed out of Congress, and to have a proposal put forward that doubles the user fee with the performance or lack thereof that has accompanied the last 3 or 4 years is something that I am not going to condone.

Now, I haven't talked with Chairman Upton or Chairman Pitts, and I am sure that there is another side to the story. But put me down as extremely skeptical that this is a good deal for the consumer or for the small medical device industry.

I had a company in my office just this week, or late last week actually, that has been making a device and marketing it for 30 years, and all of a sudden now they have been asked to have to go through the entire premarket approval process for something. I just don't accept that.

So Mr. Chairman, I am extremely glad that you are holding this hearing but don't ask this member to rubberstamp a doubling of a user fee when we have the program performance or lack thereof at this FDA.

And with that, I would yield the balance of the time to Dr. Murphy of Pennsylvania.

[The prepared statement of Mr. Barton follows.]

**Opening Statement of the Honorable Joe Barton
Chairman Emeritus, Committee on Energy and Commerce
Subcommittee on Health
“Reauthorization of MDUFA: What It Means for
Jobs, Innovation and Patients”
February 15, 2012**

Thank you, Mr. Chairman for this hearing today to discuss the reauthorization of MDUFA (Medical Device User Fee Act). Thank you for your timeliness in bringing this, and the other User Fees, before this committee.

Unless we make significant reforms to the Food and Drug Administration (FDA) and their review process, I believe we should end all user fees. The purpose of user fees is to provide the Food and Drug Administration (FDA) with the resources they need to thoroughly review products in a timely manner. However, the FDA has had a difficult time delivering on a timely basis, being predictable, consistent and proactive in its process.

I met with a small medical device company from Texas, just last week. This company has been manufacturing quality medical devices for 30 years, and has just recently been informed by the FDA that they will now have to go through the Pre-Market Approval (PMA) process. The FDA has not been clear as to why this change is occurring, or what necessitated it.

Globally, companies are seeing more and more uncertainty and lack of clarity from the FDA when trying to get their products approved. While countries around the world are fast and efficient, the FDA is dragging their feet. We cannot keep giving the FDA more money, in industry fees, and not make reforms to ensure – not promise but ensure – that there is more consistency, that there is more predictability, and that the FDA is timely and efficient in reviewing devices and drugs.

I also want to note that I do not approve of this committee rubber stamping an agreement made by the regulator and industry, without involvement in the agreement discussions from committee staff. Because, in the end, while the FDA may like the agreement and industry may sign off on it, higher fees means higher costs on the consumers, the American people.

Like my colleagues here, I want to see safe products approved quickly. I want the best products on the market to be made available to the consumer. But, the current process is not working. And more of the same is not going to make things better.

OPENING STATEMENT OF HON. TIM MURPHY, A REPRESENTATIVE IN CONGRESS FROM THE COMMONWEALTH OF PENNSYLVANIA

Mr. MURPHY. I thank the gentleman.

A few weeks ago, several of my colleagues and I met with Professor Ralph Hall, who will be testifying a little bit later today on a panel. At that meeting, Professor Hall explained how the review process at the FDA is driving investment in medical technologies overseas as well as sending jobs overseas. Now, according to Professor Hall, 40 percent of venture capitalists have already reduced investment in medical technology in the United States and many more are planning this. About 61 percent of venture capitalists cite regulatory challenges with the FDA as having the greatest impact on their investment decisions.

Now, this may seem like financial jargon but in reality, it points to a tragic bottom line: no money, no research, no treatments, no cures. This is about saving lives of people with untreatable diseases who are waiting in line for Washington's rules and bureaucracy to get out of the way and for the treatment and cures to move forward. It is cruelty, not comfort, when a doctor must tell a patient that bureaucratic barriers prevent patients in the United States from getting the treatment that they need.

We need to and we must help American patients have better access to the latest, safest medical advancements while also improving FDA's review process to allow more investment in U.S. medical technology. It is something we ought to be doing out of compassion for people who are sick.

And with that, I yield back to Mr. Barton.

Mr. BARTON. I have no further comments. If there are other members, I will be happy to yield, Mr. Rogers or Mr. Latta, anybody? I yield back to the chairman.

Mr. PITTS. The Chair thanks the gentleman. The Chair now recognizes the ranking member of the full committee, Mr. Waxman, for 5 minutes for an opening statement.

OPENING STATEMENT OF HON. HENRY A. WAXMAN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CALIFORNIA

Mr. WAXMAN. Thank you very much, Mr. Chairman, for holding this important hearing.

Our goal today is to start the process of reauthorizing the Medical Device User Fee Act, and I commend FDA and the industry for finally coming together to agree on a user fee proposal. I know it was a hard-fought compromise and I look forward to seeing the details. But I am pleased that there has been an agreement because I have very little faith that Congress is going to provide the appropriations for the FDA to do the job without a user fee. I would prefer we do it that way, and those who don't like the user fee will have to acknowledge that FDA will be short-funded and we won't get these devices approved as quickly as possible.

The funds collected under this act will provide FDA's device program with critical dollars that enable the agency to fulfill its public health mission: to ensure that only safe and effective medical de-

vices are marketed in the United States. That is our essential goal here. We should work together on a bipartisan basis to get it done.

The real compassion in this country is to make sure that we can get drugs and devices that work and that are safe to consumers, not just to get them out on the marketplace because it is no one's benefit to have drugs that are not safe or medical devices that are not safe or effective. The FDA, the device industry and American patients are counting on us to do our job.

I am concerned that some may try to hijack the reauthorization to advance proposals that would put the health of patients at risk. Last year, Republican members of the committee introduced a slate of 10 bills that would make significant and harmful changes, in my view, in FDA's device program. Unless we can reach consensus on these proposals, they should not be inserted into this must-pass reauthorization.

The newspapers are full of articles about the dangers of improperly designed medical devices. The prestigious Institute of Medicine concluded that our medical device laws need to be significantly strengthened. But many of these bills ignore the need for reforms that would protect patients. Instead, they read like a wish list assembled by lobbyists for the device industry.

The device industry claims that FDA regulation is killing jobs, stifling innovation, and depriving American patients of new medical devices. But there is no evidence to back these up except anecdotes. Anecdotes from some individual companies are not enough. And I think the industry knows that they need an FDA that is going to do its job if they are going to have credibility in the marketplace.

I have been appalled by the quality of the so-called "studies" that industry is using to advance these bills. Last July, I asked the editors of our Nation's top medical journals to examine the methodology used in the leading industry papers asserting that FDA is too slow, burdensome, and unpredictable. The editors said there were serious methodological flaws in both studies—biased samples, small sample size and botched statistical analysis, just to name a few—rendering them essentially useless as part of any discussion of FDA's regulatory system. None of the editors felt that the methodology of these studies was worthy of publication in a peer-reviewed journal, and yet they are put forward as a reason why we ought to change the law here in Congress.

Many in the device industry argue that Europe should be our model and they say new technologies are available years before they are on the market in the United States. But just yesterday, the *New England Journal of Medicine* published a study by Dr. Aaron Kesselheim finding numerous examples of high-risk devices that were first approved in the E.U. but either showed no benefit, or, worse, had substantial safety risks. I am glad that Dr. Kesselheim is here today to testify about this study.

FDA's job is to protect the public health. Part of advancing public health is helping manufacturers win approval for innovative new devices. But FDA's core responsibility is ensuring that only safe and effective devices are permitted on the market.

When FDA falls short and allows dangerous devices like surgical mesh and metal-on-metal hip implants to be implanted in patients,

the suffering of victims can be incalculable. That is why I joined with Mr. Pallone, Mr. Dingell and Ms. DeGette in requesting that the committee hear from witnesses about the risks from dangerous devices, and I want to thank Subcommittee Chairman Pitts and full Committee Chairman Upton for working with us to allow these witnesses to testify today on the second panel.

The reauthorization of MDUFA should be bipartisan, so I urge all members of the committee to work together on this critically important program.

Thank you, Mr. Chairman.

Mr. PITTS. The Chair thanks the gentleman.

Our first panel will have just one witness, Dr. Jeffrey Shuren, Director of the Center for Devices and Radiological Health at the FDA. Dr. Shuren is accompanied today by Mr. Malcolm Bertoni, Assistant Commissioner for Planning for the Office of the Commissioner. We are happy to have you with us today, Dr. Shuren. You are recognized for 5 minutes to summarize your testimony. Your written statement will be entered into the record.

STATEMENT OF JEFFREY E. SHUREN, DIRECTOR, CENTER FOR DEVICES AND RADIOLOGICAL HEALTH, FOOD AND DRUG ADMINISTRATION

Mr. SHUREN. Mr. Chairman and members of the subcommittee, I am Dr. Jeff Shuren, Director for the Center for Devices and Radiological Health, or CDRH, at the FDA. Thank you for the opportunity to testify today.

I am pleased to tell you that on February 1, FDA and representatives from the medical device industry reached an agreement in principle on proposed recommendations for the reauthorization of the Medical Device User Fee Act, or MDUFA. These recommendations would authorize FDA to collect \$595 million over 5 years to help fund a portion of the agency's medical device review program with FDA agreeing to certain overall performance goals. The final details of the agreement will be resolved very soon, and as required by law, we will hold a public meeting and seek public comment on the proposed package before sending a final package to Congress.

When I came to CDRH in 2009, in response to concerns expressed by industry and others, we initiated a review of our device premarket review programs. The following year, we released two reports that concluded, as I have testified before, that we had not done as good a job managing the review programs as we should have. The number one problem we found was insufficient predictability, which was leading to inefficiencies, higher cost to industry and FDA, and sometimes delays in bringing safe and effective products to market.

In January 2011, we announced a plan with 25 specific actions that we would take that year to improve the predictability, consistency and transparency of our premarket programs. As of February 2012, 75 percent of these actions plus eight additional actions are already completed or well underway. They are intended to create a culture change toward greater transparency, interaction and the appropriate balancing of benefits and risk. They focus on assuring predictable and consistent decision-making and application of the

least-burdensome principle and implementing more efficient regulatory processes.

We believe these actions have had and will have a visible, positive impact 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 conduct clinical studies first in the United States, speeding up clinical trial approval decisions and implementing the innovation pathway.

Preliminary data indicates that the actions we have taken have started to bear fruit. For example, the backlog of 510(k) submissions that had been steadily increasing from 2005 to 2010 decreased for the first time last year. However, we still have much work to do.

Reauthorization of MDUFA will provide the resources that CDRH needs to continue improving the device review programs and help reduce the high staff turnover that has adversely affected review predictability and consistency. The proposed MDUFA recommendations we have agreed upon with industry will also include several important process improvements. For example, if a performance goal on a device application is missed, the MDUFA proposal would require FDA and applicants to work out a plan to complete work on the submission, ensuring that no submission is left behind, and requiring new substantive interaction between FDA and an applicant halfway through the targeted time for reviewing the application would help to assure sufficient time for the applicant to properly respond to appropriate questions. Clear criteria for when FDA will refuse to accept a complete application means more efficient use of resources to the benefit of both FDA and industry. These and other proposed enhancements are intended to achieve a shared outcome goal of reduced average total time to decision, which we and industry believe is an important indicator of a successful premarket review program.

The agreement in principle we have reached with industry strikes a careful balance between what industry agreed to pay and what FDA can accomplish with the amount of funding proposed. However, we are concerned that even if device user fee resources are increased under MDUFA III, additional new legislative mandates imposed on CDRH could divert resources and undermine FDA's ability to achieve the new performance goals. When PDUFA was last reauthorized in 2007, the addition of new policy-related requirements ultimately resulted in FDA's drug review program having to temporarily suspend meeting its PDUFA review goals in order to meet the statutory mandates. We want to avoid such a situation so that CDRH can focus on meeting the ambitious new proposed PDUFA program goals and achieving timely patient access to safe and effective devices, which is an objective that we share with industry, health care practitioners, patients and consumers, and I know you as well.

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

[The prepared statement of Mr. Shuren follows:]



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

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

DIRECTOR
CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE
SUBCOMMITTEE ON HEALTH
COMMITTEE ON ENERGY AND COMMERCE
U.S. HOUSE OF REPRESENTATIVES

"REAUTHORIZATION OF MDUFA:
WHAT IT MEANS FOR JOBS, INNOVATION AND PATIENTS"

February 15, 2012

RELEASE ONLY UPON DELIVERY

INTRODUCTION

Mr. Chairman and Members of the Subcommittee, 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 reauthorization of the Medical Device User Fee Act, or MDUFA.

Background on MDUFA

The enactment in 2002 of the Medical Device User Fee and Modernization Act (MDUFMA I) was prompted by growing concerns about the medical device review program's capacity and performance. MDUFMA I and MDUFA II (enacted in 2007) authorized user fees for the review of medical device premarket applications, reports, supplements, and premarket notification submissions. These additional resources enabled FDA to make its reviews more timely, predictable, and transparent to applicants. MDUFA fees and mandated appropriations for the medical device program helped FDA expand available expertise, modernize its information management systems, provide new review options, and provide more guidance to prospective applicants.

MDUFA authorizes FDA to collect user fees for certain medical device applications, the registration of certain medical device establishments, and certain other purposes. Small businesses may qualify for a waiver or a reduced fee on certain submissions to FDA.

Of the total \$292,707,540 obligated in support of the process for the review of medical device submissions in FY2010, MDUFA fees funded about 20 percent. The remainder of the funding was through appropriations. Fees currently charged for device review under MDUFA include \$220,050 for 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). For lower-risk devices cleared under the 510(k) review program, manufacturers pay \$4,049 per 510(k) application review (\$2,024 for small businesses).¹ As a point of comparison, PDUFA fees – nearly \$568 million in FY2010 – currently account for about two-thirds of the drug review program’s budget, and the current fee for FY 2012 associated with review of a New Drug Application (NDA) requiring clinical data is \$1,841,500.²

The medical device user fee program has produced benefits for public health. A better-resourced premarket device review program has enhanced FDA’s abilities to help bring more safe and effective medical devices to the market, while keeping pace with the increasing complexity of technology and changes in clinical practice. Since MDUFA II was reauthorized in 2007, FDA has approved 106 original PMAs and cleared more than 13,000 devices under the 510(k) program.

For example, approvals have included devices intended to address unmet needs in the pediatric population, such as the first heart pump designed to support the hearts of infants to adolescents until they receive a heart transplant, and the first percutaneous heart valve (approved for both children and adults).

The device program also has approved important new laboratory tests, including an emergency-use diagnostic test in response to H1N1 outbreak in humans, and the first quick test for malaria. Device reviews have significantly contributed to the very important trend toward personalized medicine through clearance of a test system that can assist in assessing the risk of tumor recurrence and long-term survival for patients with relatively high-risk breast cancer.

Other important devices that have become available to patients over the course of MDUFA II include, for example, the Implantable Miniature Telescope (IMT), used for

¹ 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/2011-19333.htm>.

² 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>.

monocular implantation to improve vision in elderly patients with stable severe to profound vision impairment associated with end-stage age-related macular degeneration (AMD)³; the Infrascanner™ infrared brain hematoma detector, a noninvasive hand-held device that uses near-infrared spectroscopy to evaluate suspected brain hematomas at the site of injury within the “golden hour” (the period following head trauma when pre-hospital analysis is needed to rapidly assess a patient’s neurological condition)⁴; and the NeuRx DPS™ RA/4 Respiratory Stimulation System, an implantable electronic device that stimulates the diaphragm and allows certain spinal cord injury patients to breathe for at least four hours a day without a mechanical ventilator.⁵

However, neither the FDA nor industry believe that the user fee program has reached the level of performance, or produced the extent of benefits, that it has the potential to achieve.

MDUFA II Performance

FDA has been meeting or exceeding goals agreed to by FDA and industry under MDUFA II for approximately 95 percent of the submissions we review each year. For example, 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. FDA’s performance over the course of MDUFA II has not been limited to achieving quantitative goals for the timely review of premarket submissions like PMAs and 510(k)s; we have also accomplished a number of “qualitative” goals set by MDUFA II in 2007, including issuing more than 50 new and updated guidances for industry. Guidance documents are important resources for industry because they describe the Agency’s interpretation of, or policy on, regulatory issues, and as such,

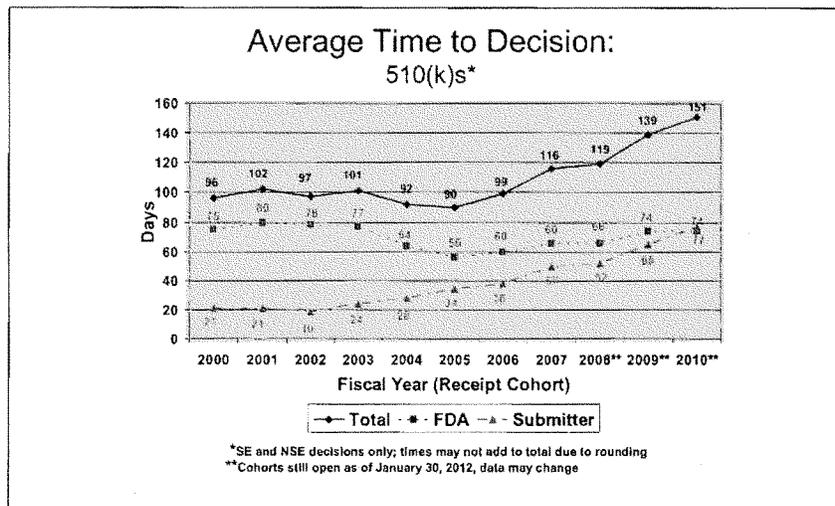
³ See FDA News Release, “FDA Approves First Implantable Miniature Telescope to Improve Sight of AMD Patients” (July 6, 2010), available at <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm218066.htm>.

⁴ See Office of Naval Research, “Naval Technology Could be a Lifesaver” (Dec. 21, 2011), available at <http://www.onr.navy.mil/Media-Center/Press-Releases/2011/Infrascanner-brain-TBI-FDA-approval.aspx>.

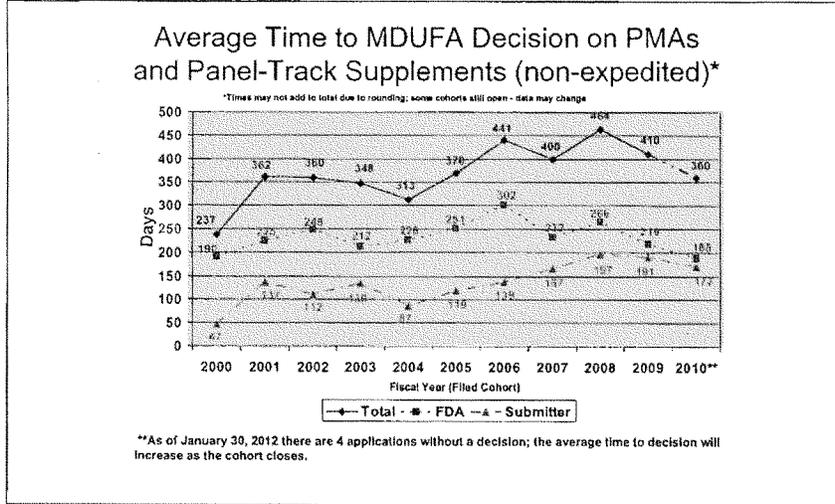
⁵ See FDA News Release, “FDA Approves Diaphragm-Pacing Device” (June 18, 2008), available at <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm116914.htm>.

are critical to support industry efforts to comply with the law and to develop new products that may benefit the public health.⁶ The availability of guidance documents also facilitates regulatory predictability and consistency.

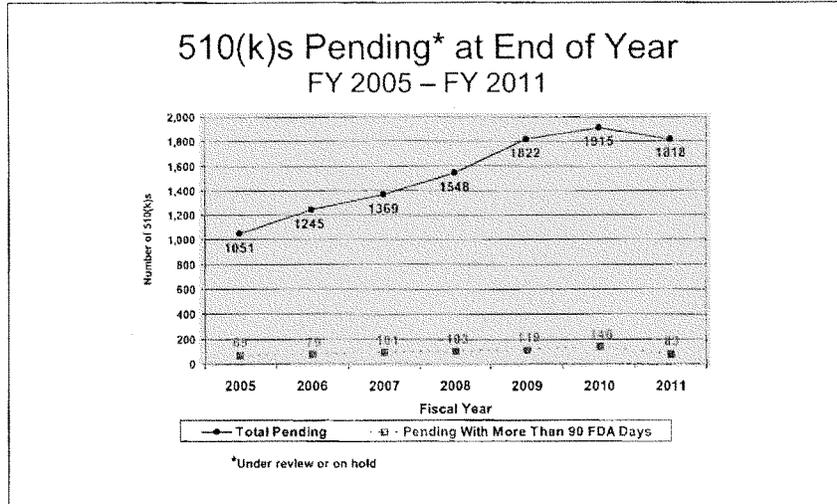
It is important to note that MDUFA metrics reflect FDA time only; they do not reflect the time taken by device sponsors to respond to requests for additional information. *Overall* time to decision—the time that FDA has the application, *plus* the time the manufacturer spends answering any questions FDA may have—has increased steadily since 2001. As the graphs below illustrate, while the time FDA spends reviewing an application has improved (for both low- and high-risk devices), average total days for the review of 510(k)s has been increasing since 2005, 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.



⁶ Guidance documents include documents that relate to: (1) the design, production, labeling, promotion, manufacturing, and testing of regulated products, (2) the processing, content, and evaluation or approval of submissions, and (3) FDA’s inspection and enforcement policies. See generally “Food and Drug Administration Report on Good Guidance Practices: Improving Efficiency and Transparency” (issued Dec. 2011), available at <http://www.fda.gov/downloads/AboutFDA/Transparency/TransparencyInitiative/UCM285124.pdf>.

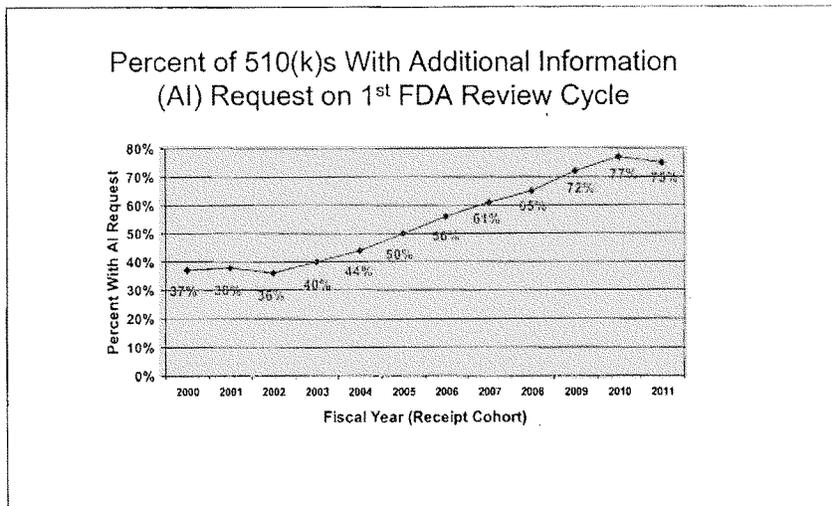


FDA bears some responsibility for the increase in total time to decision, and we have been instituting management, policy, and process changes to address this issue. As a result, in 2011, CDRH for the first time began reducing what previously was an increasing backlog of unresolved 510(k) submissions,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



There has also been a prolonged increase, since FY 2002, in the percentage of 510(k) submissions requiring an Additional Information (AI) letter⁷ after the first review cycle, as indicated in the chart below. The increasing number of AI letters has contributed to the increasing total time from submission to decision.

⁷ If, after reviewing an application, FDA determines that it cannot approve or clear the application in its current form, FDA sends a letter informing the sponsor of this decision. For 510(k) applications, this is called an "Additional Information" (AI) letter.



Smart Regulation's Role in Facilitating Medical Device Innovation

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. We are committed to continued improvements in the device approval process to address legitimate concerns raised by industry and other stakeholders.

Nearly two 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 number one 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 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 in 2011 to improve the predictability, consistency, and transparency of our premarket programs – as of February 2012, 75 percent of these actions, plus eight additional actions, are already completed or well underway.⁸ The following month, we announced our Innovation Initiative, which included several proposals to help maintain the position of the U.S. 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:

⁸ More information about FDA's progress in implementing the CDRH "Plan of Action for 510(k) and Science" is available on FDA's website at <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHReports/ucm276286.htm>.

- Create a culture change toward greater transparency, interaction, collaboration, and the appropriate balancing of benefits and risks;
- Ensure more predictable and consistent recommendations, decision-making, 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 (draft guidance released December 1, 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 (December 2011);
- Improving communication between FDA and industry through enhancements to

interactive review (some enhancements in place as of February 2012);

- 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 involves 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 decision-making (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 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).

Our efforts to improve the premarket review programs at CDRH are ongoing. We recently released our Strategic Priorities for 2012,⁹ in which we commit to completing or continuing the work we already started in four priority areas: (1) Fully Implement a Total Product Life Cycle Approach,¹⁰ (2) Enhance Communication and Transparency, (3) Strengthen Our Workforce and Workplace, and (4) Proactively Facilitate Innovation to Address Unmet Public Health Needs. Our plan for 2012 includes time frames associated with each strategy and specific actions we will take to meet those goals or make significant progress towards achieving those goals, including, for example:

- By April 1, 2012, begin the Triage of Premarket Submissions Pilot to increase submission review efficiency and better manage the premarket review workload;
- By September 30, 2012, make recommendations on how to adequately recognize good employee performance and address poor performance;

⁹ CDRH, "2012 Strategic Priorities," available at <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHVisionandMission/acm288735.htm>.

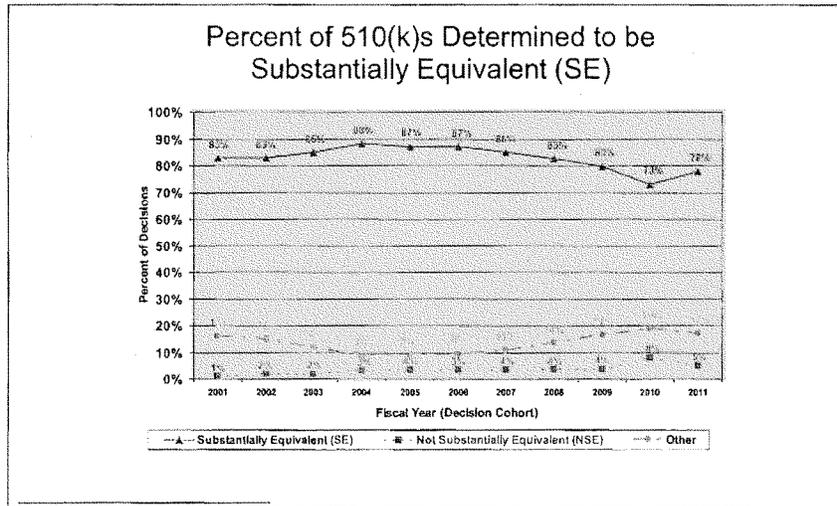
¹⁰ A Total Product Life Cycle (TPLC) Approach involves making well-supported regulatory decisions that take into consideration all of the relevant information available to CDRH, at any stage of a product's life cycle to assure the safety, effectiveness, and quality of medical devices, and the safety of non-device radiation-emitting products. The Center's TPLC database integrates premarket and postmarket data about medical devices. For more information, please see CDRH's web site at <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHTransparency/acm199906.htm>.

- By September 30, 2012, create processes and tools that will improve the pipeline for innovative medical devices and transform the way CDRH works with medical device innovators, such as the new Entrepreneurs-in-Residence program;
- By September 30, 2012, develop methods and procedures for the systematic analysis and use of medical device recall information;
- By October 31, 2012, develop a comprehensive strategy to assess real-world device performance;
- By December 31, 2012, conduct an evaluation of CDRH staffing, infrastructure, policies, and practices pertaining to medical device software;
- By December 31, 2012, review remaining Class III pre-amendment medical devices;
- By December 31, 2012, launch the Experiential Learning Program (ELP) to enhance premarket reviewer knowledge of how medical devices are designed, manufactured, and utilized by providing real-world learning opportunities; and
- By December 31, 2012, launch the CDRH Leadership Enhancement and Development Program (LEAD) to provide CDRH managers and supervisors information and tools to ensure effective leadership.

We believe the actions that we've taken and plan to take in the future will have a positive impact on the device review process 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 (consistent with conflict-of-interest guidelines), 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.

For example, I'm pleased to report that, consistent with our many improvements to the 510(k) program, the recent increase in the "not substantially equivalent" (NSE) rate¹¹ appears to be turning around. For manufacturers and FDA, NSE determinations often represent an inefficient use of time and resources. NSE determinations require significant Agency resources and time, yet fail to result in the marketing of a new product. As shown in the chart below, from a peak of 8 percent in 2010, the NSE rate has decreased to 5 percent in 2011. Just as important, we also may be seeing a reversal in the trend of declining rate in Substantially Equivalent (SE) decisions that clear a 510(k) submission for marketing. After several years of declining percentages, reaching a low of 73 percent in 2010, SE rates increased by 5 percent in 2011, as shown in the chart below.



¹¹ Among the reasons that 510(k) submissions result in NSE determinations are: lack of a suitable predicate device; intended use of the new device is not the same as the intended use of the predicate; technological characteristics are different from those of the predicate and raise new questions of safety and effectiveness; and/or performance data failed to demonstrate that the device is as safe and effective as the predicate. The vast majority of NSE decisions are due to the absence of adequate performance data, sometimes despite repeated FDA requests.

To best serve patients, both the medical device industry and FDA must have the flexibility to be innovative and entrepreneurial. CDRH must continue making critical improvements to our device program. At the same time, the medical device industry and CDRH must continue to work together to ensure that the Center receives high-quality submissions that 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. Timely reauthorization of MDUFA, as well as the Congressional appropriations process, is critical to achieving these goals.

Moving Forward: Reauthorization of MDUFA

When MDUFA was 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, as directed by Congress, we have been meeting with stakeholders, including representatives of patient and consumer groups, since January 2011 and have been making the minutes of those meetings available to the public.

Since January 2011, we also have been holding discussions with the medical device industry in an effort to develop a package of proposed recommendations for MDUFA reauthorization. We were pleased to announce last week that FDA and representatives from the medical device industry have reached an agreement in principle on those proposed recommendations. This agreement in principle, which would authorize FDA to collect \$595 million in user fees over five years (plus increases based on inflation), strikes a careful balance between what industry agreed to pay and what FDA can accomplish with the amount of funding proposed. We believe that it will result in greater predictability, consistency, and transparency

through a number of improvements to the review process.

The agreement in principle reached by FDA and the medical device industry includes numerous important improvements to the MDUFA program, including:

- Earlier and more transparent and predictable interactions between FDA and the applicant, both during the early product development or “pre-submission” stage as well as during the review process;
- More detailed and objective criteria for determining when a premarket submission is incomplete and should not be accepted for review;
- More streamlined FDA review goals that will provide better overall performance and greater predictability, including a commitment to meet with an applicant if FDA’s review of their submission extends beyond the goal date, so that the parties can discuss how to resolve any outstanding issues;
- Additional resources to support guidance development, reviewer training and professional development, and an independent assessment of the pre-market review process to identify potential enhancements to efficiency and effectiveness;
- More detailed quarterly and annual reporting of program performance; and
- A joint commitment between FDA and industry to accomplish shared outcome goals to reduce the total average calendar time to a decision for PMAs and 510(k)s.

Once the final details of the agreement in principle are resolved, as required by statute, FDA will prepare a package of proposed recommendations based on that agreement, will present that package to the relevant Congressional committees, and will seek public comment on the proposed recommendations by publishing them in the *Federal Register* and holding a public meeting. The Agency will then consider the public’s views and comments, revise the proposed

recommendations as necessary, and transmit a final package of recommendations to Congress, along with a summary of the views and comments that were received and any changes that were made to the proposed recommendations in response to the public's views and comments.

While we work with all interested stakeholders and Congress toward reauthorization of MDUFA in order to provide adequate and stable funding for the program, we will also be moving forward with our ongoing CDRH program improvements, focusing on smart regulation that will facilitate device innovation. 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 European Union (EU) before they do in the United States. While we want devices to be available to American patients as soon as possible, 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.¹²

¹² 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>.

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 from the Belgian Health Care Knowledge Centre (a governmental agency that produces studies to advise policy-makers when deciding on health care and health insurance)¹³ 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 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.”¹⁴

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.¹⁵ In the EU, more than 70 private, non-governmental 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

¹³ Additional information about the Belgian Health Care Knowledge Centre, and its mission and activities, is available at <https://kce.fgov.be/content/about-the-kce>.

¹⁴ 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.

¹⁵ 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/meddev2_7_rev_3_en.pdf.

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.¹⁶ 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.¹⁷ 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.

Most recently, France’s Directorate General for Health and its consumer safety body AFSSAPS¹⁸ issued a report¹⁹ urging stronger national and European regulation and monitoring of medical devices. In an accompanying statement, France’s Minister of Health, Xavier

¹⁶ See “Clinical evaluation of cardiovascular devices: principles, problems, and proposals for European regulatory reform,” Fraser, et al., *European Heart Journal*, May 2011.

¹⁷ “The Truth About Medical Devices,” *British Medical Journal*, vol. 342, at pp. 1115-1130 (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>.

¹⁸ Agence française de sécurité sanitaire des produits de santé, France’s Agency for the Safety of Health Products.
¹⁹ See AFSSAPS, “Poly Implant Prothèse: remise d’un rapport de la DGS et de l’Afssaps aux ministres chargés de la santé – Communiqué,” available at <http://www.afssaps.fr/index.php/infos-de-securite/Communiqués-Points-presse/Poly-Implant-Prothese-remise-d-un-rapport-de-la-DGS-et-de-l-Afssaps-aux-ministres-charges-de-la-sante-Communiqué>.

Bertrand, said that European Union rules on regulating and monitoring medical devices “must be radically overhauled.”²⁰

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. 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 long recognized that a strong and well-functioning FDA is vital to maintaining America’s preeminence in medical technology innovation, and we support the current regulatory framework in the U.S.”²¹

CONCLUSION

Over the course of MDUFA II, and especially during the last two years, CDRH has been working, with extensive input from industry and other stakeholders, 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.

²⁰ See “France Calls for Europe-wide Control on Prosthetics following PIP Breast Implant Scare.” *The Telegraph* (Feb. 1, 2012), available at http://www.telegraph.co.uk/health/women_health/9054282/France-calls-for-Europe-wide-control-on-prosthetics-following-PIP-breast-implant-scare.html.

²¹ Advanced Medical Technology Association (AdvaMed), “AdvaMed Statement on the House Energy and Commerce Subcommittee Hearing on FDA Device Regulation” (July 20, 2011).

While we work with industry, other stakeholders, and Congress in the statutory process toward the reauthorization of medical device user fees, in order to ensure adequate and stable funding of the program, we are also continuing to move forward with CDRH program improvements. 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 current law and the enactment of MDUFA III. At the same time, we must remain mindful that, unlike the PDUFA program, in which fees fund more than 60 percent of drug review costs, user fees under MDUFA III (as described in the recently announced agreement in principle) will fund about a third of the total cost of the medical device premarket review process, making it important to keep these resources focused on the performance goals identified in the MDUFA agreement.

Mr. Chairman and Members of the Subcommittee, 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.

Mr. PITTS. The Chair thanks the gentleman, and I will now begin the questioning and recognize myself for 5 minutes for that purpose.

Dr. Shuren, Chairman Upton and I have set a deadline of reauthorizing the user fees by the end of June. We received the three other user fee proposals by January 15th but we did not receive the medical device user fee proposal as required under statute. Given the need to reauthorize the user fees as soon as possible, let me ask you a two-part question. Number one, when will FDA send us the legislative language and proposed agreement for the medical device user fee so that the committee can begin its work, and two, what specific steps does the administration plan to take to expedite the process so the committee can get the device information as soon as possible?

Mr. SHUREN. So the plan we have put in place and what we have asked of the administration is for expedited review of a proposal so that we can get the proposal out to you and out to the public as we move into March, and so you will be able to see what we are proposing, we will get the public comments, we will wrap up on that. We have to follow that process. And then we will have the final package. But you will be able to see that proposed package, and our goal is to try to do that in the next few weeks.

Mr. PITTS. By mid-March?

Mr. SHUREN. That is approximately the time, and that is what we have been asking the administration to support us in doing.

Mr. PITTS. All right. The medical device legislation introduced by our committee members and Mr. Paulson of Minnesota contains critical improvements aimed at making FDA's regulation of medical devices both premarket and postmarket more predictable. This predictability is critical to getting life-saving devices to our Nation's patients and their families, as we have heard from Marty Conger, Carol Murphy and Pam Sagan at our O&I hearing in July. It is also critical in keeping medical device jobs in the United States, as we have heard from numerous innovators throughout the past year.

We have heard some argue that these device bills aren't necessary because FDA is fixing the problem. That is a little hard to believe. For example, that is what FDA has told us about the pre-amendment class III devices for the past 20 years, and the problem still isn't fixed. Class III devices are still going through the 510(k) process. Frankly, we don't have 20 years or even 6 months to wait for FDA to fix the problems. Our Nation's patients and innovators need help now. So my question is, will you commit to working with us on this legislation so we can help our Nation's patients and help keep American device jobs here in the United States?

Mr. SHUREN. Mr. Chairman, we would welcome the opportunity to work with you on legislation.

Mr. PITTS. We will follow up with that. Thank you.

What is the status of the unique device identifier rule?

Mr. SHUREN. So we have completed the rule. It is now currently under review at the administration and we are waiting for their approval to move forward with it.

Mr. PITTS. Five years ago, the committee passed the reauthorization of the medical device user fee, and when we voted for that bill,

we did so expecting that FDA would meet its end of the deal. It appears that that hasn't happened. FDA has failed to meet many of the MDUFA goals, and during the past 5 years, we have seen the total time it takes from submission to FDA decision rise dramatically. Given that track record, why should we believe that you are going to meet the goals you agreed to in the proposed user fee package?

Mr. SHUREN. Well, I won't belabor the point that there are some things that but for the user fee act, we would not have been able to enhance, but we agree, we are not happy with where the program is; industry is not happy with where it is. There are fundamental problems right now. Some of that is on our part, and that is why I made a public commitment to make those changes and started last year, regardless of whether we saw user fee dollars or not, and we are moving forward on those.

But by the same token, there are problems with the program that we cannot solve without funding. I have high staff turnover rates, just like the drug program had 10 years ago, because of too much work on their plate. We don't have enough managers to provide good oversight. The ratios are running from 1:14 up to 1:25 under a front-line manager. That is untenable in any business, and I can't solve that with changes in policies and processes. I can only change that with having the people to do the work, enough managers and enough staff to do the work. That is what comes out of the user fee dollars. And together, making those program improvements that we have underway, having the dollars from industry and having smart performance goals in place can help us achieve a successful program and the outcome we all want to see from device review.

Mr. PITTS. I have just 20 seconds left. What metrics are included in the agreement to make sure you can meet your goal?

Mr. SHUREN. In the MDUFA agreement?

Mr. PITTS. Yes.

Mr. SHUREN. So there are performance goals that pertain to FDA time but also to the average total time to the decision. So these are the things that happen that are not quite under our control but by putting in certain process improvements of greater engagement and interaction with industry, with the companies as we move forward during the review, our hope is that with that and with the more staff on board, we can actually bring down the total time for making a decision, which we think is an important indicator, through those improvements. We also have goals that go towards—it is predominantly to the performance on different kinds of applications.

Mr. PITTS. The Chair thanks the gentleman and recognizes the ranking member, Mr. Pallone, for 5 minutes for questions.

Mr. PALLONE. Dr. Shuren, I wanted to ask about the 510(k) process, and first commend you for the focus you have given to improving it. I have been interested in how to fix it for a long time. In fact, when I was the chairman of the subcommittee, we held a hearing in 2009. Quite frankly, both before and after that hearing, I was of the opinion that the 510(k) process was broken, so I am glad that FDA has focused its attention on resources and how to improve it.

I have seen your 510(k) action plan and the amount of work that CDRH did on this topic is pretty impressive. What is your sense of the 510(k) program now? Is it operating better? Is there more predictability and consistency? And what steps on your action plan would you categorize as game changers?

Mr. SHUREN. So the program is not where we would like it to be. We are not seeing the performance from it that we would like to have, but we are starting to see some early indicators, if you will, the canaries in the coalmine, suggesting instead of them dying from gas, that actually they are doing better. So starting almost 10 years ago, we saw the requests for additional information on 510(k)'s go up and up and up steadily. We saw total review times going up and up and up. We saw the backlog of 510(k)'s going up and we saw the percent of 510(k)'s being cleared going down. In 2011, for the very first time we are seeing the percent of additional requests on 510(k)'s starting to dip for the first time the other direction. We are seeing that the percent of 510(k)'s being cleared has been going up. I put all this information, by the way, in my written testimony. In 2012, that number, that percent of clearance actually went up beyond 2011. We are seeing the backlog go down. So all of these are early signs but I don't think you are going to see the real benefit from it until many of our policies go into effect.

Game changers right now—simple smart business process improvements to assure that critical decisions like asking for additional information are not made in the lowest parts of our center but they are made at the right level of management, which is why I need enough managers to provide that oversight. In fact, we created a Center Science Council of our most senior people to oversee the most important decisions. We are putting in new policies to incentivize starting clinical trials in the United States earlier. You get the clinical studies started here first, you keep the technology here because the companies come back to the same doctors over and over again, and also having benefit-risk framework that is much more focused on taking into account what patients are willing to tolerate for risk because they are the ones who get the devices, not my reviewers.

Mr. PALLONE. Thank you. Let me ask you about the conflict of interest in these scientific experts for the advisory panels. We have heard from a number of parties that the conflict of interest provisions are not working and are excluding legitimate experts. When the Commissioner was here 2 weeks ago, she indicated that there have been challenges at FDA in filling the advisory panels. Would you agree that CDRH is having similar challenges?

Mr. SHUREN. We do face challenges in moving forward, which is why we agree with you. You consider this an important issue; we consider this an important issue. And although we have not found a legislative fix yet that has a significant difference, we think this is something worth exploring. One of the reasons I would like to take the chairman up on his offer to work on legislation focused on this area is one of those areas. We are looking at internal process changes, are there other things we can be doing to sort of reduce those challenges we face.

Mr. PALLONE. I know when you testified before the Senate Health Committee in November, you indicated willingness to en-

gage with the Senators, so I guess I am getting the same assurance from you today on this.

Mr. SHUREN. Yes.

Mr. PALLONE. All right. Chairman Pitts talked about the UDI, and I think it is unfortunate that after 5 years, I think we should be closer on implementation on what I consider a very critical component. But what I wanted to ask you is, could you explain how UDI will interact with other postmarket authorities that FDA has in the device space and other initiatives that you have underway?

Mr. SHUREN. So unique device identifier will allow us to link the use of a device with a patient's experience with the device. So data is collected every day as a part of routine clinical practice, and we can't tap into that without a UDI. That is why that unique device identifier is a game changer, and it will allow us to move forward to have more robust postmarket surveillance systems that then industry and we can take advantage of and health practitioners and others in the following ways. If we have more robust postmarket surveillance, when there are problems, if we can identify them more quickly and get on top of them, it doesn't mean the device comes off the market. It means that we address it, and you don't get the front-page stories in the newspapers because you don't have so many people exposed. You have a better infrastructure that allows companies to conduct postmarket studies at lower cost because the infrastructure is there, and it will allow us to make better use of postmarket data to reduce the burden for premarket data requirements for some devices. In fact, if we are properly authorized, we may be able to even shift some of the premarket data requirements to the postmarket setting. But these are all things we could do in the future and a unique device identifier is critical to making that happen.

Mr. PALLONE. Thank you.

Mr. PITTS. The Chair thanks the gentleman and recognizes the vice chairman of the committee, Dr. Burgess, for 5 minutes for questions.

Mr. BURGESS. Thank you, Mr. Chairman.

Dr. Shuren, in this committee we worked on this a lot over the years, and it seems like there is a repetitive stream of people in my office talking about difficulties they are having in this arena. So I don't think there is any question that we have a problem. The problem generally seems to be with predictability and consistency at your agency, and whether we all agree with where the problems are and whether we all agree with how much activity is leaving our shores, I don't think there is any question that some is, and the President's own Jobs Council has raised this issue, and specifically they commented, quoting from them, "Our medical innovation system is in jeopardy. Investment in life science area is declining at an alarming rate because of the escalating cost, time and risk of developing new drugs and devices. While many factors contribute to the decline, an important factor is the uncertainty surrounding the FDA regulatory environment."

So this is not House Republicans, this is the President's Jobs Council. This is the administration that is voicing concern with the predictability and consistency within the FDA. How do you respond to what the Jobs Council is telling us?

Mr. SHUREN. I think you can add me and my own staff, who have our own concerns about the program as well, and I will say in terms of the Jobs Council, when they then came out and said what things you might want to look at for the medical device program, one of their recommendations was to have a benefit-risk determination framework that is much more focused on looking at patient tolerance for risk. We appreciate that, because when they came out with that recommendation, we had actually already proposed such a framework over the summer. In fact, we are finalizing it right now and we have committed and are already set to put out the final document and implement it come the end of March.

Mr. BURGESS. But again, you know, I just can't stress this enough. There is a steady stream of people that come in to see me and I suspect other Members of Congress have similar stories where there is a problem, and the problem seems to be centered at the Center for Devices and Radiological Health. It is clearly something that needs your highest attention and I look forward not just to your framework but we actually look forward to some performance on this, and as I reference in the opening statement, we can't just be upping in the dollars and decreasing the performance, and unfortunately, that seems to be the direction we are going.

Let me ask you a couple of specifics on some of the things I referenced. Some of the draft guidance that is coming out of your area where it appears that you are increasing your jurisdiction and your territory, and I am not sure that is in everyone's best interest and specifically in your best interest, but what about the draft guidance for industry and staff on the in vitro diagnostic products that are labeled for research use only and investigational use only? This is something that came out of your office, and depending upon the stage of development, such components are officially labeled research use only, investigational use only. That means they are neither sold nor marketed as clinical devices nor offered as services such as laboratory-developed tests, but they may be useful in developing new devices. So now it looks like your agency is wanting to regulate even the devices that are used to help develop the devices. Have I read that correctly?

Mr. SHUREN. Well, components that are being used as a part of the device are part of the device, and we regulate that. You know, the policy—

Mr. BURGESS. Well, let me ask you this then. Specifically, what are some of the deficiencies that you saw that required you to issue this draft guidance?

Mr. SHUREN. That there were companies who were actually saying that this particular device or analyte was for research purposes. They were actually marketing it for commercial use. So this policy is to clarify in terms of what you need to do to be very clear on, is this truly for research and how you handle that, or is this actually being used in patient care, and that is what it is trying to clarify.

Mr. BURGESS. And again, give us an idea of the scope of the problem of this. Is this something that you are bumping up against all the time or is this something that has happened and you are trying to get in front of it?

Mr. SHUREN. No, it is something we have been running into and we continue to see, and that is why we have a policy to clarify it.

Mr. BURGESS. And can you provide us on the committee with some examples of that so we can better understand why this mission creep is going on at your center?

Mr. SHUREN. We would be happy to come back and give you some very specifics, give you a list of examples.

Mr. BURGESS. And once again, this doesn't seem to be the flexibility built into this. It is kind of an all-or-nothing phenomenon, and one of the complaints we get is, there is no flexibility within the Center for Devices and Radiological Health. Is that something that you can help us with?

Mr. SHUREN. First of all, I would say actually we are more flexible than people give us credit for.

Mr. BURGESS. Fair statement, because you are not getting any credit at all right now.

Mr. SHUREN. I know. I mean, I will give you an example. We just recently approved a device for tears in the large artery in the chest, and in terms of flexibility, we actually approved that device based upon just 51 patients followed for just 30 days, very small, not randomized, no controls, and we did it in less than 180 days. So the opportunities are there. The changes we are trying to make in the program are also to ensure we have flexibility where we need to do it but we are also consistent in how we apply it, and like I said, we made some process improvements that just went in the end of last year. There are a lot of policy changes, good policy changes, but as you know, as a Federal Government agency, we have to get public comment. That is a good thing. We get lots of perspectives. The downside is, it takes more time. So most of the things we are trying to improve actually don't start getting finalized and kicking in until this year.

Mr. BURGESS. We want you to be consistent. That is part of our goal as well, but I would appreciate you providing us some data on this because some of the stuff we are hearing does not comport with what you are telling us.

Thank you, Mr. Chairman. I will yield back. Maybe we will have time for a second round.

Mr. PITTS. The Chair recognizes the ranking member of the full committee, Mr. Waxman, for 5 minutes for questions.

Mr. WAXMAN. Thank you, Mr. Chairman.

Dr. Shuren, one of the bills included in the Republican package would make significant changes to the device center's so-called third-party review program. Currently, that program permits third parties to review certain 510(k) applications and provide recommendations to FDA on whether the agency should clear a particular device, then FDA has 30 days to make a final decision. That is what the law is now. The Republican bill would alter this scheme to make the third party's recommendation binding on FDA if FDA fails to respond in 30 days. The bill also would expand the types of devices that these third parties are permitted to review to include permanently implantable or life-sustaining or -supporting devices. These outside reviewers are not currently allowed to review these devices. I think these changes are very worrisome.

Would FDA be concerned about these kinds of changes to the program?

Mr. SHUREN. We are deeply concerned about these changes. I mean, the hard stop, the default about their decision going into effect if we don't make a decision actually can have the perverse impact also of our being in a position to actually not approve that product. That actually can spell the death knell for the third-party review program, and I don't think that was really the intent behind the bill but that is probably the outcome that will likely happen.

Expanding the scope of the devices, I will tell you, there are over a thousand devices that are already eligible for third-party review. I mean, for 510(k), most of the 510(k)'s would be eligible. We have gone through the different categories and we have said almost 75 percent—the number may in fact be higher—could then be eligible of that set for third-party review. The problem is, that program hasn't worked all too well, and one of the big challenges we face is that those third parties don't have access to the confidential information that we do. So as a result, they end up coming back sometimes with decisions that are not fully informed.

For example, we may have already spoken to a company about what they need to do, they came to us, and then they go separately to a third party. They have no idea what that conversation was, and as a result, they can't take advantage of it. That is the challenge we really face in getting that program—

Mr. WAXMAN. Well, I was concerned about this program when we implemented it in 1997. I was never comfortable with the concept of having external third parties who have the potential for conflict of interests on their own reviewing these important devices. So when I read this bill, I was very worried about the changes that they put in place. After hearing your further description of the impact it would have, it makes me even more concerned and I feel very uncomfortable with these further changes. It is like the XL pipeline resolution. When you force a decision, you get a bad decision.

Another of the Republican slate of bills, the Premarket Predictability Act of 2011, would make certain changes to three key areas of FDA's device regulation: one, to FDA's oversight over the investigational device exemption, two, to the so-called least-burdensome provisions, and three, to the procedures for appealing decisions through the Center for Devices. I want to start with the changes to the least-burdensome provision because those are the most troubling to me.

This language was added to FDA's statute as part of the 1997 Food and Drug Administration Modernization Act at a time when the industry was asserting that FDA was requiring too much of device manufacturers and stifling innovation, strikingly similar to what we hear still today, and in essence, these provisions say that FDA must consider the least-burdensome means of demonstrating that a device is effective when the agency makes its approval or clearance decisions. So in other words, FDA should consider whether clinical data are necessary if there are other less-burdensome means for demonstrating that a device can be marketed.

The Premarket Predictability Act would change this provision by adding more-specific language like requiring FDA to consider alter-

native approaches to clinical data in evaluating device effectiveness “in order to reduce the time, effort and cost” and directs FDA to consider “alternatives to randomized controlled clinical trials and the use of surrogate endpoints” when clinical data are necessary. This seems to me overly prescriptive. Why would Congress be dictating to our premier scientific regulatory body what type of clinical data it should consider? It is also concerning because it seems that it can make it harder for FDA to require clinical data even when the agency believes it is necessary. I know that some of the language in this bill was lifted from FDA’s 2002 guidance implementing the least-burdensome provision but it looks like there were some changes to that language that could be significant. Can you comment on this?

Mr. SHUREN. Yes. First, let me say, I support the least-burdensome principle. I think as a general matter, it is good government and I support the policy we put back in our guidance in 2002. That is why I reemphasized it to my staff last year in email. It is why we are actually tailoring our guidance so we apply it specifically to specific devices.

I do have concerns regarding this legislation because as it is drafted, we are reading it as lowering the standards in the United States for devices coming on the market, and that concerns us, and also to the extent there is a difference in that language in the bill versus our guidance, we have to reconcile those differences, which means we have to change the current policy. If folks think we have the right policy but we are not applying it consistently, that is a different issue. Now, we do have concerns about not applying it consistently and that is why we put in process improvements to assure that we are getting the right level of sign-off on any decisions for actually trying to ask for more information or doing something different than we did before, and oversight on decisions to make sure we are applying the least-burdensome principle. That is the problem we think needs to be fixed and that is the one we are already working on.

Mr. WAXMAN. Thank you.

Thank you, Mr. Chairman.

Mr. PITTS. The Chair thanks the gentleman and recognizes the chair emeritus of the committee, Mr. Barton, for 5 minutes for questions.

Mr. BARTON. Thank you, Mr. Chairman.

I think it is better to have a third-party review than to have it sit on a bureaucrat’s desk at the FDA and not get reviewed at all, but that is just me.

Mr. Chairman, I want to put into the record a study of October 2011 by the National Venture Capital Association and the Medical Innovation and Competitive Coalition. I am going to put the entire study in the record, but I want to just give some of the bullet points.

This study was done in October of last year, and its conclusion and summary is that venture capital companies in the United States are decreasing their investment in biotechnology and medical device startups in the United States. They are reducing their concentration in critical therapeutic areas and they are shifting their focus away from the United States towards Europe and Asia.

The primary reason is because of FDA regulatory challenges. In the last 3 years, they have decreased by 40 percent their investments in medical devices. In the next 3 years, they expect to decrease it again by 42 percent, and 61 percent of the respondents cited as their primary reason regulatory challenges at the FDA. I am sure that you have seen this study or at least the summaries of it, Doctor?

Mr. SHUREN. Yes, I have seen it.

Mr. BARTON. Now, the proposal that the industry and your department have agreed to doubles the user fees per year for the next, I think, 4 or 5 years. The current PMA fee right now I believe is \$220,000. Is that correct?

Mr. SHUREN. That is correct, for full fee. If you are a small business, it is \$55,000.

Mr. BARTON. What does it go to in this proposal that we have yet to see?

Mr. SHUREN. So we are finalizing those details but we are thinking at the end of 5 years it would be about \$267,000, \$268,000, so it will go up by about \$48,000, and it was actually a little bit higher last year. We reduced it, because by law, if we collected a little bit more money, we had to reduce the fees so we reduced the fees this year.

Mr. BARTON. And what does the small company fee go up to?

Mr. SHUREN. I think it is about \$67,000.

Mr. BARTON. And what is the level at which you are eligible for the small company fee?

Mr. SHUREN. If your annual sales or receipts are \$100 million or less.

Mr. BARTON. And is that what it is in the current? So is that changed or unchanged?

Mr. SHUREN. No, that has remained the same, and you can compare this on the drug side. NDA is the complement on the drug side. That fee is \$1.8 million.

Mr. BARTON. And I am sure, Doctor, that you are aware that in the new health care law that passed several years ago, there is a 2.3 percent tax on medical device companies, and it is expected to raise \$20 billion over the next 10 years.

Mr. SHUREN. I am aware of the tax.

Mr. BARTON. Why could we not use some of that money and have no fee increase at all?

Mr. SHUREN. The tax isn't under our purview. That is a question for the administration. But I will say the concern about dollars, and I recognize, you know, for industry, to ask them to pay more, you know, they are figuring out how to do that. But I will you, \$595 million over 5 years, compared to what you heard the other week on the Generic Drug User Fee Act, over 5 years, they are going to collect about \$1.5 billion, and the Prescription Drug User Fee Act over 5 years is going to collect almost \$3.5 billion. So I appreciate the industry paying more and they made compromises, we made compromises to get to where we are, but to look at us and say that we are asking for way too much, the drug program is going to get six times the amount in user fees over 5 years than us. Even generic drugs, a smaller program, is going to get 3 times the amount.

Mr. BARTON. I appreciate that, but your current medical fee is \$287 million, and under this proposal, it doubles.

Mr. SHUREN. Well, not the individual fees to companies, the collections. You know, things like—most of the small companies make the 510(k) devices, and the fee right now is about \$2,000, and under the changes being made over 5 years it would go up to about \$2,600. They also pay a registration fee, and many of them have one facility. That right now is about \$2,300, and it might go up to \$3,800. If you look at the drug side, a registration fee for a facility is a little over a half a million dollars.

Mr. BARTON. My time is expired, Mr. Chairman, but put me down as very skeptical. I will look at this with an open mind, but if I had to vote today, I would vote no and I would really ask the committee staff on both sides that once we get the proposal to really scrub it and let us make sure that we protect our device user companies and the consumers who are going to have ultimately pay the increase in these fees. With that, I yield back.

Mr. PITTS. The Chair thanks the gentleman, and if you will provide a copy of that study for the minority, they would like to see it before we enter it into the record.

Mr. BARTON. Sure.

Mr. PITTS. The Chair recognizes the ranking member emeritus, Mr. Dingell, for 5 minutes for questions.

Mr. DINGELL. Thank you, Mr. Chairman.

Dr. Shuren, nowhere in the legislation is any money being diverted from the clearance of devices or pharmaceuticals. Is there any diversion of the fees to be collected under this legislation from the actual clearance in any of the programs at FDA?

Mr. SHUREN. No.

Mr. DINGELL. Now, do the agreed-upon user fees give FDA resources necessary to ensure safety and efficacy of medical devices? Yes or no.

Mr. SHUREN. Yes.

Mr. DINGELL. Insufficient staffing at FDA and high employee turnover rates were mentioned by you, and they are a matter of concern. Will the agreed-upon user fees allow FDA to hire staff to carry out functions necessary to protect patient safety and improve new innovative devices? Yes or no.

Mr. SHUREN. Yes.

Mr. DINGELL. Will the agreement allow FDA to improve training and staff to ensure consistency in the review process? Yes or no.

Mr. SHUREN. Yes.

Mr. DINGELL. Do you believe the additional staff and professional development will help lead to reduced employee turnover? Yes or no.

Mr. SHUREN. Yes.

Mr. DINGELL. This authorization of medical device user fees includes several accountability provisions. The independent assessment of the review process is one of these provisions. Do you believe that this independent evaluation of the device review process and the recommendations from this evaluation will help FDA to identify needed areas of improvement? Yes or no.

Mr. SHUREN. Yes.

Mr. DINGELL. And will you put effort into seeing to it that that transpires?

Mr. SHUREN. Yes.

Mr. DINGELL. Now, will the independent assessment help industry and FDA to evaluate how FDA is using these resources from the user fee program? Yes or no.

Mr. SHUREN. Yes.

Mr. DINGELL. Dr. Shuren, would you agree that user fees are necessary to supplement the rather miserable level of appropriations provided by Congress to FDA for the purposes in the legislation?

Mr. SHUREN. Yes.

Mr. DINGELL. Now, Doctor, I have a concern here. If a high-risk device was put on the market with no trials for efficacy whatsoever, let us say a pacemaker or a heart valve, do you believe that a provider would reasonably know when or under what conditions to prescribe the particular pacemaker to an individual?

Mr. SHUREN. No.

Mr. DINGELL. So we have a real problem. If we don't assure that these things are safe, we might be putting in a hip or a knee or a heart valve or a pacemaker that wouldn't work and then we would have a fine mess on our hands, would we not?

Mr. SHUREN. Yes.

Mr. DINGELL. All right. Now, again, if a high-risk device was put on the market with no trials for efficacy, do you believe a patient would be sure of the efficacy of the particular or specific pacemaker for their particular heart condition? Yes or no.

Mr. SHUREN. No.

Mr. DINGELL. If a high-risk device was put on the market with no trials for efficacy, can a patient or provider know that the device is efficacious for the heart conditions you are trying to treat? Yes or no.

Mr. SHUREN. No.

Mr. DINGELL. In my opinion, demonstrating efficiency and efficacy in postmarket trials as opposed to premarket approval would weaken the high standard that patients have come to expect. Do you agree, yes or no?

Mr. SHUREN. Yes.

Mr. DINGELL. Now, even industry associations have made it clear that they support the regulatory framework currently in effect at FDA. Do you agree that maintaining this framework will preserve America's leadership in medical device innovation? Yes or no.

Mr. SHUREN. Yes.

Mr. DINGELL. We are not going to be benefited by approving devices that are not efficacious and that don't help the patient, are we?

Mr. SHUREN. No.

Mr. DINGELL. That is going to have a bad effect on our sales of devices, is it not?

Mr. SHUREN. Yes.

Mr. DINGELL. Now, I want to go back to a little bit of history on this. This whole business started when I was chairman of the committee and chairman of Oversight. We found that there was a massive amount of abuse at FDA, that there were gratuities taken and

all matter of difficulties. We found that a lot of this was judgments that were being abused by FDA because it didn't have the money to do the job, and we found that industry had this awful problem of not being able to get clearance. So we found in the case of pharmaceuticals that pharmaceuticals were laying around and not getting approved and sometimes on a 17-year patent that was taking 7 to 10 years to get that done. A major U.S. pharmaceutical company would lose during that time \$250 million a year. The consequences of that were very serious. So the Congress was always plagued with legitimate demands by industry to give them an extension of patent, and I supported many of these things, simply because it was basic fairness. But we figured out that the only way to do this was to see to it that they got their clearance quickly. So with agreement of industry, the first thing we did was to move this into the pharmaceuticals, and then the over-the-counters came in and said it would be a good idea if you did this for us because it would help us, and then we found that others would agree to it, although I have to say the device manufacturers had some difficulty in swallowing it, but they ultimately did, and they found it worked and they found that they all made more money because they were getting their patents cleared in a faster and better fashion.

I hope my colleagues will learn a little bit about that history. This gives cleaner and better service to the people. It saves money. It helps innovation and it helps our manufacturers to make decent money out of their patents without the delay that was occurring previous to these events.

Thank you, Mr. Chairman.

Mr. PITTS. The Chair thanks the gentleman and now recognizes the gentleman from Illinois, Mr. Shimkus, for 5 minutes for questions.

Mr. SHIMKUS. Thank you, Mr. Chairman.

Thank you, Dr. Shuren, for being here. Do you agree that the Institute of Medicine study on the 510(k) process was widely rejected? Yes or no.

Mr. SHUREN. One of their recommendations was widely rejected.

Mr. SHIMKUS. So that would be a yes?

Mr. SHUREN. Partial yes.

Mr. SHIMKUS. I will take partial. I am under Mr. Dingell's standards here.

How much did you pay for that study?

Mr. SHUREN. About \$1.3 million.

Mr. SHIMKUS. Did you ask for your money back? I am glad we got some giggling. The reality is, I was at a breakfast this morning and someone was asking for additional Federal money, only \$21 million. The reality is, you are sitting here saying we don't have enough money, but then we fund a study through the Institute of Medicine that costs \$1.3 million that is widely rejected, and we don't get our money back. So these dollars all add up, and we are in a Congress now that says, you know, this whole saying, if you worry about the pennies, the dollars take care of themselves. So as we are talking about Mr. Barton, why is he doubling a user fee? Well, if we take care of the pennies, the dollars will take care of

themselves, and in this case, I don't think we got our money's worth out of the Institute of Medicine's report.

Mr. SHUREN. And I will say, I appreciate those concerns. They actually had a number of other recommendations that we are following up on, and if it is of interest to the committee—and I don't want to eat up your time—I would be happy whenever it is convenient, now or set a separate time, to walk through what we will be doing with the Institute of Medicine's recommendations in their report and the ones that we deferred a decision on to give them an opportunity to weigh in.

Mr. SHIMKUS. And I appreciate that, and obviously we are not pleased with the response so far.

Tell me again, we will go to the yes or format, is it important that we require reviewers to prove scientific or regulatory rationale for major decision-making?

Mr. SHUREN. There needs to be a scientific rationale.

Mr. SHIMKUS. Is that a yes? Come on. You can do it for Mr. Dingell. I mean, why can't you say yes or no? Maybe because he is on the other side of the aisle.

Mr. DINGELL. I would suggest if the gentleman does need help, I will be glad to assist him.

Mr. SHIMKUS. Do you want to read these for me?

Mr. SHUREN. Let me say with a caveat within those constructs of the question but some of the wording I might have put differently so the real meaning isn't conveyed to the committee.

Mr. SHIMKUS. Maybe I should share my questions with you prior to the hearing as other folks do to get a clarification of that in the question and answering.

Do you think it is important that we establish an expedited appeals process for any challenges to those decisions?

Mr. SHUREN. Yes.

Mr. SHIMKUS. Thank you. Do you think it is important to have qualified, trained reviewers handling applications for submissions?

Mr. SHUREN. Yes.

Mr. SHIMKUS. Do you think it is important that we have FDA publish detailed review summaries of 510(k) clearance of pre-market approval and HDE and de novo?

Mr. SHUREN. Yes, with a caveat. I mean, all of the—

Mr. SHIMKUS. We are getting there.

Mr. SHUREN. Some of these go to legislation that—

Mr. SHIMKUS. Amen, brother. That is what we are talking about.

Mr. SHUREN. Would actually—

Mr. SHIMKUS. You know, and legislation that was lampooned by the ranking member of the full committee here. I mean, he specifically took crosshairs on legislation putting it in its worst light where based upon some of your answers, maybe some of those have some merit, and that is what we do. I mean, that is what our hearing is about.

Mr. SHUREN. I know, and we would like to work through those, but some of these things in the bills and even things like detailed decision summaries if you are talking about the summaries that we are doing as opposed to what we are doing now, those have costs to them. They will divert and—

Mr. SHIMKUS. Well, we have got Obamacare, million dollars of tax increases now and fee increases, so we are not sure it is all about money. We see that the medical device folks are really ponying up a lot of money now. They are doing it in the Obamacare tax and they are doing it with this agreement.

Let me go to a final point. FDA leadership—you kind of mentioned this earlier but I wanted to follow up. FDA leadership explicitly directed staff in a memo dated November 23, 2008, to remove the “least burdensome language” from guidance documents, and of course, we have pieces of the legislation here that says the importance of the least-burdensome provision. What are you doing to make sure reviewers actually apply to the least-burdensome standard in practice?

Mr. SHUREN. So what we did is, we took out—there was boilerplate that was inconsistently being used. It was creating more confusion and actually wasn’t helping our staff apply least burdensome, so we are doing the following. First of all, you should also have—I communicated with my staff about how important it is to follow the least-burdensome principle. That went out also as a subsequent email. Secondly, what we are doing is trying to apply the least-burdensome principles to specific devices so manufacturers don’t just hear, “Well, you apply least burdensome,” to show them in fact how it can be applied to their device. That is significantly more meaningful. We put processes in place to try to assure we have got management input so that we are applying the least-burdensome principle consistently in our decision-making. And I think those changes are starting to kick in in the program. Those are meaningful, important changes to make.

Mr. SHIMKUS. Thank you, Dr. Shuren. Thank you, Chairman.

Mr. PITTS. The Chair thanks the gentleman and recognizes the gentlelady from California, Ms. Capps, for 5 minutes for questions.

Mrs. CAPPS. Thank you so much for your testimony, Dr. Shuren. I appreciate the work that has been done to reach the MDUFA deal, and I think this is a very important moment to balance the needs of the companies for increased predictability at the agency but also to increase patient safety. Congress needs to uphold our part of the deal.

As I have mentioned in previous hearings, these user fee agreements do not supplant Congress’s role in ensuring that FDA has the necessary resources to do its job. I hope we can work together to ensure adequate appropriations for the agency.

Before I begin with my questions, I want to quickly raise the issue of the unique identifier policy for medical devices that is currently stuck in OMB. No matter what one’s position on the policy itself, everyone is stuck in a holding pattern until this is released. Getting this policy out of OMB is important for industry and consumers alike, and I wanted to put on the record that Representative Schakowsky and I have sent a letter to OMB urging them to move forward on releasing the policy on the unique device identifier system. I appreciate, Dr. Shuren, FDA’s work on the policy and I look forward to its release.

Now, shifting gears with my question, Dr. Shuren, reports by the Institute of Medicine and the GAO have expressed that women have been historically underrepresented in medical research, par-

ticularly so for cardiovascular and other device trials. But due to proprietary data issues, it is hard to know for sure what is and what is not getting reported to FDA, and that is why my bill, the Heart for Women Act, which has passed the House twice with near-unanimous support, would require the GAO to examine whether clinical trial and drug and medical device safety and efficacy data are being reported by sex, by race, and by age. Perhaps we can make some headway here.

I understand that as part of MDUFA's agreement, the FDA and industry members will conduct an initial meeting to set goals, timelines and expectations. Is that correct?

Mr. SHUREN. Yes.

Mrs. CAPPs. Can you discuss to what extent the FDA will inquire about the devices use in the diverse population of patients? And, if the device is intended to be used in a diverse patient population, could the FDA use this time to encourage enrollment of a representative group on clinical trials so that the trials fully represent and reflect the usage of the product and prevalence of the disease?

Mr. SHUREN. So we have been stepping up our efforts to have better representation in medical device clinical trials, and that has been through guidance, that has been through workshops and that has been through one-on-one engagement with companies. So we believe it is important and it is something we are pursuing.

Mrs. CAPPs. And it is something you can give measurable results on?

Mr. SHUREN. To look at what may be changing in terms of representation in clinical trials, yes, that kind of data we could be able to provide.

Mrs. CAPPs. Would it be transparent enough for us to be able to see the data, or at least to get the assurances that you are giving us that there is a level of understanding and that it is a fully representative sample?

Mr. SHUREN. Yes. We will go back, because we have been trying to be more transparent about information that we are using in our decisions, and we actually have a tool starting to put up information on the clinical trials that are used in support of device approvals, and I think that is one of the components in there, but we can double-check and get back to you.

Mrs. CAPPs. I would appreciate that we have some follow-up on this particular question and look forward to working with you on it.

I want to bring up another topic in my remaining time. Several weeks ago, I asked your colleague, Dr. Hamburg, about the Sentinel system for postmarket surveillance. The PDUFA agreement will allow user fees to go towards using Sentinel for postmarket surveillance of prescription drugs, thereby protecting the public health, saving money on research and staying ahead of the curve on drug recalls, and from reports, most of the work Sentinel has done to date has been in the drug space. Now, let me ask you, can Sentinel be used in the medical device space?

Mr. SHUREN. It can be used. We have been a part of the discussions. The holdbacks right now is, one, we need unique device identifiers. Until we have that, we can't do it. The second is, I will say when Congress put the mandate to have a program for drugs, that

got a lot of people to step up to the plate to participate, and it is a very non-regulatory program. But because it is not mentioned specifically for devices, it has not had that same level of enthusiasm.

Mrs. CAPPS. I wanted to ask you to expand upon the barriers that might exist to expanding it to the device side, and you kind of hinted. Would you go further in the remaining few seconds to talk about some ways that you see as barriers that perhaps then we could—somehow there could be a pathway through to making it be effective there?

Mr. SHUREN. Well, the unique device identifiers, we need to have that system in place, and I think the fact that the legislation that passed just mentioned drugs put a lot of attention and for the folks who have data, the focus went to drugs because devices wasn't—

Mrs. CAPPS. Are you saying the legislation needs to be revisited that includes devices?

Mr. SHUREN. I think if the legislation mentioned devices, we would get more interest in having such a program for medical devices.

Mrs. CAPPS. I yield back. Thank you.

Mr. PITTS. The Chair thanks the gentlelady and recognizes the gentleman, Mr. Rogers, for 5 minutes for questions.

Mr. ROGERS. Thank you, Mr. Chairman.

Thank you, Dr. Shuren, for being here. I can see how it gets confusing. This committee asked the FDA just a very short number of years ago to regulate tobacco, and they are going to generate some \$2 billion over 5 years on a product that if you use as directed will kill you. That is a fairly confusing message to the FDA, so for that, I am going to apologize for what Congress did to you, and I certainly could find lots of places for that \$2 billion when it comes to medical research to do something pretty spectacular that is not going to find its way there.

But I guess what confuses me, and I too have been looking at the National Venture Capital Association, mainly because they are the canary in the coalmine. If they are the first ones to give an indication if in fact they are going to change their investment habits to companies who are innovating when it comes to medical devices and the survey results are a bit frightening. So you believe that medical devices that are approved by the FDA, they advance American public health. Would you agree with that?

Mr. SHUREN. Yes.

Mr. ROGERS. And would you agree with Commissioner Hamburg that the FDA has a role to play in ensuring that medical device companies stay in the United States and want to bring their products to the market here first? There is some advantage to that, is there not?

Mr. SHUREN. Yes.

Mr. ROGERS. And I know we are saying to some degree nothing to say here, we are moving on, we are trying to get through this, and I hope that you do, but would you find it concerning that according to this survey, that 44 percent of American venture capital firms are now going to invest in life science companies in Europe and Asia? I mean, it is clearly a shift. Is that concerning to you?

Mr. SHUREN. Well, it does concern me to see investments not going into development of products here for the United States, and I have to tell you, I have been on the record with that beforehand, and one of the drivers for some of the policies we have in place, we have been out meeting with the venture capital community. Ross Jaffe is going to be up here testifying. Ross and I have spoken on many occasions, and Ross can tell me if I am not telling the truth, but, you know, some of the top things of their concerns was I mentioned that benefit-risk determination, taking into account patient tolerance for risk, recognizing that when you have truly novel first-time technology that you can't expect it to be a home run, you have to view that a little bit differently. All of that is baked into this framework, a common framework between us and industry that is explicit, that will be a part of the record.

A second is incentivizing getting the early clinical studies to start here in the United States, and those policies were developed in part directly out of those concerns, the innovation pathway. Features of that were things that the venture capital community had raised as could be helpful to them to help some of these breakthrough products get to market. We have taken that—

Mr. ROGERS. Reclaiming my time. I appreciate those efforts, but what they are also saying is that the reason that investment shift is because “the unpredictability at the FDA.” So I understand you tried to make some changes. Did you hear that from those venture capital firms about the unpredictability of the FDA?

Mr. SHUREN. Yes, and that is why a number of the actions we are taking are meant to address predictability in terms of better guidance, better decision-making in terms of better oversight on the decision-making that we put in place.

For folks who may be interested, we did put out an overview that covers all the actions that we are taking and it puts a list of everything we are doing and if we achieved it, a link to all that information. I will make sure that our Office of Legislation—I think that has been passed out. We will make sure that is sent to everyone, and that is updated every time we take—

Mr. ROGERS. The one thing that worried me is a little bit is, you said you sent out an email to your staff on the less-burdensome approach. Sorry, but that doesn't sound like a great plan to me.

Mr. SHUREN. Well, that is why we follow that up in terms of specifically addressing—

Mr. ROGERS. OK, but my point being here, Dr. Shuren, I appreciate it. I hope you understand the gravity of it. And just putting out a report certainly hasn't deterred the long list of folks who come into Congress every day and saying they are having these huge problems. Investment is shifting overseas. The smaller folks are losing investment as we speak. And so we need a little fire in the belly here. If you are truly trying to change that equation, it has to happen now. We don't have time for reports and light-hearted emails about how we ought to change for the future. I appreciate you having to defend this, but at the same time, if we don't change it, we jeopardize having to have our devices manufactured and innovated in Asia and Europe. I don't think that is good for U.S. consumers. Oh, and by the way, we made it more difficult because we also applied a tax to the companies who were success-

ful enough to get through what is a very unpredictable FDA process, which means they are also hiring less and innovating less. I mean, the policies here don't work together, and that is why I think people like me are very, very frustrated with the FDA, knowing that we have asked you to do really dumb things in the past, but this stuff is so crucially important for our consumers and the folks who need these medical devices. We have to have a little urgency in our approach here, and I just don't see it.

Mr. SHUREN. Well, I would say actually we have had the urgency. You know, in 2010, we went out and we went across the country to get input from industry, from others. We pushed very quickly to get out reports and recommendations. I will tell you, I got letters from some of your colleagues telling me to slow down. I heard from industry folks, slow down, more time for conversation, and our feeling was, we can't wait. We know there are these issues and that is why we moved forward, we put in our plan in the beginning of 2010 and we have been marching relentlessly forward. I keep hearing from people, industry has even said, can you slow down, you are putting too much stuff, and it is sort of, there is a lot of things that if we don't work them together and fix, rather than just a few little things, we won't have the impact we want to have. And that email I sent out is not fluff. Quite frankly, leadership starts at the top, and to do that and communicate with my staff, I have to be out there, I have to be out in front. I have to put my name on it, and that is what that email did.

Mr. PITTS. The Chair thanks the gentleman and recognizes the gentleman, Mr. Engel, for 5 minutes for questions.

Mr. ENGEL. Thank you, Mr. Chairman.

Thank you, Doctor. Talking about medical devices, the 2011 Institute of Medicine's report on the FDA's 510(k) processes raised significant concerns about the current premarket approval and postmarket monitoring processes for these medical devices. We would all agree, I don't think there would be any disagreement on this, that there is a necessary balance between premarket and postmarket FDA processes. No matter how stringent the premarket requirements, it is obviously not possible to know everything about the safety and effectiveness of new products until they have been in use for some significant period of time, and as we improve the processes for getting products to patients more quickly, I believe we need to improve FDA's ability to detect problems that occur once products are on the market.

So let me ask you this. Can you please describe the role that postmarket data collection and surveillance play in the current FDA device approval framework, and secondly, what additional authorities or resources does FDA need to address the problems highlighted in the IOM report?

Mr. SHUREN. Well, we do use information from the postmarket setting to help inform on the premarket side. Many of the devices that are made, they constantly come back in the door through incremental innovation. So having real-world experience on those devices is critically important. Our systems in the United States are pretty good. It is not really the system the Nation deserves. We have adverse-event reporting that gives us some information, but we don't have a truly robust data collection that we really need.

The Institute of Medicine highlighted that point, and we agree with them. We need to pursue that at a national level, and that is why as a strategic priority we put out last month, we said we will go forward and put out a draft national strategy for postmarket surveillance in the spring. We will have a public meeting. We will have a public dialog how to do this because ultimately this will help companies, can help companies keep products on the market, can help companies get products on the market, can also help protect patients. It is a win-win, we need to work together, and I think things like Sentinel, unique device identifier are all critical aspects, having more registries. We have been stepping up our efforts on registries.

I will tell you, Europe has a lot of issues with the postmarket side. One thing they sometimes will do a little bit better than us is having a national registry for certain devices. I will give you an example. Just very recently we worked with the American College of Cardiology, the Society of Thoracic Surgeons and with a company, Edwards Life Sciences, on a registry for heart valves that are being inserted through blood vessels, revolutionary technology, and this now will be a national registry, not only getting information on that device but subsequent devices that come forward and you can actually do postmarket studies buried within that registry, can reduce future costs for doing those kinds of examinations.

Mr. ENGEL. Thank you, Doctor. Let me ask you a question about the regulation of laboratory-developed tests. The FDA's oversight of medical tests, the LDTs, have become controversial of late. As I understand it, there are several issues in play here. First, there are a wide variety of tests, everything from blood tests to genetic tests that can predict whether a patient would benefit from a particular therapy. Secondly, the FDA regulates the actual tests themselves while CMS oversees the administration of these tests called CLIA, the Clinical Laboratory Improvement Amendments. It is clear that the FDA has jurisdiction over these tests but the agency has historically exercised enforcement discretion with respect to so many of them but there are recent signs that the agency is going to begin regulating a subset of these tests again.

The reason I ask that is because one of the Republican medical device bills, the Modernizing Laboratory Test Standards for Patients Act, which is H.R. 3207, I believe would make radical changes in its regulatory scheme. The bill would remove FDA from the picture entirely and give complete control of these tests to CMS. My understanding is that CMS does not believe this is a good approach.

So let me say this. I am very concerned about the direction of this bill, and by all accounts, these tests are at the cutting edge of new medical therapies, and to take the responsibility of ensuring that these tests are clinically effective away from the FDA, our premier scientific regulatory body, and give it to one that lacks entirely the scientific expertise to me makes absolutely no sense. Do you have concerns about the approach to laboratory-developed tests laid out in H.R. 3207?

Mr. SHUREN. We do have concerns about it, and we appreciate the fact that the bill recognizes the fact that finally laboratory-developed tests need to be regulated. The days of the Wild West need

to stop, that CLIA is not adequate for the oversight of that. The law as it currently stands is not good enough, and the standard of analytical validity and clinical validity, the standard that FDA uses, that it is the right standard. The problem is, it creates a duplicative Federal bureaucracy at a much higher cost, grows government unnecessarily and it maintains an unlevel playing field between traditional manufacturers and labs who make the exact same kind of test, and as a result, just continues to stifle innovation and can actually kill jobs on the flip side, and then it allows those tests to come out on the market and then for CMS to make a decision after it goes on the market. So you can have a bad test that is out there, and we have seen plenty of laboratory-developed tests, ones for diagnosing ovarian cancer that have been inaccurate, so women are having their ovaries out and didn't need to, making decisions about treatment for breast cancer, treatment on chronic Lyme disease, I mean tests for autism that are just wrong and they need to be regulated but they need to be regulated right, and CMS did say they are not the right place for it, they don't have the expertise, and the cost would be at least \$50 million to \$100 million a year plus \$20 million startup. For our framework in the first few years, we are talking about a cost that is probably less than \$3 million in fees to industry, so I don't know why we want a more costly, less effective kind of approach and this duplicative oversight that actually would not help.

Mr. ENGEL. Thank you. I agree.

Thank you, Mr. Chairman.

Mr. PITTS. The Chair thanks the gentleman and recognizes the gentleman from Kentucky, Mr. Guthrie, for 5 minutes for questions.

Mr. GUTHRIE. Thanks, Dr. Shuren. We had a meeting in your office about this important issue. I am from a manufacturing background and a big believer in making in the USA and remaking it in the USA and have been concerned about some companies making them in the Europe because of the regulatory environment. We talked about that.

I actually have a bill on guidance documents, and a lot of companies like guidance documents because it gives them regulatory predictability, but some of the problems—your process for reviewing internal guidance documents because some companies have said that they have submitted a guidance document—that guidance document no longer reflects FDA thinking, and so what process do you review those and because how they can submit to you or to a dated guidance document? Just kind of talk about what you are doing with the guidance process to improve it.

Mr. SHUREN. Yes. So with guidance documents, you can actually continue to submit comments about it after the comment period has closed. It is different from rulemaking. So that docket remains open and we will look to see if new comments come in. We made a concerted effort to improve our guidance development process. In fact, in 2011, our production of guidance documents improved by about 22 percent over 2010, and 2010 was better than 2009, but we sort of squeezed, you know, the fruit and gotten maybe about as much juice as we can from the internal processes improvements, and it is one of the reasons as a part of the MDUFA III reauthor-

ization agreement we are getting a little bit of extra dollars, about five additional people to help us for the oversight of guidances. What is critical is, we need people who are more technical writers on guidances so our experts who are doing reviews can provide their expertise but not write the documents themselves. That is what is going on now. And so they get diverted away from doing premarket reviews. The little bit extra help will help us take some of that tension off. It will also help us do a better job at looking at guidances that have already been put out to see if changes need to be made and also to try to make sure that we are finalizing draft guidances more quickly.

Mr. GUTHRIE. And one other point I wanted to bring up. On page 7 in your testimony, there is a chart that says about from 2000 to 2011 has been increasing additional request additional information from 510(k) requests whereas now it says in 2011 three-fourths of all 510(k)'s had additional information requests coming back. And I think the implication is that companies aren't submitting the information that you need, therefore, you haven't asked for more, and I am a manufacturing person, quality engineer, so I used to be responsible for submitting our tool and dies once they came in and we got paid based on them being approved, and let me tell you, they were only wrong if I didn't have the right information because I had to answer to somebody because literally once our customers signed off on that, they were by contract supposed to cut a check. So sometimes I felt delayed because the other parts of the project weren't ready.

So the question is, you see the trend. Are three-fourths of the applications really inadequate or are you not letting them know what you need? I mean, that is the question that I have. Because it does seem like a disturbing trend to go from a third to three-fourths.

Mr. SHUREN. Yes, and actually because it was a disturbing trend, we did an analysis of 510(k) decisions, the first 130 we had done, or 110 in 2010. We put that analysis on our Web site, and it is a mixed bag. I mean, there are times—

Mr. GUTHRIE. You have been willing to show that. I appreciate these charts because it does show the issues, and I appreciate that.

Mr. SHUREN. Yes, but it also shows the problems have been longstanding, like a decade, and this was a canary in the coalmine that then led to increased total times for review. The data just marches up starting around 2002. But when we looked at it, so a number of different reasons behind it. There are companies who we have put out very clear guidance on what to do and they opted not to follow it, and they could do something different but they didn't even justify doing something different. I mean, even where for years you provide a little bit of clinical data. If you want to measure oxygen through the skin, you take a blood sample and compare it. A company comes in and never even did the blood samples. We go back, do the blood samples.

Mr. GUTHRIE. That is legitimate. That is absolutely legitimate. It is hard to believe companies whose products are based on that.

Mr. SHUREN. Believe it or not, it happens, but then we have companies where if we had better clarity on what to do, that would help, and the last is, there are times where we ask for things that we shouldn't be asking for, and that was one of the drivers behind

our changing our decision-making within the center, making sure we have that level of oversight that the staff can't suddenly decide to ask for something extra until you have the proper level of sign-off. In fact, if you want to ask for a new kind of clinical study across a type of device, that is made at the highest levels in the center by the Center Science Council where those kinds of decisions in fact should be made. I just need enough managers to provide that oversight.

Mr. GUTHRIE. I have a chart here from the venture capitalists, like 38 percent of their decisions, FDA regulations are about 38 percent of their decision whether to invest, and about two flights down there is a meeting now, and I am going to run back to it, on manufacturing and so we have talked about that. That is a concern. That is why we are here and why we are real concerned about it because we want it made in America and made safely and securely and efficiently. I appreciate your efforts. Thanks.

Mr. PITTS. The Chair thanks the gentleman and recognizes the gentlelady from Illinois, Ms. Schakowsky, for 5 minutes for questions.

Ms. SCHAKOWSKY. Thank you, Mr. Chairman.

You have heard a lot today from many that the FDA has become too risk-averse in terms of what the agency requires device manufacturers to do in order to obtain FDA clearance or approval, and we have heard that the FDA is insisting on too much clinical data prior to approval and that this has resulted in a decrease in venture capital investment as well as an export in innovation and jobs abroad, and to help address the situation, some have suggested that the FDA's mission statement should be changed to include things like job creation and innovation, and a bill has been introduced that would accomplish this. But even if we assume there is some truth to these reports, and I think there is a lot of evidence to suggest that in fact there is not, revising FDA's mission statement seems drastic to me. So I wanted you to comment on the implications of revising the FDA's mission statement to include things like job creation.

Mr. SHUREN. Well, we are concerned about a change to mission statement that would include job creation, economic growth, competitiveness because we read that, so are we looking at job growth in the context of product approvals? Are we now going to—I mean, to do that, then we are asking for financial data on the companies, we are looking at reimbursement opportunities, market analyses become part of approval decisions, and then whose jobs? Jobs in the United States or jobs overseas? What about jobs of the competitors? I mean, the devices most at risk will actually be the most disruptive technologies because they are more likely to adversely affect the competitors in the short term and could hurt job growth in that direction.

So those are the kinds of, I really think, unintended consequences happen with those changes, and there are a number of other things in this bill as you march down the list that would lead to, we think, very troublesome changes in what we do. It can change the standard for evidence for our product approval decisions. I mean, one of them is on public participation. So we then say OK, so we are talking now about public participation in prod-

uct approval decisions. That means, so should we revisit what information we have considered confidential and start making more of that information public and some people may think it is a good thing. We hear from industry, please don't do that, but that is where this bill is actually directing us. It talks about using the most, you know, innovative tools. Well, innovative doesn't mean it is the best tool. So we start using bad tools and we talk about, well, make sure you are using modern tools. Well, sometimes the newest tools aren't the best ones. Old ones are just as good but why we should change the goalpost on industry every time there is some modern tool? It may not be necessary to do that.

Ms. SCHAKOWSKY. So you think that this could slow down, complicate and actually make less efficient the process?

Mr. SHUREN. Oh, yes. I think it could lead to some fairly dramatic changes in how we make product approval decisions and I think it would adversely affect industry and adversely affect patients.

Ms. SCHAKOWSKY. If you look at the language of the bill, and that is called the Food and Drug Administration Mission Reform Act, there is some language that may on its face seem less controversial like changing the mission to require FDA to take into account the risks that certain patients are willing to take. Am I correct in saying that these are things the FDA is already doing, and if so, proponents of the bill would argue that there should be no harm in revising the mission statement to encompass things that the FDA is already doing, and I wondered if you could comment on that.

Mr. SHUREN. Yes, this is something we already are doing as part of the benefit-risk determination framework we put out. That is already out there publicly, and it will go final and begin implementation at the end of March. That is going to happen.

But this is an activity. It is not really a mission. And so this isn't exactly the right way of sending a message about having a benefit-risk determination framework because it is really an activity. It is an action.

Ms. SCHAKOWSKY. Well, I am concerned about revising FDA's mission statement. I think it is a pretty drastic step and it doesn't seem that there is a record for why such a dramatic change would in fact be necessary.

So I thank you for your comments, and I yield back. Thank you.

Mr. PITTS. The Chair thanks the gentlelady and recognizes the gentleman from Louisiana, Dr. Cassidy, for 5 minutes for questions.

Mr. CASSIDY. Dr. Shuren, a friend of mine, an orthopedist, went to—I am a doctor—went to a conference in San Francisco and said he was struck that there was, relative to previous years, a paucity of new equipment being displayed. So what I am speaking of is somewhat influenced by the conversation I had with him. I assume there must be some difference in terms of how you regard the bigger manufacturer or the bigger innovative company versus the smaller. Fair statement?

Mr. SHUREN. Yes. Actually, we try to do a lot more hand-holding with the smaller companies.

Mr. CASSIDY. What in this bill—I mean, if I were to go and say to those smaller companies, first, how do you define a small company, and secondly, if I were to go to those innovators and say these are the specific provisions that pertain to you, what would be your summary?

Mr. SHUREN. So small businesses for purposes of the user fee act is \$100 million or less in annual sales or receipts.

Mr. CASSIDY. I want to have such a small business, by the way, but continue.

Mr. SHUREN. And what we will do is actually work with them in terms of what they may need to do to bring a product to market. We are very used to dealing with small companies because they make up the largest segment of the device industry, although most of the devices on the market are made by big companies. But I will tell you, one of the challenges we are seeing is some of the data suggesting we are seeing an uptick of some of the first-time sponsor companies coming to us, and because they are small companies, they oftentimes don't have a good understanding of what they need to do to come to market. I quite frankly think——

Mr. CASSIDY. But that suggests a regulatory complexity as much as anything, correct?

Mr. SHUREN. No. You come to it with what you know, and for people who understand that system, can work a lot better. I think you don't suddenly—you need to have efficient systems, you need to have clear systems. They need to be predictable and consistent. But you don't just suddenly lower the bar simply because someone says——

Mr. CASSIDY. That is a fair statement. Are your fees the same for larger and smaller companies?

Mr. SHUREN. No, they are smaller for smaller companies.

Mr. CASSIDY. And do they remain constant relative to the previous authorization or do they increase or decrease for smaller companies in this regard?

Mr. SHUREN. So in MDUFA III, they will go up, and what we are talking about now is for PMA going from about \$55,000 now to \$67,000 by 2017, and the first PMA for a small business is free. It is on the house.

Mr. CASSIDY. Now, I presume that if you have a small company, you would still be required for the double blind control trial insofar as that is practical to test your invasive device. I assume that is the case?

Mr. SHUREN. The evidence you have to provide wouldn't change. I mean, the device is the device. It shouldn't change based upon who made it. That has been one of the issues with laboratory-developed tests.

Mr. CASSIDY. That is a fair statement.

Mr. SHUREN. But by the same token, we are trying to apply least burdensome, so actually most of our clinical trials are not placebo-controlled double blind clinical trials. They are either not practical or they may not be necessary.

Mr. CASSIDY. Now, let me ask you as regards the increased revenue you all are requesting, I have again seen stuff and I have learned to say what I have been told, not what I know. Let me first say that. But you in your testimony can see that there is an in-

creased time for approval over the last several years. You are working to address that.

Mr. SHUREN. Yes.

Mr. CASSIDY. But I have also seen that your revenue increased under the last MDUFA authorization. Your revenue significantly increased, and I think I know that your number of employees similarly increased. And so it seems like the lack of resources was not there. I mean, you have the resources. You had more money, you had more people, and yet the time to approval increased. So since we are being asked to give you more resources, why did more resources not work last time but they are going to work this time?

Mr. SHUREN. So two parts to that. One, there are program issues that need to get fixed, and those are things we have identified and we are fixing, and that is separate from resources if you are going to make it work.

But the second is the resources we got weren't sufficient for the work we had to do, and one of the things in MDUFA II was we didn't take into account the increase in workload that would occur. So we got more people to try to meet the goals but then the workload was also going up and sort of outpaced the resources we got, and we never addressed the fundamental issue of having enough people to do the work and enough managers to provide oversight, and so we constantly have this high turnover rate, which industry has complained about because it disrupts the review of the device.

Mr. CASSIDY. I see you have a high turnover rate, but you did increase your number of employees. So what you are saying is, you just needed to increase them even more?

Mr. SHUREN. That is correct, and we have the same problem, by the way, in the drug program. About a decade ago, they had the same high turnover rate, same issues. The drug industry said—and they were not concerned about—they were very concerned about performance. And so what happened was, there were process improvements in the drug program and they got more money. They were able to get over that hump and they were able to put the drug program on the right track.

Mr. CASSIDY. So you feel like your process improvements are not enough, just to use your existing employees with existing revenue more efficiently, but rather you need both efficiency and much more money?

Mr. SHUREN. That is correct.

Mr. CASSIDY. I yield back.

Mr. PITTS. The Chair thanks the gentleman and recognizes the gentleman, Mr. Matheson, for 5 minutes for questions.

Mr. MATHESON. Thank you, Mr. Chairman.

Thank you, Dr. Shuren, for being here today. I am glad that Mr. Barton and Mr. Rogers both made reference to the Venture Capital Association study. I was going to note that, but I think they covered what the substance is, is the troubling trend of investment going offshore. I have grave concern for a couple of reasons. One is, of course, I want folks in the United States to have access to the best devices possible to maintain their health and safety, number one, and secondly, the medical device industry is the great U.S. success story over time and it has tremendous presence throughout

the country including in my home State of Utah, and I am worried about investment shifting offshore.

I do applaud your goal that you stated of bringing greater consistency and efficiency and transparency at the device center, and I want to ask you about your proposed guidance document on when device modification requires a 510(k). Last year, as you know, FDA released its draft guidance to industry detailing when a manufacturer needs to submit a new 510(k) for a change to an existing device. Obviously, FDA has had a policy on the books for many years that industry understood and was well accepted, but the new policy could, from what I have been told, dramatically increase FDA's workload, by estimates of 200 to 500 percent, I mean, that many more applications coming to the FDA for 510(k). Is it your interpretation of the guidance document that it would require manufacturers to file 510(k)'s in that much of an increased magnitude in terms of workload within the FDA?

Mr. SHUREN. It is not, and we had put out the guidance actually to clarify when to submit a modification, predominantly in areas that were gray where we didn't provide clarity in the past, and we were not intending to raise the bar but to clarify to make it easier. We recognized, though, the concerns that had been raised by industry. We take them seriously. And I will tell you, we have got companies in, we have had trade associations in, and we are actually working very closely with them, sort of marching through to see what would be the real impact, did we get some things wrong, did we not clarify properly and we are going through that. We are doing that very methodically.

You know, one of the downsides is, one of the bills on guidance document development would actually limit the time frame to get a final guidance out, and if that was in effect and we had just the one year to do it, I would be in a position to take that guidance and rush to finish it whereas I would rather take the time and work with industry to get it right. I think that is ultimately the right thing to do and that is what we are trying to do now.

Mr. MATHESON. Let me ask you a specific component of the guidance. Is it your interpretation that the new guidance would require manufacturers to file a 510(k) when a manufacturer would need to change suppliers due to a supplier goes bankrupt or there is a fire or some other emergency? Would they need to file a new 510(k) with the agency?

Mr. SHUREN. Just to change suppliers, no. They would have to document it as part of their design controls. That is just internal records. But they don't have to submit a 510(k).

Mr. MATHESON. It is my understanding that the guidance proposed last year would require manufacturers to file 510(k)'s for likely uses. Can you comment as to how or why the FDA would require manufacturers to anticipate likely off-label uses of their devices and file a 510(k)?

Mr. SHUREN. They would not have to file a 510(k) for off-label uses. They don't have to go and say well, it could be used this way so I have to file a 510(k) then. That is the guidance.

Mr. MATHESON. But there is something in the guidance about likely uses. Is that correct?

Mr. SHUREN. There is something in there about if the manufacturer on their own puts a contraindication in their labeling about a particular likely use, then there is something called a changes being affected manifestation that they would submit to us. So it just that one circumstance where they are actually making this change in the labeling and it is just a certain kind of update to 510(k).

Mr. MATHESON. So absent the manufacturer listing on their labels another likely use, you are suggesting that if there some off-label use, the manufacturer is not going to be compelled to file a 510(k)?

Mr. SHUREN. That is correct.

Mr. MATHESON. OK. Thank you, Mr. Chairman. I yield back.

Mr. PITTS. The Chair thanks the gentleman and recognizes Ms. McMorris-Rodgers for 5 minutes for questions.

Mrs. MCMORRIS RODGERS. Thank you, Mr. Chairman, and thank you, Dr. Shuren, for being here. This is a very important discussion, and when it comes to new cutting-edge medical research, exciting new medical devices, the FDA can either help make it happen or the FDA can close the doors to an entire industry, and as Mr. Matheson just said, the medical device industry in America is a great success story over the last 50 years, and we have been the world leader. Americans have benefited and lives have been saved. And yet today we hear because of the FDA, we hear about delays, we hear about increased cost, increased user fees. We hear about regulatory unpredictability. And it is not just—it is not the regulations themselves, it is the fact that the goalpost changes so often. And then along with that, we know that this industry is also facing huge tax increases because of the President's health care bill. We also know that it takes on average now 4 years longer in America to bring a new device to market than in Europe, and I don't believe that Europe is using bad tools and I don't believe it means that we have to lower the bar, but we do need to address what is happening.

And so my first question is, do you believe that the current regulatory environment at FDA is negatively impacting the development of new medical devices here in America and sending jobs overseas?

Mr. SHUREN. I think the program that we have here needs to be improved so that we are actually having devices, more devices developed over here and that we are keeping and actually creating more jobs over here in the United States, and I take it seriously very much from a public health standpoint. I am a physician myself. I would like to see more treatments and diagnostics for patients. I am a neurologist. That space, if there is ever a space that could use more help, that is the one. But I don't think Europe is the answer. Europe actually does have a lower standard. You don't show effectiveness over there. You don't show that there is any benefit to patients, and as a result, you do have products—we are finding more products that have been approved over there later shown through subsequent studies, often through the United States, that it is unsafe or it is ineffective, but they don't have a centralized database of their approvals so it is very hard to follow much of this.

And there has been a growing chorus in Europe for change, particularly for high-risk devices. Like the European Society of Cardiology, the British Medical Journal are all coming out to say high-risk devices should be treated more like the United States: demonstrate effectiveness, more robust clinical trials over there, putting out guidance to clarify what to do. Believe it or not, for the need for more guidance, we put more guidance than Europe does. So I don't think the answer is that the United States should become Europe. I think we should keep the American standard but the program behind it needs to be predictable, consistent, transparent and timely. I don't know what—

Mrs. MCMORRIS RODGERS. Do you believe that that program currently is predictable?

Mr. SHUREN. Well, I don't think it is sufficiently predictable, consistent, transparent, and we have said that, and I wouldn't be making these changes, I wouldn't have my staff spending the time to make those changes if we didn't believe it, and I will tell you, in spite of their working hard to try to get products out and the added effort to make these changes in the program, we are actually now starting to see early signs of improvement in performance. It is going to take a little time to really show bigger impact but it goes to show you, making those investments on our part can pay off dividends, but what we really need is, we need the support to go ahead and do it and then ultimately between our changes and the extra dollars with the user fee program, we can get ourselves back on track and we can keep the American standard.

Mrs. MCMORRIS RODGERS. Well, at the current rate, we are going to run out of time, and I have introduced legislation regarding harmonization, and I wanted to ask you what role you believe harmonization with other countries could play in terms of getting devices to market more quickly.

Mr. SHUREN. I actually consider harmonization critically important. We had what is called a global harmonization task force, which was us, European Union, Canada, Australia, Japan working on harmonization. I will tell that most of the members of that group had felt that that group had kind of run its course. We put out—

Mrs. MCMORRIS RODGERS. Now, when was this?

Mr. SHUREN. This is the global harmonization task force, and it put out many high-level documents that were more helpful to developing countries who didn't have a regulatory program in place or just developing but didn't lead to a lot of true harmonization. We, the United States, I will tell you I personally felt we needed to do better and so we put a new proposal on the table for an international medical device regulators forum to broaden the participation. It can't just be those few countries because the rest of the world was at risk of moving in different directions. We had to broaden our scope and we had to focus on real implementation on harmonization, and that group, I will tell you, to the credit of the members of GHTF, they agreed to do it and the very first meeting of that new forum is at the end of this month.

Mrs. MCMORRIS RODGERS. So are you seeing products being brought to market any quicker because of these efforts?

Mr. SHUREN. No, this effort is going underway. That was the problem with GHTF. We actually weren't focusing on critical questions about could we actually be relying on data submitted or in some cases decisions being made by other regulatory bodies in support of bringing the product here to the United States.

Mrs. MCMORRIS RODGERS. Thank you. I have run out of time. Bottom line, we are running out of time and we have to start making it happen. Thank you.

Mr. PITTS. The Chair thanks the gentlelady and recognizes Ms. Blackburn for 5 minutes for questions.

Mrs. BLACKBURN. Thank you, Mr. Chairman, and I thank you all for being here.

And Dr. Shuren, I hope that you realize and appreciate that we would like to see a sense of urgency coming from you to do more than just talk about issues but actually have some demonstrable actions, and when you talk about a global task force, when you talk about, you know, time, as Ms. McMorris-Rodgers said, we are running out of time with a lot of our constituents and their companies who complain about the way they are dealt with by the FDA, and in their mind, time is money.

Now, you all in government have an additional, a continuing appropriation but I think it is important that you realize what we see from you is that you may not get additional money. The Federal Government doesn't have additional money to give. Taxpayers are saying we want to see them show some successes and some changes in behavior, and right now, perception is reality, and the reality is, the FDA is a very difficult agency with which to deal. You can look at the Jobs Council. You can look at the ODE annual report, the GAO, the Venture Capital Alliance. You can look at all of these, and there are problems dealing with you and the regulatory burden that you impose and the method in which you impose that.

Now, let me ask you a question. You may have seen this article about mobile devices. This is something that is important to my constituents in Tennessee. And this is from February 7th Washington Times. So I want to ask you about mobile devices, and how do you plan to move forward with regulation of mobile devices? Do you think you have got enough on your plate with that? And if you do move forward with mobile devices, do you intend to subject them to the device tax? If somebody goes out and buys their iPad and places a mobile device on that, some monitoring device on this, are they going to be subject to the device tax? So please speak specifically to the mobile device.

Mr. SHUREN. So specifically for mobile devices, we actually took a very unique approach for FDA. Normally if something is a device, you regulate it like a device, and we said, "Wait a minute, why do we need to do that?" Quite frankly, if there is not sufficient value added to do that, and keeping in mind the value of having certain technologies out there and recognizing the more rapid innovation cycles we see, then we shouldn't do it. So the policy we put out—and that article is dead wrong. They got it wrong, and you should see the commentary in other publications on that article saying what was this person thinking. No, what we actually said is, while the world of mobile apps is maybe this big for devices, we are only

interested in this, and in reality, what we are interested in is, it is the same thing as devices we already regulate. It shouldn't matter if the device is on a desktop versus on a mobile application. It is still a device. It is something we already regulate. That doesn't change it. And that is really the very narrow universe that we focused our attention on. That is essentially it. That makes a lot of sense.

What we got back from comments is, can you provide more clarity on the boundaries, give us more examples about it, but for the most part, the read we have been getting from people is that very narrow look makes a lot of sense, and for the rest we have said even if you are a device—

Mrs. BLACKBURN. What about expediency? Because right now it is taking about 3 years and about \$75 million to get something through your process, and I have to tell you, some of the innovators that I am talking with, they don't think this was completely wrong. They saw a lot of commonalities in the article, and so I would just highlight with you, when you look at the speed of innovation that is taking place in the medical mobile applications that you can't spend 3 years trying to get through all of your filings and reviews and the repetitiveness and switching reviewers. Sir, there is a tremendous amount of frustration with the FDA by our innovative community. So talk with me about expediency.

Mr. SHUREN. Sure, and again, when we are talking about the mobile apps that we are looking at, it is things like you have technology that is pulling down X-rays and reading the X-rays, I mean, the stuff we normally regulate, or EKG machines to measure heart rhythm. We have been regulating those for years. But when we deal with just software, we recognize too that the paradigm we have, the framework we have in place for devices does not work well. Actually, that was one of the recommendations from the Institute of Medicine to look at software because it was so challenging. So maybe we don't have to get the \$1.3 million fully backed. We can let them keep a few dollars. But we are actually underway to sort of revisit our entire framework as regard software, recognizing exactly the point that you make, that you have these rapid changes, and you need to allow for that kind of business model and constant updates. By the same token, there may be other ways to assure you have a good product that we might be able to avoid even looking at it premarket, and the other is, there is a whole bunch of things for clinical decision support, things to help you make decisions that while they could be medical devices, we are going through it and saying leave it alone, just leave it alone completely, and that is what we are working on by way of policy. Because we agree, we have to have a rationale approach.

Mrs. BLACKBURN. When do you think that your policy will—when are you going to have some guidance? And my time has expired. I will ask you to answer, and yield back.

Mr. SHUREN. OK. Our goal is on mobile medical apps to close out that one this year and also to put out the draft policy on the clinical decision support software this year as well.

Mr. PITTS. The Chair thanks the gentlelady. That concludes the questions by the members of the subcommittee. Without objection, we will go to members of the committee for questions. Dr.

Christensen, you have been very patient, you were here the whole hearing. We will recognize you first for 5 minutes for questions.

Mrs. CHRISTENSEN. Thank you, Mr. Chairman and Ranking Member. It has been very informative to sit here and listen to the questions and the answers.

I wanted to follow up on Mr. Waxman's questions about the Pre-market Predictability Act of 2011. The bill would make changes in two areas in addition to the least-burdensome provisions, one, to the investigational device exemption, and then second, to the procedures for appealing decisions through CDRH.

On the first, the bill would change the investigational device exemption process in ways that appear designed to permit companies to conduct studies that are not necessarily geared towards an approval or clearance decision. That seems to run counter to the company's interest, so can you explain where this is coming from, if you know, and whether you believe a change like this is necessary?

Mr. SHUREN. Well, we actually find problematic the change that is put in there because that change in standard for approving a clinical trial will mean that we will approve a clinical trial that is supposed to be the pivotal trial to show it is safe and effective and we will approve a trial that isn't going to be good enough so it will go forward, and then when the product comes back in the door with the results, we want to approve the product. And we suffered in that circumstance previously and so we were watching our approval of products going bad. It wasn't working well.

Now, on the flip side, we sort of changed that but didn't change it well enough so that we said look, let us stop doing it, but what we didn't allow is, there may be extra questions we don't need an answer to right now, and they are nice to know but we shouldn't worry about them, and so we put out new policy in November of 2011 to actually set that balance right on approving clinical trials, and we think that is the smart approach. That will get us to actually approving clinical trials more quickly but appropriately. This change in the standard will actually adversely affect products coming on the market.

Mrs. CHRISTENSEN. That was my impression as well.

And the Pre-market Predictability Act would also make changes to CDRH's appeals process to make it easier to have you as the center director be directly involved in appeals. In fact, it appears that under that bill, you would not be doing much else other than just dealing with appeals. So can you comment on that section of the bill and what impact those changes to the appeal process would have on the center?

Mr. SHUREN. Well, if folks would prefer that I just work on appeals and not improving the premarket program and making the changes necessary to do, this is a good way to do it. I would actually prefer just being sent on vacation, but that is a problem with this bill. And I will tell you, most appeals actually get resolved at the office level. In fact, of the appeals filed in the past 2 years, 26 to 28 percent wind up getting changed in whole or in part. So it goes to show you, the appeal process can actually work.

Mrs. CHRISTENSEN. Thank you. I just wanted to get that on the record.

And on the guidance issue that was raised, H.R. 3204, the Guidance Accountability and Transparency Act of 2011, appears aimed at making FDA guidance development a more public process and ensuring that they remain up to date. I think we all agree that government procedures should be as transparent as possible and that the ability of government to make informed and sensible decisions is dependent on receiving and making use of information stakeholders, and we certainly agree that guidance should be finalized in a timely manner and kept up to date.

At the same time, though, I think we all understand that the principal purpose of FDA guidance is to enable the agency to provide advice in a more timely and flexible manner than it can through regulations. For instance, when FDA learns of new information relevant to certain product approvals, the agency needs to be able to communicate this information to the regulated industry as quickly as possible. Otherwise the industry could waste valuable time and money doing clinical trials on other work that won't necessarily help with approval of clearance of their product. So we need a workable process that balances the need.

But I am concerned that the processes that would be required would actually make the guidance more onerous and more time consuming. So as my time is getting short, I know that the legislation would apply to all FDA guidances but could you tell me how it would affect CDRH and are there any aspects of that legislation that you agree with that might be helpful?

Mr. SHUREN. The bottom line is, we will issue fewer guidance and there will be less predictability in our programs. I mean, there are all these additional hoops and hurdles. You have to announce that you are going to do this particular guidance 3 months in advance. We already put out a list. Then we have to meet both before and after putting out the draft so the cost just dramatically increases, and where we have been trying to improve our productivity, productivity is going to go into the toilet and we know that is not good for industry.

Mrs. CHRISTENSEN. And if you have to issue your final guidance in 12 months, that just makes you say no, I can't do it, so—

Mr. SHUREN. Well, that is one of the problems, and industry sometimes asks for longer comment periods because they want more time to look at it. I can't grant the longer comment period. Modifications guidance, we couldn't be working through those issues. And if I have HHS or OMB who are reviewing it, that just adds on a lot of additional time. We understand the need to kind of try to move quickly and rapidly but this actually would have unintended consequences. And the other part about expanding what is under a guidance document actually can have adverse consequences for patient safety because it includes notices that involve a complex scientific issue. Those are public health notices that we have to get out quickly to tell the public about a big public health concern would not be subject to this good-guidance practice more onerous. So we would have to say there is something coming up on this device, we will announce it in 3 months, stay tuned. That doesn't help patients.

Mrs. CHRISTENSEN. Thank you for clarifying those issues for us. Thank you.

Mr. PITTS. The Chair thanks the gentlelady and recognizes Mr. Bass for 5 minutes for questions.

Mr. BASS. Thank you very much, Mr. Chairman, and I appreciate your accommodation. I am also not a member of this subcommittee.

Dr. Shuren, I represent a State, New Hampshire, with a number of important medical device manufacturers as well as laboratories that are at the forefront of developing new medical devices, some of which are very common now and in use not only in America and around the world, and to say that some of them at least are very frustrated with the length of time and the quality of the decisions that are coming out of the FDA on the medical device side would be an understatement and perhaps in some cases we can work together on some of these issues.

But I am here to ask you a question about a bill that I have introduced as part of, I think there are 10 altogether, on MDUFA having to do with humanitarian-device reform. As you know, we haven't had nearly as much success since the 1990s in developing humanitarian devices for rare diseases as we have had with the orphan drug program, just 55 devices compared to 350 orphan drugs. But that isn't FDA's fault or the industry's fault. There are flaws in the law that chill investigator and sponsor interest and demand targeted reforms. The bill that I have agreed to introduce, H.R. 3211, the Humanitarian-Device Reform Act of 2011, would lift the profit restriction on current law but maintain FDA's current oversight of humanitarian devices. The Act would simply do it for adult HDEs what the 2007 pediatric device law has already done for pediatric HDEs. Today, there is evidence that this has already led to more interest in pediatric HDEs.

My question to you is, do you agree that lifting the no-profit restriction on adult HDEs while maintaining FDA oversight is a win-win reform that would encourage more innovation, ensure safety and result in more treatment for rare-disease patients?

Mr. SHUREN. So the honest answer is, I don't know what the ultimate impact would be on the flip side for pediatric devices. We happen to agree with you that there is a need for more incentives to develop devices for these rare conditions. I know the National Organization for Rare Disorders has said look, lift the cap on adult products. That makes a lot of sense. The American Academy of Pediatrics has a concern that if you broaden it, then manufacturers won't make devices for the pediatric population, and we have seen a fivefold increase in companies coming forward to actually get a fivefold increase in designations for humanitarian-device exemption for pediatric indications.

So this is exactly the kind of topic, quite frankly, that we agree Congress should be tackling. We would like to be a part of that conversation. We suggest get all the players in there, because I don't think we have enough information to make a firm decision but we fully support this is an area that it is critical that we take a closer look at.

Mr. BASS. I appreciate that, and I appreciate the fact that you are willing to work with me and other members of the subcommittee. I would point out that there are other patient groups that disagree with AAP, and the reality is that we could really ben-

efit significantly if we had an honest debate and could work out some sort of a legislative remedy for this.

And with that, Mr. Chairman, I will yield back. Thank you, Doctor.

Mr. PITTS. The Chair thanks the gentleman. That concludes the first round of questioning. We will now take one follow-up per side. I recognize Dr. Burgess for 5 minutes.

Mr. BURGESS. Thank you, Mr. Chairman.

I vowed to be good today, but someone on the other side took the first shot, so let us talk about laboratory-developed tests for just a moment and the reason why H.R. 3207 was in fact necessary because of draft guidance coming out of your shop, the Center for Devices and Radiological Health, appeared to be overstepping the boundaries. In fact, there appeared to be a basic change in the standard regulatory paradigm that had been established, and if one even wanted to draw it to its further conclusion, there appeared to be violations of the Administrative Procedures Act coming out of your office by issuing this draft guidance. You are going to require people to do things that had never previously been required, and this was all happening without any legislative authority. It was simply happening upon the will and the whim of the Center for Devices and Radiological Health.

So I have got several letters from laboratories across the country that are in support of keeping this jurisdiction within CMS, within the purview of CLIA. Laboratory tests must be accurate, they must have clinical utility, and that is the correct place. To ask these companies to literally be sucked into the maelstrom of the regulations of the devices, you can't do what you are already supposed to be doing and you are asking for more jurisdiction. How is this helpful? How does this move anything in the proper direction?

So Mr. Chairman, I did want to submit these letters on the laboratory-developed tests for the record, because again, I think this is an important part of the discussion. Maybe this legislation is not the correct final product but this discussion needs to be part of the reauthorization of the user fee agreements. I will certainly allow you time to respond.

Mr. PALLONE. Mr. Chairman, I would have to review those before I could agree to unanimous consent to put them in the record.

Mr. PITTS. OK. We will provide copies to you.

Mr. SHUREN. So laboratory-developed tests, we have been clear for years, they are medical devices. I mean, it is the test. It doesn't matter who makes the test and that is how the law is, but we have exercised enforcement discretion but the world changed, and we have more-complex tests that are actually putting patients at significant risk. I would be very interested to see the framework you are talking about because we actually never issued draft guidance, so maybe it is another group that put it out there, but we have yet to put anything out there for people to react to. But it makes absolutely no sense to have the same kind of test that is regulated by two different government agencies, depending upon who makes it.

And CMS has been clear when they looked at the legislation, this is not the right place for doing it. In fact, one of the changes under CLIA was about where you make determinations in terms of the risk on the test, and it moved from CDC to FDA, specifically to re-

duce duplication and try to have more of one-stop shopping, and this actually goes the opposite direction of—

Mr. BURGESS. No, sir. The indications of the draft guidance you were going to put out, that would be the duplication that this legislation is seeking to avoid. And CLIA, remember, in its inception in the late 1980s, I was never a big fan of CLIA as a practicing physician but their whole purpose, the purpose that Senator Kennedy and others worked on this was so that laboratory tests could be certified as accurate and have clinical utility. That is their job. Don't tell me they don't want to do their job. If a Federal agency doesn't want to do its job, then perhaps we will have that discussion, but this is their job. This is what they were required to do under the amendments in 1988.

Mr. SHUREN. No, the amendments actually don't address these issues on analytical and clinical validity. In fact, your bill now changes that so you have to provide the data to actually show that. The problem is, it is not set up in a good way to get there and it creates duplicative government.

This is actually a problem for personalized medicine. We have heard this from companies who are making drugs and then devices to actually have the devices diagnose who is the right population to get the drug, and you now have companies, they make the device, they make the drug, they do the data. Everything works out and moves forward. In fact, one of them, two of them that just came out, we and our Center for Drugs, we approved it, both the drugs and the diagnostic, in less than 5 months. But then the day that they go out with their test and with their drugs, labs come out and say oh, I have got the exact same thing and in fact we are better. Really? And so now people can go use those other tests. Who knows if they are actually any good. Because none of the studies was even done with the drug. It is not even out there. And so what do you have now? Now you have tests that actually may be directing patients to get treatment they shouldn't get or not get a treatment they should get, and that is a disaster.

Mr. BURGESS. Well, I would submit that the duplication actually exists within your center, and albeit there is work to be done here but to simply ignore that there is a problem is to do no service to anyone at all.

Thank you, Mr. Chairman, for your indulgence and I will yield back.

Mr. PITTS. The Chair thanks the gentleman and recognizes the ranking member for 5 minutes for follow-up.

Mr. PALLONE. Thank you, Mr. Chairman.

Dr. Shuren, H.R. 3202, the Novel Device Regulatory Relief Act, appears to be intended to streamline the de novo process for FDA approval of medical devices. Although it is important to ensure that FDA review processes are efficient, I am sure we would all agree that the fundamental goal of the FDA is to ensure the safety of the public and to protect Americans from unsafe and ineffective medications and devices.

The proposed new language in this bill would allow device companies to require that their new device be evaluated under the de novo process without first submitting a 510(k) application demonstrating a substantial equivalence to another device already on

the market, which is what is currently required under the de novo procedures, and it changes the timelines under which a de novo application must be submitted.

So my question is, do you think this change under this proposed legislation would add to the efficiency of your clearance process? Does it give you enough time to do the reviews for products that presumably will be more novel than most 510(k) submissions?

Mr. SHUREN. We do think that the change of not having to be required to submit a 510(k) before going down the de novo pathway makes sense. So taking that requirement out of the law makes sense. Giving us only 60 days to do it, however, isn't enough time. I mean, even a 510(k), which is less complicated, is 90 days by law, and even that, we all know that that is not enough time for many of these as well. So not enough time but it is the right thing to do to take out the 510(k) if they don't want to submit it. Some companies, you actually don't know and they don't know, and they submit a 510(k) and then we will look at it. They actually never the requirements for a 510(k).

Mr. PALLONE. All right. Then I wanted to ask you a second question. As you know, the Safe Medical Devices Act of 1990 mandated that FDA evaluate pre-amendment class III devices and on a case-by-case basis either reclassify them to class I or II or require them to go through premarket approval as most post-amendment class III devices. What I would like to know is why FDA hasn't completed its mandated task of reclassifying pre-amendment class III devices or requiring them to go through premarket approval. Can you tell us how far you have gotten in this activity and how many devices remain, and are there unnecessary procedural hurdles in the law that keep you from finishing this activity?

Mr. SHUREN. So when I came on board, we put a new refocused energy into trying to get these done, and we have on our Web site each of the devices that we have to go through and where they are in the process. There are five steps. Four of them, we have wrapped up on. Another six we have proposals out and we will be issuing some actually final rule coming up and another proposed rule. So we are marching down the list. The challenge for us are the statutory requirements to go through this process, advisory committee meetings and doing rulemaking. In fact, this challenge—I mean, you all in legislation are telling us do this faster. This is a challenge when we have to change classification on a product. It is by rulemaking, and it cuts both ways. On the one hand, it is a weakness with 510(k). If you have a device that is in the 510(k) pathway and we have new data to say there are concerns, it should not be under 510(k), it should have been under PMA, a higher classification. It will take us several years to go there and puts a terrible quandary on doctors and patients who are out there and have the technology and they don't have the data behind it, or we take it completely off the market and that doesn't make sense in a lot of cases. We want to leave it there. That process is too burdensome.

On the flip side—and that is a safety issue. On the flip side, though, when we want to down-classify so we have something at a high risk or moderate risk and we want to make it lower risk and reduce regulatory burdens, we have so many statutory burdens on us, it is hard to do that. So it is hard for us to be deregulatory

and it is hard for us to set the bar in the right place. And if that were fixed, that would solve a big challenge. It would actually buttress things like the 510(k) program where the attention goes on these few devices where there are a lot of issues but it will also allow us to free up resources by down-classifying devices that should be subject to a lower standard.

Mr. PALLONE. You know, just an editorial comment. I don't envy you your job because it is a constant problem which is on the one hand, we want innovation, we want approvals to move more quickly, but we also have to balance that with public safety, and we get it at both ends. I mean, I as a politician get that from both ends, you know, "Why aren't you moving quickly?" On the other hand, everything has to be safe. You know, it is tough. I mean, I know a lot of my colleagues, particularly on the other side of the aisle, have been saying there are too many hurdles, but you can't sacrifice public safety, either, so it is a difficult quandary. Thank you.

Mr. SHUREN. I appreciate that. Actually, not even my dog is talking to me these days.

Mr. PITTS. The Chair thanks the gentleman.

The Chair has two unanimous consent requests. One, the report by the National Venture Capital Association entitled "Vital Signs." You have seen that?

Mr. PALLONE. That is fine.

Mr. PITTS. Without objection.

[The information appears with Mr. Jaffe's prepared statement.]

Mr. PALLONE. And the other being from—

Mr. PITTS. Mr. Burgess's letter?

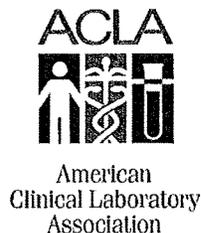
Mr. PALLONE. My colleague is fine too, yes.

Mr. PITTS. Without objection, those will be entered in the record.

[The information follows:]

October 14, 2011

The Honorable Michael Burgess, MD
United States House of Representatives
2241 Rayburn House Office Building
Washington, D.C. 20515



Dear Congressman Burgess:

The American Clinical Laboratory Association (ACLA) is extremely pleased to offer our full and strong support for H.R. 3207 the Modernizing Laboratory Test Standards for Patients Act. This Bill is in lock-step with the need for existing regulation to keep pace with the advancements in science that will move our health care delivery system to one focused on what is best for the patient, public health, and the economy. In particular, we note the legislation's effectiveness in reaching these goals by strengthening the current regulatory structure and eliminating duplicative regulation; enhancing public transparency for patients, providers and regulatory agencies; forging public/private partnerships with qualified non-governmental organizations; and strengthening reporting for adverse events-- all without additional government expenditures.

As such, the Modernizing Laboratory Test Standards for Patients Act will accelerate progress toward a personalized medicine revolution. A hallmark of that revolution is the contribution that clinical laboratory developed tests continue to make in enabling better informed diagnosis and better targeted care. The clinical laboratory industry is constantly innovating with new tests that detect and diagnose disease as well as inform the treating physician whether a drug or biologic is an effective means of treating a particular patient. This Bill will help ensure the accuracy and reliability of these tests while maintaining the integrity of the current regulatory framework.

On behalf of our membership, ACLA thanks you again for demonstrating such strong leadership in improving healthcare delivery by introducing legislation that enhances patient care and public health in a cost effective manner without stifling innovation, economic growth and job creation.

Sincerely,

A handwritten signature in cursive script that reads 'Alan Mertz'.

Alan Mertz
President

4770 Regent Boulevard
Irving, TX 75063



October 14, 2011

The Honorable Michael C. Burgess, M.D.
Member of Congress
2241 Rayburn House Office Building
Washington, DC 20515

Dear Congressman Burgess:

As the Managing Director of Quest Diagnostics Incorporated's Texas Gulf Coast Business Unit, I am pleased to offer the company's full and strong support for H.R. 3207, the Modernizing Laboratory Test Standards for Patients Act. This legislation is aligned with the need for existing regulation to keep pace with the advancements in science that will move our health care delivery system to one focused on what is best for the patient, public health, and the economy. In particular, we note the legislation's effectiveness in reaching these goals by strengthening the current regulatory structure and eliminating duplicative regulation; enhancing public transparency for patients, providers and regulatory agencies; forging public / private partnerships with qualified non-governmental organizations; and strengthening reporting for adverse events-- all without additional government expenditures.

Quest Diagnostics is the world's leading provider of diagnostic testing, information, and services that patients and doctors need to make better health care decisions. In Texas, Quest Diagnostics employs over 3,400 employees at 180 locations state-wide, including over 860 people at our Irving laboratory in your congressional district. The company offers the broadest access to diagnostic testing services through its national network of laboratories and patient service centers and over 40,000 employees, and offers interpretive consultation through its extensive medical and scientific staff. Quest Diagnostics provides clinical and anatomic laboratory testing services to touch the lives of approximately 150 million patients on an annual basis as ordered by thousands of physician practices and over one-half the hospitals in the United States.

It is our firm belief that this legislation will accelerate progress toward a personalized medicine revolution. A hallmark of that revolution is the contribution that clinical laboratory developed tests continue to make in enabling better informed diagnosis and better targeted care. The clinical laboratory industry is constantly innovating with new tests that detect and diagnose disease as well as inform the treating physician whether a drug or biologic is an effective means of treating a particular patient. This bill will help ensure the accuracy and reliability of these tests while maintaining the integrity of the current regulatory framework.

On behalf of our colleagues in Texas and nationwide, Quest Diagnostics thanks you again for your leadership and stewardship of patients' access to quality, affordable health care by introducing legislation that will benefit hundreds of thousands if not millions of patients nationwide and allow clinical laboratories to continue to develop new tests to improve patient health as well as enable economic growth.

Sincerely,

A handwritten signature in black ink, appearing to read 'Michael A. Peat'.

Michael A. Peat, Ph.D.



Laboratory Corporation of America® Holdings
531 South Spring Street
Burlington, North Carolina 27215

October 14, 2011

Donald E. Horton, Jr.
Vice President
Public Policy & Advocacy
Telephone: 336-436-5040
Fax: 336-436-1411
Email: hortond2@labcorp.com

The Honorable Michael Burgess
United States House of Representatives
2241 Rayburn House Office Building
Washington, D.C. 20515

Re: H.R. 3207 – Modernizing Laboratory Test Standards for Patients Act of 2011

Dear Congressman Burgess:

Laboratory Corporation of America Holdings (LabCorp) is extremely pleased to offer its support for H.R. 3207, the Modernizing Laboratory Test Standards for Patients Act of 2011. Enactment of this bill will enhance patient care and public health in a cost effective manner while supporting innovation, economic growth and job creation. In particular, we note the legislation's effectiveness in reaching these goals by enhancing the current regulatory structure for oversight of laboratory developed tests (LDTs) while eliminating duplicative regulation; improving public transparency for patients, providers and regulatory agencies; forging public/private partnerships with qualified non-governmental organizations; and facilitating reporting of adverse events -- all without additional government expenditures.

As such, enactment of the bill will accelerate progress toward achieving the promise of personalized medicine to improve care and reduce costs. The innovative contributions of LDTs have been, and will continue to be, essential in enabling physicians to detect and diagnose disease, as well as to assist physicians in determining the right treatment for the right patient at the right time. Enactment of this legislation will provide further assurance of the accuracy and reliability of these tests while maintaining the integrity of the current regulatory framework and providing regulatory certainty.

On behalf of its 31,000 employees, LabCorp thanks you again for demonstrating such strong leadership in improving healthcare delivery by introducing this important legislation, and we look forward to working with you towards its enactment.

Very truly yours,

Donald E. Horton, Jr.
Vice President, Public Policy & Advocacy



500 Chipeta Way, Salt Lake City, Utah 84108-1221
phone: (801) 583-2787 | toll free: (800) 242-2787
fax: (801) 583-2712 | www.aruplab.com

AN ENTERPRISE OF THE UNIVERSITY OF UTAH AND ITS DEPARTMENT OF PATHOLOGY

October 18, 2011

The Honorable Michael Burgess, MD
United States House of Representatives
2241 Rayburn House Office Building
Washington, D.C. 20515

Dear Congressman Burgess:

ARUP Laboratories, Inc. is extremely pleased to offer our full and strong support for H.R. 3207, the Modernizing Laboratory Test Standards for Patients Act. This Bill improves existing regulation to keep pace with the medical advancements in medical laboratory services. It will allow clarity for clinical laboratories, like ARUP, and permit us to focus on what is best for the patient, public health, and the economy. In particular, we note the legislation's effectiveness in reaching these goals by strengthening the current regulatory structure and eliminating duplicative regulation; enhancing public transparency for patients, providers and regulatory agencies; forging public/private partnerships with qualified non-governmental organizations; and strengthening reporting for adverse events – all without additional government expenditures.

As such, the Modernizing Laboratory Test Standards for Patients Act will accelerate progress occurring in the personalized medicine revolution. Central to that revolution is the contribution that clinical laboratory developed tests continue to make by enabling better informed diagnosis and better targeted care. The clinical laboratory industry is innovating constantly by providing new tests that detect and diagnose disease as well as inform the treating physician whether a drug or biologic is an effective means of treating a particular patient. This Bill will help ensure the accuracy and reliability of these tests while maintaining the integrity of the current regulatory framework. On behalf of ARUP, thank you for demonstrating such strong leadership in improving healthcare delivery by introducing legislation that enhances patient care and public health in a cost effective manner without stifling innovation, economic growth and job creation.

Sincerely,

A handwritten signature in black ink that reads 'Edward R. Ashwood MD'.

Digitally signed by Edward Ashwood
DN: cn=Edward Ashwood, email=ashwood@aruplab.com,
o=ARUP, ou=ARUP, c=US
Date: 2011.10.18 14:39:20 -0600

Edward R. Ashwood, MD
President and CEO
ARUP Laboratories, Inc.



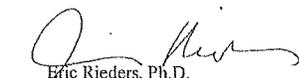
October 25, 2011

Dear Congressman Burgess,

I am writing to express my strong support for H.R. 3207. Our laboratory is a specialized reference laboratory, established in 1970, and employs nearly 250 professionals in our Pennsylvania location. We provide well over 1000 esoteric toxicology diagnostic tests to healthcare providers throughout the United States. Our clients rely upon us to be first to market with diagnostics that address emerging needs within our area of expertise. A recent example of this is NMS Labs' development of testing to identify abuse of so-called "designer drugs", often sold as "bath salts" or "synthetic pot".

Virtually all of our tests fall under the category of "LDTs" and the uncertainty surrounding future regulation of such innovative tests has been of major concern to us. We believe that you have performed a great service by tackling this issue in a measured and thoughtful fashion. This bill accounts for the critical need to insure clinical laboratories continue to adhere to appropriate standards demonstrating the quality of their operations through a focus on patient safety, while preserving the access patients and their physicians will have to innovative, relevant and economical diagnostic testing in the evolving era of personalized medicine.

Thank you for your attention and dedication,


Eric Rieders, Ph.D.
President and CEO
NMS Labs



November 3, 2011

The Honorable Michael Burgess, MD
 United States House of Representatives
 2241 Rayburn House Office Building
 Washington, DC 20515

Dear Congressman Burgess:

I am writing on behalf of GeneDx, a Gaithersburg, MD company that specializes in the genetic diagnosis of rare and ultra-rare hereditary disorders. GeneDx was established in 2000, by myself and another NIH scientist, when we saw the need for diagnostic services for the underserved community of patients and families with rare disorders. Working with the Maryland Department of Health, we learned what was needed to obtain our CLIA certification so that we could begin providing diagnostic services. As the laboratory has grown over the years (from 2-200 employees; from testing in 14 to testing in 400 disorders; from 140 patients tested in 2000, to over 20,000 in 2011), the CLIA regulations have guided us in how we run the laboratory and provide accurate, timely, and quality test results. All of these tests have been developed as Laboratory Developed Tests (LDTs).

I believe that HR 3207, the Modernizing Laboratory Test Standards for Patients Act, is the appropriate next step in continuing to guide laboratories in providing the best care for patients, especially as we move toward personalized medicine. This Act will allow laboratories to continue to innovate and move forward in providing patients with rare hereditary disorders the best possible diagnostic tests, while staying within the proven regulatory framework of CLIA and reducing or eliminating duplicative regulatory pathways that would slow innovation.

Thank you for introducing this important bill, and we at GeneDx want you to know that it has our complete support.

Sincerely,

A handwritten signature in black ink that reads "Sherri J. Bale".

Sherri J. Bale, PhD, FACMG
 Managing Director



January 25, 2012

The Honorable Michael Burgess
 U.S. House of Representatives
 2241 Rayburn House Office Building
 Washington, DC 20515

Dear Representative Burgess:

On behalf of the American Association of Bioanalysts (AAB) and the National Independent Laboratory Association (NILA), representing independent community and regional clinical laboratories, I am writing to thank you for your attention to the oversight of laboratory developed tests (LDTs) and for introducing H.R. 3207, *The Modernizing Laboratory Test Standards for Patients Act of 2011*. Your legislation provides a good start for discussion on how to appropriately regulate these tests. Our organizations look forward to working with you to address this important issue as the Energy and Commerce Committee focuses on legislation to reauthorize FDA-related programs.

As you know, LDTs offer patients the potential for preventing disease, obtaining early diagnoses, and receiving the most accurate and best course of treatment from their health care provider. Any regulatory process to oversee LDTs must appreciate the promise these tests hold without stifling innovation, while simultaneously ensuring that patient safety remains paramount. As health care providers, we feel strongly that this technology must be appropriately validated to ensure that the tests are accurate, reliable and reproducible.

We support the approach of your legislation to build on the current system in place to regulate the laboratory industry through the Clinical Laboratory Improvement Act (CLIA). We want to work with you and the Committee to identify the best way to establish a fair and sustainable regulatory process that appropriately assesses the quality and safety of LDTs.

Thank you again for your efforts in addressing this important issue. We look forward to continuing to work with you and your staff as this legislation moves forward in the process. Should you have any questions, or require additional information, please contact Julie Allen, our Washington representative at (202) 230-5126 or julie.allen@dbr.com.

Sincerely,

Mark S. Birenbaum, Ph.D.
 Administrator

Mr. PITTS. That completes panel one. Thank you very much, Dr. Shuren. We look forward to sitting down with you and working with you as the process goes forward.

At this point we will take a 5-minute recess while panel two sets up on the table, and we will reconvene in 5 minutes.

[Recess.]

Mr. PITTS. I will ask all of our guests and witnesses to please take their seats, and I will introduce the second panel. First of all, thank you all for agreeing to testify before the subcommittee today. Let me quickly introduce each one of you, and you can present your testimony, summarize your statements in this order. Mr. David Perez, the President and CEO of Terumo BCT; Ms. Elisabeth George, Vice President of Global Government Affairs, Regulations and Standards for Philips Healthcare; Mr. Ralph Hall, Professor at the University of Minnesota Law School; Dr. Ross Jaffe, Managing Director of Versant Ventures; Dr. Aaron Kesselheim, an Internal Medicine Physician at Brigham and Women's Hospital; Dr. Art Sedrakyan, an Associate Professor at Weill Cornell Medical College; Ms. Lisa Swirsky, Senior Health Policy Analyst at Consumers Union; and Mr. Jim Shull from the State of New Jersey.

Again, thank you all for coming. We have your prepared statements, which will be entered into the record. Mr. Perez, we will begin with you. You are recognized for 5 minutes to summarize your testimony.

STATEMENTS OF DAVID PEREZ, PRESIDENT AND CHIEF EXECUTIVE OFFICER, TERUMO BCT; ELISABETH M. GEORGE, VICE PRESIDENT, GLOBAL GOVERNMENT AFFAIRS, REGULATIONS, AND STANDARDS, PHILIPS HEALTHCARE; RALPH F. HALL, PROFESSOR OF PRACTICE, UNIVERSITY OF MINNESOTA LAW SCHOOL; ROSS JAFFE, MANAGING DIRECTOR, VERSANT VENTURES; AARON S. KESSELHEIM, ASSISTANT PROFESSOR OF MEDICINE, HARVARD MEDICAL SCHOOL, DIVISION OF PHARMACOEPIDEMIOLOGY AND PHARMACOECONOMICS, BRIGHAM AND WOMEN'S HOSPITAL; ART SEDRAKYAN, ASSOCIATE PROFESSOR AND DIRECTOR, PATIENT-CENTERED COMPARATIVE EFFECTIVENESS PROGRAM, WEILL CORNELL MEDICAL COLLEGE AND NEW YORK PRESBYTERIAN HOSPITAL; LISA SWIRSKY, SENIOR HEALTH POLICY ANALYST, CONSUMERS UNION; AND JAMES SHULL, BROWNS MILLS, NEW JERSEY

STATEMENT OF DAVID PEREZ

Mr. PEREZ. Thank you, Chairman Pitts, Ranking Member Pallone and members of the committee for this opportunity to testify today.

My name is David Perez and I am the President and Chief Executive Officer of Terumo BCT and Chairman of Terumo Corporation's Blood Management Business board, and I am responsible for leading the strategic direction, the growth and the execution of this global organization.

At Terumo BCT, we believe in the potential of blood to do even more for the world than it does today. This belief unites our organization, inspires our innovation and strengthens our collaboration with customers, which ultimately benefits the patients that we all

serve. Working with the American Red Cross, community blood centers throughout the United States as well as hospitals, we unlock the potential of blood as we strive to make even safer high-quality transfusions available to people. We help our customers bring even more treatment options to patients with advanced blood therapies, and we support researchers in developing cell therapies that may fundamentally improve health care.

I want to thank you for convening today's hearing and for your interest in improving medical device regulation for patients in our industry.

Over the course of the last year, members of this committee have demonstrated their focus on improving the efficiency and effectiveness of FDA regulation in your outreach to the agency and to the policy proposals that show your commitment to this important issue.

The medical technology industry is an American success story. Our industry directly employs more than 400,000 workers nationwide including 22,000 in the State of Pennsylvania, 20,000 in New Jersey and over 11,000 in my home State of Colorado, making these among the States with the largest med tech employment. In 2011, our company alone added 297 jobs, 224 of which were in manufacturing.

Whether the firm is large or small, success in our industry comes only from innovation, the creation of diagnostics, treatments and cures that extend and enhance lives. While we are very proud of our contribution to the U.S. economy, we are even more proud of our contributions to improving patient care.

Even though we are making progress in improving patient care and see immense future opportunities, we are also very worried. Today, America is the world leader in medical technology but there are warning signs that our lead is slipping, and a key factor in our loss of competitiveness has been the decline in the FDA's performance. Put simply, FDA is a crucial partner to our company's efforts to bring safe and effective medical devices to patients. Without a strong, effective and efficient FDA, we cannot have a strong and competitive industry.

While the FDA has consistently maintained an excellent record of assuring the safety and effectiveness of the products it reviews, delays in product approval, inconsistency in the review process and the resulting downstream effects on investment and innovation have undermined the competitiveness of our industry and harm patient access to new treatments, diagnostics and cures.

I am pleased to be able to report that after extensive negotiations, industry and FDA recently reached an agreement in principle for a new user fee package, which we believe has the potential to help achieve meaningful change in FDA performance through groundbreaking accountability and transparency measures.

The FDA leadership and Dr. Shuren in particular have recognized the need to vigorously address the issues affecting the device center, and I want to applaud them for this commitment. The user fee agreement is a huge step in the right direction. It is good for industry, it is good for the FDA, and most of all, it is good for patients.

The user fee agreement builds the conditions for success in a number of major ways. For the first time ever, this user agreement establishes average total time goals for FDA product review. All previous agreements have set goals in terms of time on the FDA clock. What matters to companies like my own and patients is the time it actually takes to get the product to patients. By setting in place this new goal, we will helping the FDA focus on the metric that is truly the most important to all concerned.

The agreement also includes process standards that we anticipate will improve the consistency and timeliness of the review process independent of the specific time goals, and the agreement provides for meaningful pre-submissions interactions where agreements reached will not change so that companies know what the FDA expects and the FDA is bound by its commitments. And a new procedure, what we call No Submission Left Behind, will be instituted so that if the FDA time target is missed, the company and the FDA will meet to work out a schedule to resolve the remaining issues so that the submission doesn't go to the bottom of the pile.

The agreement also provides for greater accountability so that FDA's success will be transparent to FDA management, to industry, to patients and to Congress so that any problems that arise can be corrected promptly. There will be quarterly and annual reporting on key metrics both the FDA and the industry have agreed are very important. In addition, this agreement requires analysis of FDA's management of the review process by an independent consulting organization coupled with an FDA corrective action plan to address opportunities for change and improvement.

Finally, to give FDA additional tools to meet these goals, the agreement provides \$595 million in user fees, additional reviewers, lower management-to-reviewer ratios, enhanced training, and other resources provided by the agreement will give FDA what it needs to improve performance.

I appreciate the committee's work and its focus on enactment of this reauthorization package as soon as possible, and once again, I thank you for the opportunity to testify.

[The prepared statement of Mr. Perez follows:]

Testimony of David Perez, Terumo BCT
House Energy and Commerce Health Subcommittee
Reauthorization of MDUFA: What It Means for Jobs, Innovation and Patients
February 15, 2012

Thank you Chairman Pitts, Ranking member Pallone, and members of the Committee for this opportunity to testify today.

My name is David Perez and as the president and chief executive officer of Terumo BCT and Chairman of Terumo Corporation's Blood Management Business board I am responsible for leading the strategic direction, growth and execution of this global organization with revenues in excess of \$875 million.

As a dedicated and active industry leader with nearly 30 years of experience within the medical device and healthcare industries, I lend my expertise to numerous boards and councils including the AdvaMed board, where I serve as a member of the board of directors and on the executive committee, chairing both the Technology and Regulatory Affairs Committee and the Blood Products and Technology Sector.

I share this with you because both AdvaMed and Terumo BCT are vested in innovation, job creation, and increasing the availability of life-improving and life-saving medical devices. At Terumo BCT, we believe in the potential of blood to do even more for the world than it does today. This belief unites our organization, inspires our innovation and strengthens our collaboration with customers, which ultimately benefits the patients we all serve. We unlock the potential of blood as we strive to make even safer, higher-quality transfusions available to more people. We help our customers bring even more treatment options to patients with advanced blood therapies. And we support researchers in developing cell therapies that may fundamentally improve health care.

From the inception of the company, our inspiration has always been and continues to be to improve the lives of patients in need. With more than 2,500 associates in over 45 countries, supporting customers in 120 plus countries with an average relationship spanning more than 20 years, Terumo BCT is a leading global provider of innovative technologies, products and services in blood collection, processing, safety, clinical procedures and cell therapies focused on such customer segments as Blood Banking - by providing products to increase the value of blood donations and to make even safer, higher-quality transfusions available to more people; Hospitals and Therapeutic Apheresis Centers - by expanding the number of treatment options for patients and Biotech and Cell Processing - by enabling scalable production of cells and supporting researchers in developing cell therapies that may fundamentally improve healthcare.

I want to thank you for convening today's hearing, and for your interest in improving medical device regulation for patients and industry. Over the course of the last year, members of this committee have demonstrated their focus on improving the efficiency and effectiveness of FDA

regulation, and your outreach to the agency and the policy proposals that have been introduced show your commitment to this important issue.

The U.S. Medical Technology Industry

The medical technology industry is an American success story. Our industry directly employs more than 400,000 workers nationwide, including over 22,200 in the state of Pennsylvania, 20,400 in New Jersey, and over 11,000 in my home state of Colorado, making these among the states with the largest medical technology industry employment. In 2011, our company alone added 297 new jobs, 224 of which were new manufacturing jobs. And, if indirect employment is included, the employment impact is substantially higher. Typically, for every worker our industry directly employs, another four workers are employed by businesses supplying components and services to our industry and our employees.

Our industry is heavily skewed toward small companies—the kind of companies that begin with a doctor, and engineer, and an idea to improve patient care. Almost two-thirds of the 7,000 medical technology firms in the U.S. have fewer than 20 employees. A high proportion of the breakthrough products in our industry come from these small, often venture-capital funded companies.

And whether the firm is large or small, success in our industry comes only from innovation—the creation of diagnostics, treatments and cures that extend and enhance lives. Our industry's investment in research and development is more than twice the national average. Our product life-cycle is only 18-24 months.

The jobs our industry provides are good jobs—the kinds of jobs that allow employees to live the American dream. Industry pay levels are 38 percent higher than average pay for all U.S. employment and 22 percent higher than other manufacturing employment. While the number of manufacturing jobs was plummeting across the larger economy, even before the current recession, employment in our industry was expanding. Between 2005 and 2007, medical technology employment grew 20.4%, adding 73,000 jobs. During the recession, between 2007 and 2008, MedTech employment dropped 1.1 percent, compared to 4.4% for manufacturing as a whole.

Our industry is so competitive that price increases have averaged only one-quarter the rate of other medical goods and services and just one-half the general CPI for almost 20 years.

With \$33 billion in total exports in 2008, medical technology ranks eleventh among all manufacturing industries in gross exports. Notably, unlike virtually every other sector of U.S. manufacturing, medical technology has consistently enjoyed a favorable balance of trade. With the aging of both U.S. and foreign populations, the projected explosive growth of large middle class populations demanding modern health care in developing countries like China and India, and the accelerating pace of biomedical discovery, the potential for growth of our industry is great.

While we are very proud of our contributions to the U.S. economy, we are even more proud of our contributions to improving patient care. For patients, medical progress has been remarkable. Between 1980 and 2000, medical progress added more than three years to life expectancy. The death rate from heart disease was cut in half; the death rate from stroke was cut by one-third, and the death rate from breast cancer was cut 20%.

FDA Regulation of Medical Devices – MDUFA III

While we are making progress in improving patient care and see immense future opportunities to provide jobs and contribute to long-term economic growth, we are also worried. Today, America is the world leader in medical technology. But there are warning signs. As a recent PriceWaterhouse Coopers report showed, our lead is slipping on a number of dimensions of competitiveness. And a key factor in our loss of competitiveness has been the decline in FDA's performance in ensuring timely patient access to safe and effective medical devices. Put simply, FDA is a critical partner in our companies' efforts to bring safe and effective medical devices to patients. Without a strong, effective, and efficient FDA, we cannot have a strong and competitive industry. The predictability, consistency and efficiency of FDA decision-making, as well as reasonable, risk-based standards of evidence to assure the safety and effectiveness of medical technology products, is essential to drive new innovations for patients and for the long-term success of the medical device industry. While the FDA has consistently maintained a strong record of assuring the safety and effectiveness of the products it reviews, delays in product approval, inconsistency in the review process, and the resulting downstream effects on investment and innovation have undermined the competitiveness of our industry and harmed patient access to new treatments, diagnostics, and cures.

I am pleased to be able to report that after extensive negotiations, industry and FDA recently reached an agreement in principle for a new user fee package which we believe has the potential to help achieve meaningful change in FDA performance through groundbreaking accountability and transparency measures.

The FDA leadership and Dr. Shuren have recognized the need to vigorously address the issues affecting the device center and are already taking a number of steps that we believe have the potential to bring significant improvements. The user fee agreement our industry representatives just concluded with the agency is a huge step in the right direction. It is good for industry. It is good for FDA. And most of all, it is good for patients.

The user fee agreement builds the conditions for success in a number major ways:

Total Time Goal

For the first time ever, this user fee agreement establishes average total time goals for FDA product review. All previous agreements have set goals in terms of time on the FDA clock. When the FDA asks sponsors for additional information or data, the FDA clock stops. The result was that while FDA may have been meeting the goals for 510(k) submissions, the total time from submission to final decision increased 43% between the average for 2003-2007 and 2010.

Of course, what matters to companies and patients is not an artificial construct like time on the FDA clock, but the time it actually takes to get the product to patients.

FDA, of course, often has legitimate questions about an application and it cannot control the amount of time it takes for a sponsor to respond to questions about any individual application. But all sponsors want to submit applications that meet FDA standards, and total time is the best indicator of whether FDA is consistent and efficient in its review and is providing sponsors with adequate information in advance of what data is needed for different types of products. We refer to this new standard as a shared performance goal, because industry also has an obligation to submit good applications. AdvaMed will, in cooperation with FDA, be carrying out additional training to help smaller companies meet this standard, and FDA will have new authority to decline to begin review of an application that is obviously deficient when it is submitted.

By setting in place this new goal, we will be helping FDA management focus its efforts on the metric that is truly most important to all concerned.

Improved FDA Day Goals

Second, the agreement also establishes significantly improved goals for time on the FDA clock. For example, for PMAs receiving panel reviews—which tend to be the most innovative products—the current FDA performance is that only 38% receive a decision in 320 days. By the end of this new agreement, 90% will achieve this goal, and many, of course, will be reviewed more quickly.

Process Improvements

Third, the agreement includes process standards that we anticipate will improve the consistency and timeliness of the review process independent of the specific time goals.

The agreement provides for meaningful presubmission interactions where agreements reached will not change, so that companies know what FDA expects and FDA is bound by its commitments, unless, of course, new information arises that requires a change to protect public health.

Additionally, there will be a substantive interaction between FDA and the company midway through the review process. This will assure that both companies and FDA identify any problems with the application early, so that they can be corrected promptly.

A new procedure that we call “no submission left behind” will be instituted, so that if the FDA time target is missed, the company and the FDA will meet to work out a schedule for resolving remaining issues, so that the submission doesn’t go to the bottom of the pile.

Greater Accountability

Fourth, the agreement provides for greater accountability. Greater accountability means that FDA’s success under this agreement will be transparent to FDA management, to industry, to

patients, and to Congress and the Administration, so that any problems that arise can be corrected promptly. Under the agreement, there will be quarterly and annual reporting on key metrics, tracking of new performance indicators that both FDA and industry have agreed are important.

In addition, the agreement requires an analysis of FDA's management of the review process by an independent consulting organization, coupled with an FDA corrective action plan to address opportunities for improvement.

Appropriate Resources

Finally, to give FDA additional tools to meet the new goals, the agreement provides \$595 million in user fees for 2013-2017. Additional reviewers, lower manager-to-reviewer ratios, enhanced training, and other resources provided by the agreement will give FDA what it needs to improve performance. Overall, the agreement will allow FDA to hire approximately 200 additional FTEs, the vast majority of which will be put into place where needed most – additional reviewers and more supervisors to ensure consistency in the review process.

Each of the provisions of this agreement has the potential to make a significant difference in improving FDA performance. But the whole is truly greater than the sum of its parts. Each of the elements of the agreement reinforces the others. For example, the combination of total time goals and faster FDA time goals should result in greater improvements than either one would achieve separately.

And, of course, no agreement, no matter how good on paper, is self-executing. Making it work as intended will require the full efforts of FDA's dedicated staff and managers. Our industry is committed to work with FDA in any way we can to make it a success. Continued oversight and interest from the Congress will also be important. Patients are depending on all of us.

Conclusion

Finally, I should note that a number of legislative proposals have been introduced with the goal of improving the FDA's operations. We are appreciative of efforts by all Members who seek to give the FDA the tools and structure it needs to succeed. Legislative reforms that do not alter the substance of the negotiated agreement between FDA and industry hold the potential to create a legislative reauthorization package that maximizes the opportunity for success at the agency, which should be the shared goal of all involved.

For example, legislation has been proposed to streamline the de novo process by eliminating the statutory requirement that a sponsor receive a finding of "not substantially equivalent" before even beginning the de novo process. The Institute of Medicine and FDA itself have recognized that the current process is cumbersome, and FDA is looking at using its regulatory discretion to improve that process. However, statutory change may be the most effective way to address the problem, which will help FDA, industry, and ultimately patients.

Another example is the proposals that would ease the conflict-of-interest restrictions for participation on FDA advisory panels. Advisory panels can be a useful mechanism for providing FDA reviewers with important expertise, but the agency has experienced difficulties securing qualified experts, slowing the approval process and patient access to the latest medical innovations.

I appreciate the committee's work in considering these and other appropriate measures that enhance and compliment the underlying user fee agreement, and its focus on enactment of this legislative package as soon as possible.

Once again, thank you for the opportunity to testify.

Mr. PITTS. The Chair thanks the gentleman and now recognizes Ms. George for 5 minutes for an opening statement.

STATEMENT OF ELISABETH M. GEORGE

Ms. GEORGE. My name is Elisabeth George and I represent Philips Healthcare as their Vice President of Global Government Affairs, Regulations and Standards. I want to start by thanking Chairman Pitts and Ranking Member Pallone for holding today's hearing. I also want to thank you for your particular interest in medical innovation and for leading a policy discussion on how we can work together to collectively improve the medical device user fee program.

It is clear to me that we all share the goal of getting safe and innovative products to U.S. patients in a timely and predictable manner. Philips Healthcare employs over 15,000 hardworking Americans in cities and towns across the country. We are just one in a global industry. Philips Healthcare's current activities are organized across four businesses: imaging systems, patient care and clinical informatics, home health care solutions, and customer services. We have appreciated your steadfast support in ensuring the access to medical technology and particularly imaging and its important appropriate use for patients.

I have worked for Philips Healthcare for more than 15 years. I have managed strategic planning and technical aspects for global affairs, regulations and standards. I have also served on multiple FDA advisory panels through the years and have most recently represented the medical imaging industry during the MDUFA negotiations with the FDA. As an industry negotiator, I am pleased to talk with Congress today about the agreement in principle between the medical device industry and FDA. We believe that this agreement will facilitate improved transparency and consistency leading to better predictability and more timely access for patients.

After negotiating for more than a year, we believe that this agreement is balanced and is fair to all stakeholders. We hope this package will lead to a timely reauthorization of the medical device user fee program. The goal of this agreement is to ensure timely patient access to safe, effective treatments and diagnostics. Although it is not formerly proposed to Congress until it receives full administrative approval and the FDA completes its public commenting period, the package as negotiated includes commitments from the agency that will improve the device review program through additional predictability, transparency and accountability. In a time of tremendous advances in medical technology, the agreement enables the industry to bring innovative, lifesaving technologies to market faster so that patients receive the highest quality care.

The explicit goal of the device user fee program has been to achieve more timely clearance of safe and effective devices by providing the FDA with supplemental funds to independently evaluate applications. However, despite clear Congressional intent, FDA performance has declined steadily over the past several years. For example, fiscal year 2006, it took an average of 105 calendar days to make a final decision on a submission. The number increased to 154 days in 2009 despite the fact that the user fees had increased

by over 50 percent over the same period. The decline in timeliness has been an overarching concern for industry. Our goal in this agreement was to reverse this downward trend and to ensure value for our user fee investment for both patients and innovators. The increase in resources to the agency under this agreement corresponds to a more timely approval process, which will benefit patients and the manufacturers who develop these innovative technologies.

The agreement includes several new quantitative goals to hold the FDA accountable. These goals include total time for decisions as well as improved annual targets for 510(k) applications. The agreement also works to ensure an improved review process that is more predictable and transparent for manufacturers, patients and other stakeholders such as through enhanced clarity in the pre-submission process, enhanced guidance development and an independent assessment of the FDA's performance. These improvements are important for patients, innovation and jobs in America.

I believe it is important that Congress do everything possible to encourage high-tech 21st century industries like the medical device manufacturing that will continue to create jobs and necessary to grow the U.S. economy. We are very appreciative of members of this committee who have held a series of hearings and introduced a number of bills in an effort to respond to these concerns and improve the FDA review process for medical devices. I believe that our collective efforts will lead to constructive improvements.

Thank you for your consideration of these important issues. As the legislative process moves forward, we look forward to continuing to work with Congress and the administration to ensure patients are guaranteed timely access to medical technologies.

I again thank you for this invitation.

[The prepared statement of Ms. George follows:]

**Philips Healthcare**

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Elisabeth M. George
Testimony before the House Committee on Energy and Commerce
Subcommittee on Health
Hearing Entitled "Reauthorization of MDUFA:
What It Means for Jobs, Innovation and Patients"
Wednesday, February 15, 2012

Introduction

My name is Elisabeth George, and I represent Philips Healthcare as Vice President of Global Government Affairs, Regulations and Standards. I want to start by thanking Chairman Pitts and Ranking Member Pallone for your holding today's hearing. I also want to thank you for your particular interests in medical innovation and for leading a policy discussion on what the flaws are in our system and how we can work together to collectively improve it during this reauthorization of the medical device user fee program. It is clear to me that we all share the goal of getting safe and innovative products to U.S. patients more quickly.

Philips Healthcare's current activities are organized across four businesses: Imaging Systems (X-ray, computed tomography (CT), magnetic resonance (MR) imaging, nuclear medicine and ultrasound); Patient Care and Clinical Informatics (patient monitoring, hospital respiratory systems, children's medical ventures, cardiac care systems, healthcare informatics and image management services); Home Healthcare Solutions (sleep management and respiratory care, medical alert systems, remote cardiac services, remote patient management); and Customer Services (consultancy, clinical series, education,

equipment financing, asset management and equipment maintenance and repair). Especially because of our diverse portfolio, we have appreciated your steadfast support in ensuring the access to medical technology and particularly imaging and its appropriate use for patients. I am confident that today's hearing will serve to further ensure patient access to safe and effective technologies.

I have worked for Philips Healthcare for more than 15 years and have managed strategic planning and technical aspects for global affairs, regulations and standards including quality, reliability, safety, product security, privacy and sustainability compliance for Philips Healthcare business around the world. My responsibilities include supporting the organization in ensuring worldwide compliance and continual improvement in product submissions, post-market surveillance, product reliability improvement, International standards and regulations, quality systems (ISO13485, 21CFR), and environmental management system (ISO14001 & OHSAS 18001) for Philips products in the area of Home Healthcare, Patient Monitoring Systems, Healthcare Informatics, External Defibrillators, Cardiographs, X-Ray Systems, MR Systems, CT Systems, Nuclear Medicine Solutions and Generators.

I have also served on multiple FDA advisory panels through the years and have most recently represented the medical imaging industry during the Medical Device User Fee Agreement negotiations with the FDA.

As an industry negotiator, I am pleased to talk with Congress today about our first successful step in the process to final reauthorization: the agreement in principle between medical device industry representatives and the FDA. We believe that this agreement will facilitate improved transparency and consistency from the agency leading to better outcomes and more timely access for patients in need of safe and effective medical devices.

After negotiating for more than a year, the FDA and the medical device

manufacturing industry have successfully come to this agreement in principle, which we feel is balanced and fair to all stakeholders. We hope that the balanced approach taken by this package will lead to a timely proposal to Congress on reauthorizing and improving the Medical Device User Fee Program.

The goal of this agreement is to ensure timely patient access to safe and effective treatments and diagnostics. Although the agreement is not formally proposed to Congress until it receives full Administration approval and the FDA completes its public commenting process, the package as negotiated includes commitments from the Agency that will improve the device review program through additional predictability, transparency, and accountability. In a time of tremendous advances in medical technologies, the agreement enables the industry to bring innovative, life-saving technologies to market faster, so that patients receive the highest quality care.

What Medical Devices Mean to Patients

Philips is a manufacturer of a diverse range of medical devices, from patient monitoring systems that can be used in the home to advanced medical imaging equipment for use in a hospital or physician office setting. These technologies are critical to patient care, and we are committed to ensuring that the FDA device review process works effectively. An effective and efficient process not only benefits us by ensuring our products get to market, but it also prevents patients from being left unable to access the device that helps them rest comfortably at home or the advanced imaging technology that detects their cancer early, when it is most treatable.

The devices we produce are central to patient care. For example, the *New England Journal of Medicine* declared that medical imaging is one of the top “developments that changed the face of clinical medicine” during the last millennium – as important as anesthesia and antibiotics.¹ Physicians who care for patients each day have echoed that

assessment and have ranked MRI and CT technology as the most valuable medical innovations in the last 30 years.ⁱⁱ Indeed we know that the term “exploratory surgery” is all but obsolete due to the advancements made in medical imaging. Wait times to diagnosis and treatment have been shortened, allowing Americans to put an illness or injury behind them and get back to their lives and their families more quickly than ever before.

Additionally, in the field of medical imaging, Philips has focused on patients are exposed to the lowest radiation dose possible, while giving physicians an image resolution that allows them to make an accurate diagnosis. Philips and the entire medical imaging industry are dedicated to the ALARA dose management principle, which stands for “as low as reasonably achievable” Medical imaging manufacturer have produced groundbreaking innovations to make this principle a reality. As a result, today’s medical imaging technologies make imaging procedures safer than ever.

These technologies are critical for patient care and diagnosis, and give patients and physicians peace of mind. Because these technologies are so important to patients and central to physician standards of care, we have worked with the FDA over the years on ways to improve the timeliness, consistency and transparency of the pre-market approval process. When that process is broken, it not only stifles innovation, but also patient care.

History of MDUFA Negotiations

As you may know, medical device user fees arose following widespread concerns with the lengthy FDA approval time and the associated harm that this delay had on innovation and patient care. Congress initially gave FDA the authority to collect medical device user fees in 2002. The original negotiation between the FDA and industry established user fees for premarket applications (PMAs), premarket notifications (510(k)s), and other types of requests to market medical devices. The original negotiated agreement listed specific performance goals for FDA for premarket device reviews only.

Since that time, that basic structure has remained. During the last negotiation, the Medical Device User Fee and Modernization Act (MDUFMA), in 2007, industry agreed to increase fees for additional performance improvements from the FDA.

The explicit goal of the device user fee program has been to achieve more timely clearance of safe and effective devices by providing FDA with supplemental funds to independently evaluate applications. In fact, the 2007 law specifically states that “the fees authorized under the amendments made by this title will be dedicated toward expediting the process for the review of device applications”ⁱⁱⁱ.

However, despite clear Congressional intent, FDA performance has unfortunately declined steadily over the past several years. For example, in FY2006, FDA took an average of 105 calendar days to make a final decision on a 510(k) submission. That number increased to 154 calendar days in 2009 despite the fact that user fees had increased by more than half over the same period. Concern with the decline in FDA device approval timeliness has been an overarching concern for industry during the years leading up to our most recent negotiation period. Our goal in negotiating this agreement was to reverse this downward slide and ensure value for our user fee investment for both patients and innovators.

Highlights of the MDUFA Agreement in Principle

As you may have seen in the published minutes from the official negotiation meeting with the FDA and industry negotiators in January 31st, the negotiators have put in place what we believe is a strong and fair agreement in principle. At this point that agreement needs to receive further review and approval by the Administration.

The new agreement negotiated by FDA and industry would make key improvements to the review program while providing the Agency with the resources it needs to expedite the pre-market process. Under the agreement, industry would provide a total of \$595

million to FDA in user fees from Fiscal Year 2013 to Fiscal Year 2017. When combined with Congressional appropriations, this resource level will enable FDA to substantially increase the resources it can dedicate to the review process. It will be incumbent upon the FDA to ensure that these employees are qualified and quickly and thoroughly trained to ensure the Agency meets the goals set forth in the tentative agreement.

Ensuring Patient Access to Innovative Technology

The increase in resources to the agency under this agreement corresponds to a more timely approval process, which will benefit patients and the manufacturers who develop these innovative technologies. The agreement includes several new quantitative goals to hold FDA accountable for its commitment to reducing review times.

Total Time Goal: For the first time, FDA has agreed to establish a “total time” goal, which will hold FDA accountable for the length of time— importantly, in clearly understandable calendar days—between the submission of a device application and a final review decision. In prior agreements, performance goals were based solely on “FDA days”, which allow the Agency to “stop the clock” and therefore technically meet the goals without expediting reviews. The total time goal will ensure that both the FDA, industry, and all other stakeholders understand the time it takes to bring a new or improved technology to market. This goal will hold both the FDA as well as industry to a new standard of accountability, as each party works to improve efficiencies to ensure patient access to innovative devices is not unnecessarily delayed.

Substantive Interaction Goal: Another new goal, the “substantive interaction goal”, will require FDA to initiate a productive discussion of Agency concerns between reviewer and manufacturer early in the review process. This early interaction is invaluable in helping manufacturers understand the Agency’s questions or concerns about a device and improving industry responses.

510(k) Approval Time Improvements: As you may know, most of the devices produced by Philips Healthcare are approved through the 510(k) program. Over 90 percent of all medical devices entering the market in the United States go through the 510(k) process. This pathway is absolutely essential, as it gives patients access to important incremental improvements in medical device technology. Meanwhile, this process also allows increased investment in research and development by manufacturers—producing exciting new technological developments.

Fortunately, the agreement in principal between FDA and industry strengthens and reforms existing 510(k) program review goals in very important ways. Under the existing user fee goals, FDA is expected to make a final decision on 90% of 510(k) submission decisions within 90 days. The new agreement would improve the Agency's performance goal to 95% in 90 days for 510(k) decisions by FY16. The new agreement also eliminates the existing and counter-productive 150 day performance goal, replacing it with a process that encourages a meaningful discussion between FDA and the manufacturer on every stalled submission. This new process will require extensive management involvement in delayed applications, which will better enable Agency managers to respond to recurring process problems. In addition, this change also avoids the negative consequence of the existing metric, which unintentionally creates a perverse incentive for reviewers to delay final decisions for reviews that miss the initial 90 day performance goal.

FDA's commitment to meeting these new and improved review time goals will expedite the review process and help ensure patients have access to innovative medical devices.

Improving Predictability, Transparency, & Accountability

The agreement also works to ensure an improved review process that is more predictable and transparent for manufacturers, patients, and other stakeholders.

Enhanced Clarity in the Pre-submission Process: The agreement requires FDA to enhance its pre-submission meeting process to provide more robust feedback to a manufacturer prior to a submission. The improved process prevents FDA from changing the requirements communicated at this stage, barring the development of important new issues that materially affect safety or effectiveness.

Enhanced Guidance Development: The agreement also requires FDA to dedicate resources to developing guidance documents for industry and Agency staff with the goal of ensuring both the reviewer and the manufacturer understand the FDA's current thinking on important questions of safety and effectiveness.

Detailed Performance Reports: Under previous MDUFA agreements, often FDA has been slow to provide industry and other stakeholders with the information necessary to judge the Agency's performance and provide constructive input on how the Agency could improve. The MDUFA III agreement requires FDA to increase transparency by publishing more detailed performance reports. This information will help industry identify areas where FDA and manufacturers can work together to remove obstacles to effective and timely device reviews.

Independent Assessment of Performance: Perhaps one of the most valuable new items for improving transparency and accountability is that the FDA has agreed to an independent assessment of its management of the device review process, which will provide an unbiased analysis of how FDA can improve its performance. The FDA has committed to respond to this audit with a corrective action plan that addresses problem areas and improves the Agency's management of both the taxpayer dollars and industry user fees that fund the device review program.

Conclusion

I can't overstate the importance of an effective and efficient medical device pre-

market review program. That's why I greatly appreciate this Committee's demonstrated interest in improving the review process in the United States, to ensure innovative companies can continue to advance innovation in medicine.

Philips Healthcare employs over 15,000 hardworking Americans in cities and towns across America—and we are just one company in a global industry. One recent study found that the American medical device industry employs over 422,000 American workers, with jobs in every state.

I don't think our industry can take a single job for granted in times like these. Unfortunately, the current system's lack of predictability and the trend of increased review times have combined to force many investors to put their capital into projects in Europe—where device reviews are often significantly shorter than in the United States. This trend has raised concerns across the industry of where the American medical device industry is headed without improvements to the regulatory environment in the U.S. like those included in the MDUFA III agreement.

That's why we simply can't afford to delay reforms that expand patient access to safe and effective medical devices while fostering the kind of innovation that will improve care and reduce costs. In fact, I believe it's more important than ever that Congress do everything possible to encourage high-tech 21st century industries—like medical device manufacturing—that will continue to create the jobs necessary to grow the U.S. economy.

We are very appreciative of Members of this Committee who have held a series of hearings and introduced a number of bills in an effort to respond to these concerns and improve the FDA review process for medical devices. I believe that all our efforts have been constructive. We certainly can't afford to move in the opposite direction and make it more difficult for patients to access devices the FDA deems safe and effective.

Thank you for your consideration of these important issues. As the legislative

process moves forward, we at Philips Healthcare, along with our industry partners, look forward to continuing to work with Congress and the Administration to ensure patients are guaranteed timely access to medical technologies. We believe that timely access will continue to improve quality of life for millions of Americans and patients around the world. I thank you again for this invitation to testify.

ⁱ The Editors. "Looking back on the millennium in medicine." *New England Journal of Medicine (NEJM)*, 342: 42-49, 2000.

ⁱⁱ Fuchs VR and Sox HC Jr. "Physicians' Views of the Relative Importance of Thirty Medical Innovations." *Health Affairs*, 20(5): 30-42, 2001.

ⁱⁱⁱ P.L. 110-85, Sec. 201(c)

Mr. PITTS. The Chair thanks the gentlelady and recognizes Mr. Hall for 5 minutes for an opening statement.

STATEMENT OF RALPH F. HALL

Mr. HALL. Chairman Pitts, Ranking Member Pallone, members of the committee, I appreciate the opportunity to address you on these important issues of medical device regulation. I serve on the faculty of the University of Minnesota Law School. I am also part-time counsel with Faegre Baker Daniels and am CEO of a four-person startup company.

I am here to focus on two matters: the agency's authority in the area of medical device regulation and the safety performance of FDA in its actual review. I believe it is important to differentiate between questions of authority from questions of implementation. Authority is whether the agency can act or has the power to compel action, while implementation goes to issues such as resources, skill sets, timing, processes, etc. The user fees that are under discussion specifically today primarily address implementation challenges and are intended to address those.

On the authority front, the agency has extensive authority for the entire lifecycle or, as we call it, total product lifecycle, of a device from initial design to final obsolescence. There are of course improvements, some of them which have been discussed in the de novo process or HDEs, for example, but fundamentally, the agency has the current authority to require products to meet the statutory standard of a reasonable assurance of safety and effectiveness. This is true under both the 510(k) system and the PMA system. There are differences in how we achieve that objective or that test but that same statutory standard applies to all products.

Along the same lines, the agency has extensive postmarket authority. Examples include the MDR system, the 522 orders, MedSun, registries, and there have been discussions about registries. It is important to note again on the authority front that the agency currently has the authority under the 510(k) system to mandate patient registries for products for which it believes such registries are appropriate and valuable. The agency likewise has extensive authority in the areas of recalls and dealing with product issues including the authority to ban products where that is necessary and the authority to mandate recalls.

The major question then is, how is the agency performing on the safety aspects. I leave to others the issues of impact on innovation, timeliness, predictability, etc. We have performed a study looking at medical device recalls. We have analyzed 5 years of data. We are actually in the process right now of analyzing another year's worth of data. That is not yet completed. The conclusion of this study is that the agency is doing a very good job on the safety aspect. The vast majority of products that get through their system do not have significant safety issues. It is obvious and critical to remember that all medical devices have risks and the statutory standard is a balance between the benefit and the risk of the product. So one of the key aspects and requirements of the system is to identify the risks so that a knowing balance can be made between the risks and the benefits, and when you look at the data, you can see that greater than 99.5 percent of all product approvals do not result in a class

I recall, that the majority of recall safety issues that do occur are postmarket issues: manufacturing mistakes, labeling errors, etc. And changes to a premarket system obviously can impact events that take place after product approval.

Quality systems are the key to improving product safety. Of all recalls, as we have looked at the data, approximately 90 percent of all of those have some relationship to quality systems and improvements in quality systems therefore provide the greatest leverage. Very preliminarily, we have looked at 2010 data, as I mentioned. That data seems consistent with what we have seen to date with the other data, with a slight increase in manufacturing issues. We are not clear if that is statistical or not. We have also taken a look at class II recalls, and preliminarily, the reasons for recall appear to be consistent between class I and class II recalls.

So in conclusion, the agency has multiple control points to ensure product safety and effectiveness, not just one: quality systems, premarket approval, postmarket approval. The agency has authority, extensive authority both pre- and postmarket, and the agency's safety record has been very good over the past years.

Thank you very much.

[The prepared statement of Mr. Hall follows:]

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Written Statement

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U.S. House of Representatives Energy and Commerce Committee

Subcommittee on Health

Medical Device Safety: An Overview of FDA's Authority and a Review of Safety Data

February 15, 2012

Good morning, 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 discuss FDA's medical device regulatory system including, specifically CDRH's post-market authorities and its recall authority and practices. In addition, I will review research I have done into the safety of 510(k) products. 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 Practice 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 Faegre 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 start-up medical device company

working on a new technology for cardiac rhythm devices generally regulated under the PMA process.

The research that is the focus of many of my comments 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.¹

Overview:

While medical device regulation can appear to be obtuse and convoluted, there are core themes and policies that can be readily discerned.

- 1) The system created by FDA and Congress rarely has just a single regulatory control point or tool to protect public health. In almost all situations, FDA has multiple tools it can use to ensure that only products with a reasonable assurance of safety and effectiveness (the statutory standard)² are permitted onto the market or permitted to remain on the market.
- 2) It is critical to separate questions of FDA's authority from questions about FDA's implementation of its authority. My comments focus on the agency's authority.
- 3) FDA has clear statutory authority under the 510(k) system to assess the safety and effectiveness of products under review.

¹ 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 the first study. Their talents, hard work and dedication are vital to this research and I appreciate all that they did. Chris Walker continues his strong support as he is conducting a detailed data review for recalls posted in 2010..

² 21 U.S.C. §393(b).

- 4) FDA has a substantial number of post market tools currently available to it. These tools, while not perfect, give CDRH significant authority to identify post market product issues and to compel corrective action.
- 5) Overall FDA has done well in providing the reasonable assurance that medical devices are safe and effective before they are approved or cleared. The majority of Class I recalls (the high risk situations) involve post market issues. The most powerful tool to improve this safety record is an emphasis on quality systems (so-called "QSR" systems) rather than changes to pre-market authorities.

Safety and effectiveness

FDA has the explicit statutory mandate to provide a reasonable assurance that medical devices are safe and effective for their intended use. What can be confusing is that FDA uses different means to achieve this universal goal. This reasonable assurance of safety and effectiveness for Class I devices³ is provided through the implementation of "general controls". A medical device is in Class I if these "general controls" "are sufficient to provide reasonable assurance of the safety and effectiveness of the device".⁴

Class II devices use both general controls and "special controls" to provide the reasonable assurance of safety and effectiveness.⁵ These special controls can include clinical trials, specific bench testing, post market obligations and patient registries as some of the tools available to FDA to meet the statutory objective of safety and effectiveness. The 510(k) system has the explicit statutory authority to address safety and effectiveness issues and to keep unsafe products

³ Congress has created three risk based device classes. Class I devices are the lowest risk devices. Class II devices pose medium risk and, obviously, Class III devices present the highest risk. See 21 U.S.C. §360c for an overview of the classification system and processes.

⁴ 21 U.S.C. §360c(a)(1)(A)(i).

⁵ 21 U.S.C. §360c(a)(1)(B).

off the market. Class II products generally go through the 510(k) system for premarket clearance (there are some exceptions not relevant to this discussion).

CDRH has explicit authority to create special controls for life supporting or sustaining Class II devices to ensure that these products have a reasonable assurance of safety or effectiveness. The statute states:

For a device that is purported or represented to be for a use in supporting or sustaining human life, the Secretary shall examine and identify the special controls, if any, that are necessary to provide adequate assurance of safety and effectiveness and describe how such controls provide such assurance.⁶

Class III devices are those high risk devices for which general controls and special controls are not adequate. These products use the PMA process to assess safety and effectiveness.

I want to make two key conclusions. First, no matter the device classification, CDRH is charged with providing a reasonable assurance of safety and effectiveness for the intended use. No medical device bypasses this requirement. What changes is the means (or tools) CDRH uses to meet this objective. Second, all devices – like all drugs – have some risk. The challenge to CDRH, physicians and patients is to ensure that the benefit outweighs the risk.

Post-Market Authorities

In addition to the premarket control systems outlined above, FDA has a variety of post market authorities. Whether it uses them in the way Congress desires is a different question. The post market systems include information collection processes, information analysis mechanisms and corrective action systems.

⁶ 21 U.S.C. §360c(a)(1)(B)

These authorities can be categorized as either general (or universal) requirements applicable to all medical devices or requirements specific to a particular product type or specific product use. The first group is applicable to all devices; the second are applicable to defined subgroups. The agency uses all of these tools detailed below to implement a systemic post market control and information system.

Universal Post-Market Requirements

The following post market legal/regulatory structures generally apply to all medical devices.

I. MDR Reporting

Pursuant to 21 C.F.R. § 803 (and related authorizing statutes such as 21 U.S.C. § 360i(a) and (b)), medical device manufacturers are required to submit any reports of deaths or serious injuries allegedly associated with the device and, in addition, are required to report device malfunctions which could, if such a malfunction were to occur in the future, cause death or serious injury. Failure to submit MDR reports can (and often do) lead to serious civil and criminal enforcement actions.

The regulatory definition of “serious injury” includes a wide variety of events including events in which medical intervention prevented an actual serious injury. For example, a product issue that extends the time of the operation by ten minutes would be “serious injury” under 21 C.F.R. § 803 even if there was no other patient impact. Stated differently, the regulatory definition of “serious injury” is much broader than what the lay person or physician might consider serious.

MDRs are required to be submitted within specified time frames even if the allegations are unproven or open to debate. Causation need not be established and an investigation need not be completed before the MDR must be submitted.

Approximately 180-200,000 MDRs are reported each year.

Properly implemented, the MDR system provides an ongoing assessment of product performance in real world situations and operates as an “early warning system” for unknown safety issues or changes in the frequency or severity of known risks.

2. Recall Reporting

Under 21 C.F.R. § 806 (and related statutes and guidance), companies are obligated to report to FDA within ten days any field action (technically, either a correction or removal action) related to product issues or regulatory matters.

These recall reports, subsequent recall effectiveness checks conducted by FDA and recall close outs processes provide FDA with information about field performance issues and to ensure that field performance issues related to that product or similar products are properly addressed.

As discussed in more detail below, FDA has the explicit statutory authority to mandate a recall.⁷

⁷ 21 U.S.C. §360h(a) and (e).

3. MedSun

The MDR system is a “passive” data collection system in that it relies on third parties to submit reports. To complement this “passive” system, CDRH has implemented (and is currently upgrading) the MedSun program. The program actively collects product performance data from approximately 350 hospitals covering different geographies and types of patient base (urban and rural, small and large, academic teaching centers and non-academic centers, etc.). CDRH has special relations with these institutions and has trained these institutions to actively report product issues.

The MedSun system provides enhanced field surveillance and the collection of more data in a structured, organized fashion.

In a related program, CDRH is working to implement MDEpiNet.⁸ This system links together 10 major academic networks in order to bolster post market and field information collection and analysis.

4. QSR Systems

A critical element in CDRH’s post-market safety and surveillance systems are the Quality System Regulations (or QSRs) generally set forth in 21 C.F.R. § 820. These require, among other obligations, each company to collect and analyze all product complaints (i.e. post market information) and related internal product quality information. All such issues must be investigated to determine root cause and appropriate reporting (often MDR filings) must take place. The company has

⁸ <http://www.accessdata.fda.gov/FDATrack/track-proj?program=cdrh&id=CDRH-OSB-MDEpiNet>

an obligation to look not just at events in isolation but to trend events and look for commonality of issues across product lines. This event trending is a key tool to identify signals of issues and to understand any appropriate corrective action.

Properly implemented, these QSR processes (and related manufacturing and product development and testing systems), are robust tools to identify and analyze product performance. FDA routinely inspects these processes and, in fact, audits of these "CAPA" systems are part of the QSIT inspection system.

5. Inspections

FDA has the authority to inspect any medical device manufacturer. These inspections routinely cover QSR systems, compliant files, complaint investigations, root cause analysis, event trending, product modifications and recall activity. Inspectors have access to all relevant documentation and to individuals responsible for these various activities. Such inspections can be either "routine" or "for cause" if FDA suspects or has knowledge of some product performance issue. A failure or refusal to supply relevant information or documents or supplying false information can be a criminal offense.

6. Product Tracking

Post-market surveillance (and recalls as discussed below) is intended to link products to events and identify specific products. This is no small challenge given the literally billions of devices on the market that are used in a wide variety of settings outside the knowledge or control of the manufacturer by users or

consumers over which FDA has little if any regulatory authority. In addition, multiple devices are used in a single therapeutic setting and are often serving an ancillary role to the more obvious therapy delivery. There may be literally hundreds of devices used in a cardiac surgical procedure.

FDA's unique device identification (UDI) program should significantly improve the agency's ability to track devices and link specific devices to events. The agency is in the process of developing the UDI system as mandated by Congress in 2007.

In addition, FDA can, for implantable and high risk devices, impose specific device tracking requirements under 21 U.S.C. § 360i(e) (FDCA § 519(e)).

7. Reports of Product Modifications or Changes

Under both the PMA and 510(k) systems, companies are also obligated to report to CDRH product modifications made to address field issues (whether safety or effectiveness issues). This process provides CDRH another view into product performance and can trigger inquiries about related products or systems. Product modifications that must be reported include physical changes to the device and also changes in the labeling such as new warnings or instructions for use.

Specific Post-market Systems or Obligations

For certain products, more tailored or specific post-market surveillance may be appropriate. These are in addition to, not in lieu of, the general or universal post-market obligations described

above. CDRH has a wide variety of statutory authorities by which it can impose such tailored post-market surveillance obligations.

1. Conditions of Approval

PMA product approvals include mandatory “conditions of approval” (see 21 C.F.R. § 814.82(a)(2)). These vary between product types but can include enhanced post-market surveillance, post-market testing, increased reporting, patient registries, etc. These post-market obligations can be tailored to the particular needs of the patients and products themselves thus allowing for more focused and relevant post-market surveillance.

2. Special Controls

In an analogous way, Class II products can be subjected to special controls under 21 U.S.C. § 360c(a)(1)(B) (FDCA § 513(a)(1)(B)). These special controls can require any number of post-market obligations including patient registries, dissemination of product use guidelines, post-market surveillance plans, etc. In addition to these specifically enumerated tools, the FDA can mandate “other appropriate actions as the Secretary deems necessary to provide such assurance [of safety and efficacy].”

3. Section 522 Orders

In 1997, Congress added 21 U.S.C. § 360I (FDCA § 522). Under Section 522, FDA may order manufacturers of Class II or Class III products which are implantable products, life sustaining products or products for which a failure

“would be reasonably likely to have serious adverse health consequences” to conduct post-market surveillance studies. These orders can be imposed as part of a PMA (or sPMA) approval or applied to 510(k) products. FDA has the power to review the proposed post-market surveillance plan to ensure that it is adequate and is being implemented by qualified individuals and the power to review compliance to the Section 522 order.

Section 522 orders are in addition to, not in lieu of, other post-market authorities.

4. International Controls and Information

In addition to these U.S. centric obligations, companies are obligated to report to FDA adverse events occurring or reported outside the U.S. and to include adverse event information from non-U.S. sources in many submissions. The various regulatory agencies also have information exchanges such that a product issue in one jurisdiction is reported to regulators in other countries. International or domestic information can trigger field actions in the United States, corrective actions by the manufacturer and detention or refusal of entry of imports.

Recall Overview

FDA has a number of existing statutory mechanisms to address field issues. In a number of cases, these don't use the term “recall” but perform the functions of a recall.

1. Voluntary Recalls

In the event that industry takes a voluntary field action to address a product or regulatory issue, the company is obligated to inform FDA under 21 C.F.R. Part 7

and 21 C.F.R. § 806 within 10 days. The agency oversees the field action and conducts recall effectiveness checks of varying intensity based on the seriousness of the risk.

2. Mandatory Recalls and Notifications

If the company refuses to take action, FDA has a variety of actions it can take generally under 21 USC §360h (FDCA §518). These include the right to mandate a public notification if the device in question “presents an unreasonable risk of substantial harm to the public health” and notification is necessary to eliminate that risk. §518(e) also gives FDA the authority to order a mandatory recall in situations of a risk of serious adverse health consequences.

3. Seizure and Detention Actions

FDA also has the well-established authority to conduct seizure and detention actions pursuant to 21 USC §§331 and 334. In a seizure action, the government can go into the company and into the market place (including distributors and stores) and take physical control of the product to prevent any further movement in interstate commerce. Violation of a seizure order is a standalone criminal violation.

4. Publicity

Under 21 U.S.C. § 375, FDA has the authority to publicize issues or products which present an imminent danger to health or gross consumer deception.

5. Repair, replacement and refund

Section 518(b) gives FDA the authority to order the company to provide repairs or placements of defective products. FDA can also order a monetary refund to consumers. FDA has additional power under court decisions such as *Lane Labs* to order restitution to consumers.

6. Banning and suspension of approvals

FDA also has the authority under FDCA §516 and 515(e) to ban further distribution of products or to suspend (temporarily or permanently) PMA approval.

As can be seen, FDA has substantial statutory authority to take (or mandate) actions to protect consumers from unsafe products in the market. It is hard to imagine some action that FDA should be able to take action relating to an unsafe product in the market for which it does not already have statutory authority.

The existence of such authority is a very different question from whether FDA, industry and physicians are appropriately using or complying with such authority.

Recall Suggestions

There are, however, some ways in which the general recall process under 21 C.F.R. Part 7 and 21 C.F.R. § 806 could, in my opinion, be improved.

First, the term “recall” implies a physical removal or explants. That causes unnecessary patient anxiety and possibly unnecessary explants. It is also inaccurate. While in some cases a physical removal or explants may be the best medical course that is often not the case. Implying that the product should be physically removed can mislead patients. Of course one does not want to

dilute or hide the importance of the field action. Calling it something like a “Safety Alert” while reserving the term “recall” for those situations in which a physical removal is appropriate conveys the seriousness of the situation in an accurate, non-misleading fashion.

Second, I would strongly encourage the agency to immediately classify any recall reported to it so that the field notification can accurately state the seriousness of the situation. Assigning a classification six weeks after the physician notification occurs serves no physician or patient communication purpose and can mislead physicians and patients into thinking that there is a second recall when that is not the case.

Finally, having more objective criteria for classification of recalls would improve the communication value of the classification.

Medical Device Review Decisions – Study Summary

The safety of medical devices is, of course, of prime importance to patients, physicians and other stakeholders. Rather than look at individual events, opinion or anecdote, I am interested in the performance of the system as a whole. It is critical to remember that all devices carry with them some risk.

With the aid of a number of research assistants, I studied the overall safety profile of medical devices approved or cleared by FDA from 2005-2009 by using Class I safety recall data.⁹ This study¹⁰ evaluated Class I (or high risk) recalls of all medical devices, regardless of whether they

⁹ We are currently in the process of analyzing 2010 recall data.

¹⁰ 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, reviewed with FDA.

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:

7. Overall, 510(k) regulated medical devices have an excellent safety profile. Over 99.5%¹¹ of 510(k) submissions assessed during this study period did not result in a Class I safety recall. Over 99.7% of 510(k) submissions did not result in a Class I recall for any reason relevant to the 510(k) premarket system.
8. Products approved through the PMA system also have an excellent safety record. Again, greater than 99.5% of PMA or sPMA submissions do not result in a Class I safety recall during the study period.
9. Very few (less than 9%), 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.
10. The majority (approximately 55%) 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 three 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.
11. A very significant majority (over 90%) of all Class I recalls (including both premarket and post-market issues) are directly related to quality system issues (so-called QSR

¹¹ All percentages have some margin of error given the relatively small data set.

systems¹²). Improved QSR systems will have the greatest effect in reducing the number of Class I recalls.

12. 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 review process should be targeted to demonstrate problems rather than applied in some random, shotgun way. In fact, following the initial public discussion of this data, CDRH has instituted two initiatives – one directed to infusion pumps and the other to AEDs.
13. Finally, one should not confuse classification for premarket review processes with recall classification. These are very different things and serve very different purposes.

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 and am familiar with the numerous issues relating to delays in submission reviews and changing data requirements. I was, however, struck by the belief among some that the 510(k) system did not assess or consider product safety in making clearance decisions and that there was some major issue with the safety of products being cleared by the 510(k). First, it is critical to note that FDA does consider safety when deciding whether to clear a 510(k) submission. Second, some stakeholders were advocating making major changes in the 510(k) system to address presumed safety problems. I was particularly struck by the fact that there was no good, objective data to support or refute the

¹² 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 post-market assessments. See, generally, 21 C.F.R. § 820.

assertion that the 510(k) system needed to be changed because of these presumed safety issues and, if some changes were warranted, the s.

In fact, at an early public meeting held by FDA to discuss making major changes to the 510(k) system, I commented that this was a “ready, fire, aim” exercise in which various interest groups were advocating major changes without any understanding of the actual performance of the system and any issues with the system. It struck me then and now that data, not opinion, should drive policy changes.

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. This study was funded by the private, nonpartisan Kauffman Foundation. I am solely responsible for the study and its results.

Study Methodology

This study assessed the overall safety profile of medical devices approved or cleared by FDA from 2005-2009 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.

Using FDA databases, we identified all Class I recalls posted by FDA on public databases during 2005-2009. 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).

118 unique recalls were 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 one of thirteen reasons for recalls. Generally speaking, these thirteen 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), post-market issues and miscellaneous (counterfeit and “quack” products). We used FDA websites and publicly available information for this coding.

All data was entered into a standard Excel spreadsheet following quality control.

This study must be assessed in light of the following factors¹³:

1. We relied entirely upon publicly available data.
2. 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 in number because of the penalties for non-compliance and the variety of

¹³ We considered other methodologies; including reviewing adverse event reports (generally referred to as Medical Device Reports or MDR reports) and also tried to assess number of products involved in each recall. In these cases, the data is hopelessly inaccurate and incomplete, inaccurately counts actual events as compared to the risk of a malfunction or is not related to the binary decision to approve or not approve the submission.

information sources that would alert FDA and the public to any undisclosed 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. 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 represent a valid safety picture. Class I recalls represent the majority of actual patient risk and it seems that FDA (the entity doing the classification) tends to err in the direction of more serious recall classifications. 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. 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 ten-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.

Study Results and Data

Initially, we looked at the reasons for recalls for these 118 Class I recalls. It must be remembered that all devices carry risk and that Congress has balanced patient access to new technology with premarket processes by creating the standard that there must be “reasonable assurance” of product safety before the product should be marketed. We determined the reason for the recall by examining FDA’s public databases and also reviewing publically 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% of the recalls and had a complete match with the initial determination of the reason for the recall.

The following table shows the number of recalls by regulatory pathway and the reason for recall. Reasons for recall in blue are those related, at least potentially, to premarket review processes. The others are recall reasons that are completely unrelated to any premarket process.

Primary Reason for Recall	PMA	510K	Class 1	Other or Unknown	TOTAL
Manufacturing	6	31	2	1	40
Labeling Error	0	4	0	0	4
Design Issue	6	25	1	0	32
Software Design	1	9	0	0	10
Software Manuf. Failure	0	2	0	0	2
Supplier Issue	2	5	0	0	7
Failure to Identify Clinical Risk	0	0	0	0	0

Failure to Warn/Inadequate Instructions	0	8	0	0	8
Missing Parts	0	0	0	0	0
Sterilization	1	4	2	0	7
Regulatory Violation	0	1	1	0	2
Packaging/Handling	0	0	0	0	0
Other (Counterfeit, Sham)	0	6	0	0	6

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

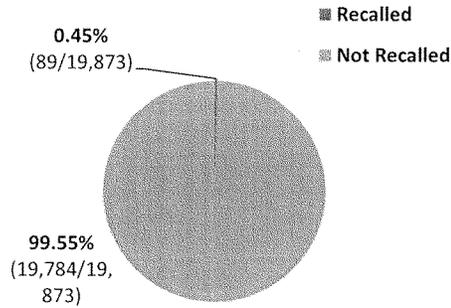
	Total Recalls	Recalls for Pre-Market Issues	Recalled for Post-Market Issues	Recalled for Other Issues	Percent of Recalls to Total Recalls
Class I or u/k	7	1 (14.2%)	6 (85.7%)	0 (0%)	5.9%
510(k)	95	43 (45.3%)	46 (48.4%)	6 (6.3%)	80.5%
PMA	16	7 (43.8%)	9 (56.3%)	0 (0%)	13.56%
TOTAL	118	51	61	6	118

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.

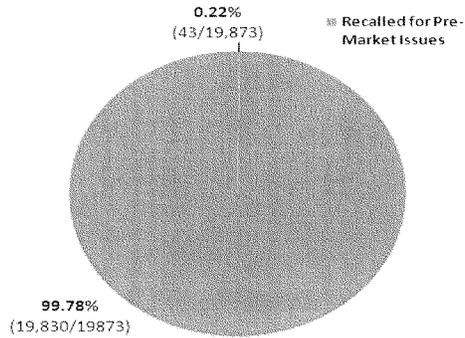
This data shows that CDRH and the submission sponsors have done an admirable job in identifying potential device risks, particularly clinical risks, prior to the approval or clearance decision. These risks can then be explicitly balanced against benefits as part of that premarket decision. Very few, if any, recalls in the device world are related to undiscovered clinical issues.

Based on this data, approximately 99.55% 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% 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% 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)



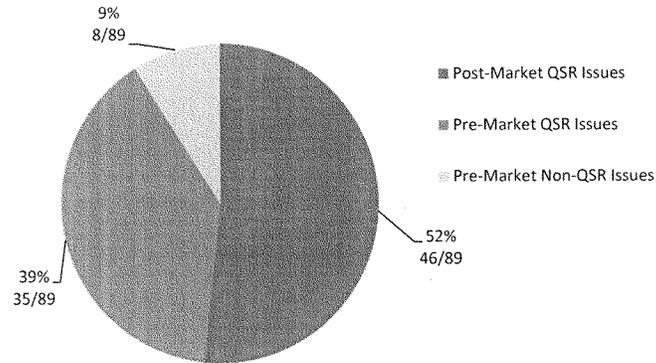
Total 510(k) Recalls for the Last 5 years – Premarket issues



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 Pre-Market 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 post-market issues, not premarket processes, should be the focus to improve patient safety.

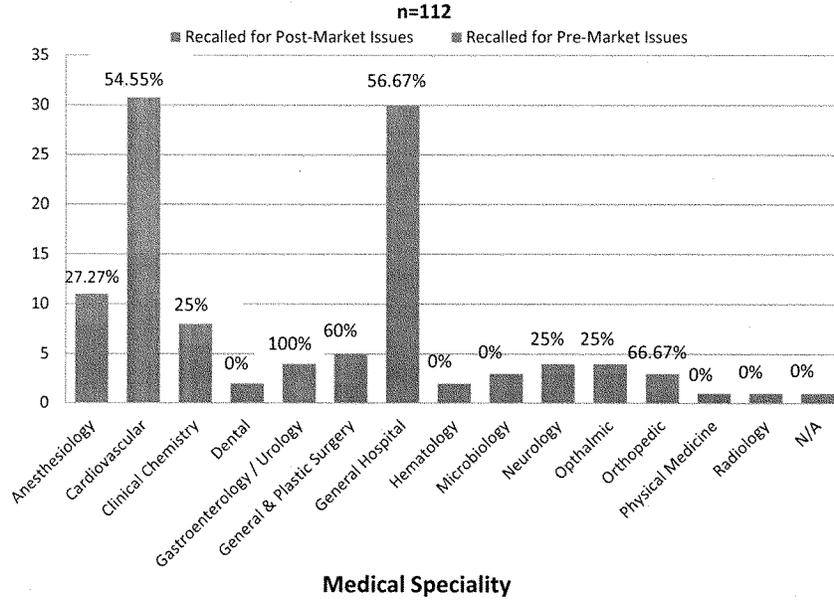
This conclusion is reinforced when we reviewed the role of quality systems in recalls. As shown below, over 90% of all Class I safety recalls are related to quality system issues and not to other factors such as a lack of clinical trials.



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



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

This data also shows remarkably few Class I recalls for a number of product areas, including some product types that have been recently argued demonstrating flaws with the 510(k) system, such as orthopedics, radiology and OB/GYN.

We also assessed the data to see whether implantable products or submissions that went through the third party review process had any concentration of Class I recalls. Our analysis showed that Class I recalls for implantable devices almost exactly matched the expected percentage of recalls and that there were fewer recalls for submissions reviewed under the 510(k) third party review system than might be expected.

Study Conclusion

This study demonstrates that very few 510(k) medical device submissions — less than 0.5% — 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 post-market 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% 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.

Overall Conclusion

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 impact.

FDA also currently has substantial post-market surveillance authority and recall authority. It is difficult to imagine actions that FDA may want to take when faced with a serious public health issue for which it lacks authority. Implementation and compliance by all stakeholders may well be the most fruitful area of focus.

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

Mr. PITTS. The Chair thanks the gentleman and recognizes Dr. Jaffe for 5 minutes for an opening statement.

STATEMENT OF ROSS JAFFE

Mr. JAFFE. Chairman Pitts, Ranking Member Pallone, members of the subcommittee, thank you for the opportunity to testify today. My name is Ross Jaffe. I am a physician trained in internal medicine who for the last 21 years has had the privilege of working to help develop innovative medical technologies.

In my role as a physician and venture capitalist, over the last few years I more and more frequently face a frustrating paradox. On the one hand, we live in a time of incredible innovation in science and medicine that I see embodied in fascinating technologies every day. On the other hand, more and more often I am forced to turn down many of these important medical innovations because our unpredictable regulatory system here in the United States has stretched development time frames and increased capital requirements needed to fund these technologies, precluding adequate investment return for my investors.

It is important to note that our investors are primarily university endowments, foundations and pension funds, which rely on us to generate a positive return on their capital. If we do our jobs well, not only do patients benefit and physicians have access to more innovative medical technologies, high-quality jobs are created, universities can educate more students, foundations can do more good works, and people can retire in greater comfort, a real win-win-win system that supports medical innovation and the U.S. economy.

Colleagues of mine who have testified during previous hearings have described how most medical innovation comes from small venture-backed companies. However, the growing uncertainty with the FDA has dramatically reduced the amount of investment available to fund innovative medical companies. According to data from PriceWaterhouseCoopers, in 2007, 116 early-stage companies raised approximately \$720 million in initial financing. In just 4 short years, that investment amount has dropped by more than 70 percent to just 55 companies raising only \$200 million. To put this in perspective, 2011 saw the lowest level of venture capital investment in medical startups in the last 16 years.

In a recent survey by the National Venture Capital Association, which has been referenced this morning, 42 percent of health care venture firms expect to decrease investment in medical device companies over the next 3 years. In addition, 31 percent of firms expect to shift health care investment and operational focus away from the United States towards Europe and Asia. In both cases, regulatory challenges here in the United States were cited as the primary factor for declining investment and driving investment overseas. Indeed, it is now common for many innovative lifesaving technologies, for example, percutaneous heart valves, to be available for patients in Europe years before they are available to patients here in the United States.

Fortunately, within the last year or so, the FDA leadership including Dr. Shuren has acknowledged how regulation is slowing innovation and driving product development overseas. They have begun internal efforts to improve FDA processes as illustrated by

a series of draft guidance documents released over the past few months.

One notable effort seeks to make explicit FDA considerations and risk-benefit determinations for premarket approval. Under the law, FDA is supposed to assess medical technologies to assure that the probable benefits are greater than the probable risks. Unfortunately, over the past few years, many FDA reviewers appear to be applying a different standard, weighing the probable benefit against any possible risk, which is not the standard in the law. If implemented appropriately, this guidance should make risk-benefit determinations more patient-centric and evidence-based and therefore improve the transparency, consistency and accountability of FDA decision-making, and I was pleased to hear today that that should be moving forward very quickly in the next few months.

Beyond administrative changes under consideration by the FDA, the MDUFA reauthorization being discussed at this hearing will include additional process enhancements as well as needed resources to increase the predictability of the process. However, resources alone are not enough. We also need meaningful operational improvements, not only through MDUFA but also through additional legislation that leads to better application of the least-burdensome principle, streamlining the de novo process and revision of conflict of interest policies to allow more leading experts to sit on FDA advisory panels.

In closing, let me be clear about one thing. We are not asking for increased regulatory predictability, consistency or efficiency at the expense of public safety. Innovation and safety are not a trade-off. It is not an either-or. We absolutely need both. As investors, my colleagues and I pursue medical innovations precisely because they are safer and more effective for patients, preferably when they also can reduce health care costs. We need to work together to assure a regulatory system that supports the timely development of innovative products and therefore enables safer and more effective patient care.

Thank you.

[The prepared statement of Mr. Jaffe follows:]

Written statement of:

Ross Jaffe, M.D.

Versant Ventures

Before the:

U.S. House of Representatives

House Energy and Commerce Committee

Subcommittee on Health

Hearing:

**“Reauthorization of MDUFA: What it Means for Jobs, Innovation and
Patients”**

February 15, 2012

Chairman Pitts, Ranking Member Pallone, and Members of the Subcommittee, thank you for the opportunity to testify today. My name is Ross Jaffe. I am a physician trained in internal medicine who for the last 21 years has had the privilege of working to help develop innovative medical technologies. I am a founder and Managing Director of Versant Ventures, a California-based venture capital firm that focuses on investing in early stage medical device and life science companies to fund and guide their development of medical solutions for some of the most daunting diseases and afflictions facing patients today.

As a physician venture capitalist, I am increasingly facing a frustrating paradox, one that I never thought I would face in 21st century America. On the one hand, we live in a time of incredible opportunity for medical innovation. Our understanding of human physiology and disease grows almost daily. In addition to this new understanding of clinical problems, we have constantly evolving information technology, new and novel materials, and expanding engineering capabilities that enable smart inventors to conceive fascinating new products to solve important clinical problems. With the aging of the population and increasing pressure for healthcare reform, new and better technologies are critical to reduce the costs and improve the quality of healthcare. The potential for innovation in medical technology has never been greater.

On the other hand, as a venture capitalist I am forced to turn down investing in too many promising medical innovations -- technologies that you and I would want access to in order to help our loved ones if they needed them -- because it is difficult to predict how long and how much capital it will take to get a particular innovation approved by the FDA and into patient care. In this day and age of phenomenal medical innovation, regulatory uncertainty is the largest deterrent to venture capitalists bringing potentially valuable new technologies to market.

America currently leads the world in medical innovation through our unique medical device innovation ecosystem which has developed over the last fifty years. Most medical technology innovation comes from small, entrepreneurial companies, often fueled by venture capital, that take on the risk of promising science and, over time, transform ideas and research into critical technologies that advance science in areas of unmet needs for patients. I am sure that you have heard the statistics before: 80 percent of medical device companies have less than 50 employees, and 98 percent of the medical device companies have less than 500 employees.¹ If successful, these companies grow, create jobs, and deliver innovative devices and technologies to medical providers that improve patient care.

It is important to note where venture capitalists get their funding. Our investors are primarily university endowments, foundations, and pension funds. If we do our job well, not only do patients and physicians have access to innovative medical technologies and high-quality jobs are created, but universities can educate more students, foundations can fund more good works, and people can retire in greater comfort. This is an incredible win-win-win system that fuels medical technology innovation – a system which has allowed the United States to be the world leader in medical product development, manufacturing, and exportation.

While this medtech innovation ecosystem has traditionally worked very well, funding of medical technologies has slowed, largely because regulatory pathways are increasingly difficult to predict and unexpected regulatory delays increase the time and capital required to build companies. Increasing time frames and capital needs are causing many venture capital firms to move away from medical device investing, and many traditional investors in venture capital – the university

¹ "Medical Technology and Venture Capital: A Fruitful Yet Fragile Ecosystem," MDMA and NVCA, June 2009, <http://www.medicaldevices.org/node/656>.

endowments, foundations, and pension funds that provide most of the capital to venture investors – are no longer putting their money with venture firms investing in the life sciences space.

This loss of capital has caused a dramatic decline in medical devices start-up funding over the last five years. In 2007, the MoneyTree report by Pricewaterhousecoopers and the National Venture Capital Association (based on data from ThomsonReuters) shows 116 early stage device companies raising approximately \$720 million in initial venture capital. Since then we have seen more than a 60 percent decline in the number of device companies receiving initial venture capital investment and more than a 70 percent decline in the amount of capital invested -- with only 55 new companies raising just under \$200 million in 2011.² This is the lowest level of medical device start up activity since 1996. What makes this data more troubling is that initial start-up company financings are a leading indicator for innovation and job creation in the medical device sector.

When you ask my venture capital colleagues why they are no longer funding new medical device start-ups, whether in formal surveys or informally, the answer is the same: unpredictability in the U.S. regulatory process makes it too risky to commit the capital required to build a company through to success. Since 2005, the time and capital it takes our companies to get a clear definition of the required regulatory path, negotiate pre-clinical and clinical requirements, and obtain an approval decision once a completed application has been submitted have risen dramatically. Small, venture-backed companies typically spend \$500,000 to \$2 million per month to operate as they prepare for clinical trials. A six to twelve month delay in getting to agreement with the FDA staff about a clinical trial design

² NVCA/PWC MoneyTree Survey, "VC Investments Q4 – MoneyTree – National Data", http://nvca.org/index.php?option=com_content&view=article&id=344&Itemid=103

issue, which is not unusual, can result in millions of dollars of extra capital that the company has to raise from investors to get through the approval process and into the market.

In a recent survey that the National Venture Capital Association³ performed, 42 percent of healthcare investors responded that they were decreasing their investment in medical device companies because of the increased time frames to regulatory approval. 61 percent of respondents noted that regulatory challenges with FDA was the primary factor driving their healthcare investment decisions, making this challenge by far the most commonly cited factor. As these investments are disappearing at home, they are moving overseas and into other emerging markets. The NVCA survey found that 31 percent of VC respondents expected to decrease healthcare investment in the U.S. while 44 and 36 percent expected to increase investments in Asia and Europe, respectively. I have included the entire report as an addendum to this testimony, but the message of this and other surveys⁴ is clear: The current regulatory environment is an increasing deterrent to investment in innovative medical technologies.

My venture capital colleagues and I would greatly prefer to have our companies do our development work here in the U.S., but the challenges of our regulatory

³Vital Signs: The Crisis in Investment in the U.S. Medical Innovation and the Imperative of FDA Reform, NVCA and MEDIC, October 2011, http://www.nvca.org/vital_signs_data_slides.pdf

⁴"FDA Impact on US Medical Technology Innovation", Dr. Josh Makower, November 2010, <http://nvcaccess.nvca.org/index.php/topics/public-policy/155-fda-impact-on-innovation-study-out-today.html>;

"Competitiveness and Regulation: The FDA and the Future of America's Biomedical Industry", California Healthcare Institute, February 2011, http://www.chi.org/uploadedFiles/Industry_at_a_glance/Competitiveness_and_Regulation_The_Future_of_America%27s_Biomedical_Industry.pdf;

"Comprehensive Analysis of the 510(k) Process, Northwestern University, May 2011, <http://www.inhealth.org/wtn/Page.asp?PageID=WTN004937>;

environment have compelled us to take most of our initial clinical work to foreign shores. We routinely seek regulatory approval and commercialize new products overseas ahead of seeking U.S. regulatory approval. It is now common for many innovative and often life-saving technologies – such as percutaneous heart valves – to be available to patients in Europe years before they are available here in the U.S. In our Versant portfolio, we have several examples of products approved and first commercialized in Europe -- a novel, leadless cardiac defibrillator; a novel treatment for chronic atrial fibrillation; a retinal implant to restore functional vision in blind patients; and a spinal implant – all approved overseas years before we could obtain regulatory approval and offer them to patients here in the U.S.

Fortunately, within the past year, the FDA has acknowledged how delays, indecision, and inconsistency are slowing innovation and driving product development overseas, and have committed resources to addressing these problems.

One recent guidance document that has the potential to improve the regulatory environment significantly is intended to make explicit the risk-benefit analysis used by FDA staff to make regulatory decisions in each pre-market application. Under the law, FDA is directed to assess medical technologies on the basis of whether the probable benefits outweigh the probable risks from the use of the technologies. Unfortunately, over the past few years many reviewers seem to be applying a different standard that weighs the probable benefits against any potential risk. This departure from the law is one of the key drivers that makes getting to agreement on pre-clinical and clinical requirements more difficult and time consuming. By making the assumptions behind the risk-benefit assessment for a new technology explicit, and documenting them for future reference, adoption of this guidance should improve the dialog between applicants and FDA staff.

While we await the finalization and implementation of this risk-benefit guideline, I am hopeful that this guidance will make a significant improvement in the transparency, consistency and accountability of FDA decision-making.

Beyond the administrative changes under consideration by FDA, I am cautiously optimistic that the user fee package that industry and FDA are developing will have additional process enhancements which will provide patients with timely access to safe and effective products. Medical device innovators simply need greater predictability in the review process if we are to attract future investment and lead the world in medical technology innovation. At the same time, resources alone will not solve FDA's problems. The additional funding needs to be accompanied by real administrative improvements and legislative reforms.

Currently, there are a series of bills before the House that may further improve the FDA situation. Rather than discuss specific bills, I would just highlight the potential value of legislative efforts that reinforce and clarify the "least burdensome" standards; streamline the *de novo* process; and revise conflict of interest guidelines to increase the ability of knowledgeable experts to participate in FDA decisions processes.

Let me be clear about one thing: We are not asking for increased regulatory predictability, consistency, and efficiency at the expense of patient safety. While some insist there is a tradeoff between encouraging innovation and protecting patient safety, the reality is that we need both. We need a regulatory system that is conducive to the timely development of innovative products that result in safer and more effective patient care than existing options. As investors, we pursue medical innovations precisely because they are better for patient care and are safer and more effective, preferably while also reducing overall healthcare costs. Many new

products we back are designed to specifically overcome limitations of existing technology, or to offer clinically valuable new solutions that improve patient care.

The public's health and our national economic competitiveness are compelling enough reasons to recognize the urgency of our challenges, but in the end it is in all of our individual interests to improve the transparency, predictability, consistency, efficiency, and effectiveness of the FDA. I am in an unusual role where I invest in innovative medical technologies which, I hope, I or my loved ones – or you and your loved ones – never have to use. But if we or any of our family or friends ever needs one of those technologies, we will be extremely grateful that it was developed, approved, and is available here in the United States. Getting the FDA regulatory system right so that it achieves its dual goals of assuring the safety and effectiveness of medical technology as well as encouraging innovation is of critical value to each of us and those we love.

In closing, I would like to reiterate just how fragile the U.S. medical technology ecosystem is, primarily as a result of the regulatory uncertainty at FDA. If the U.S. is to maintain our global leadership in medical technology innovation and our patients are to have timely access to the safest and most effective therapies available, Congress, FDA, industry and the medical community must work together on meaningful reforms to restore predictability, reasonableness and transparency to the premarket review process.

Thank you.

Addendum



Summary

A 2011 study found that U.S. venture capitalists have been and will continue to:

- **Decrease their investment in biotechnology and medical device start-ups**
- **Reduce their concentration in critical therapeutic areas, and**
- **Shift focus away from the United States towards Europe and Asia**

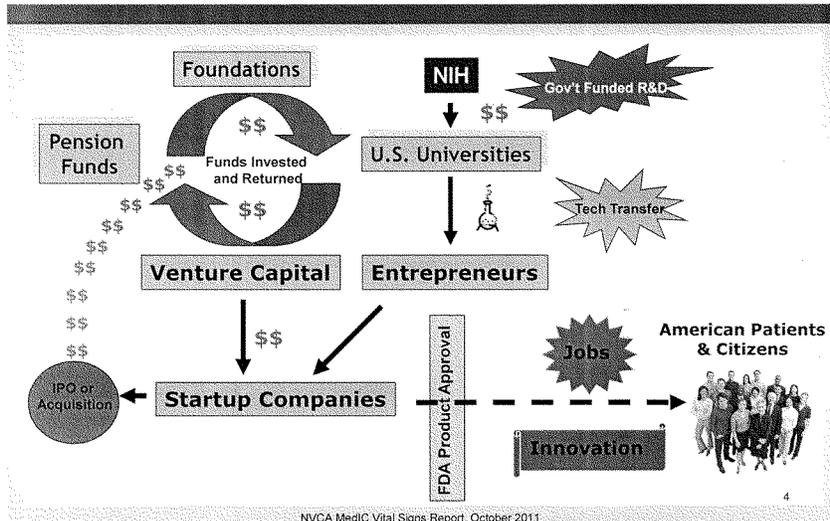
FDA regulatory challenges were identified as having the highest impact on these investment decisions.

We must act now or lose our leadership position in medical innovation, job creation and access to life-saving treatments in the United States.

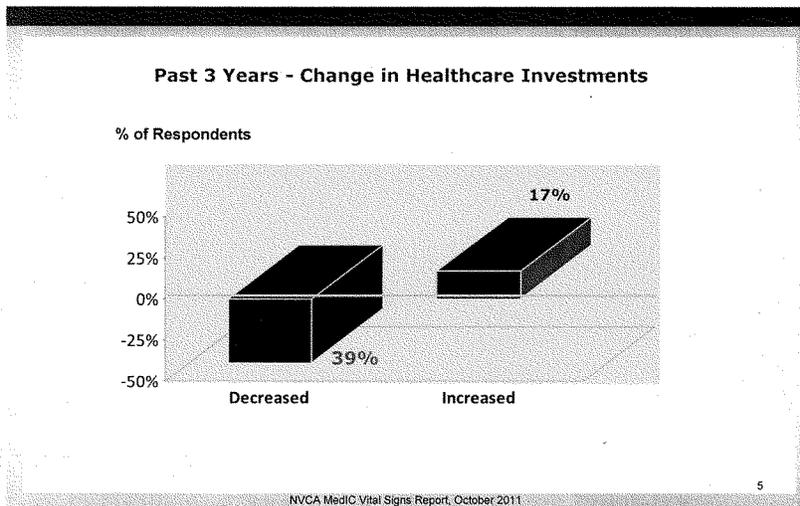
Study Methodology

- **Online survey conducted July–September 2011**
- **Sent to 259 NVCA member firms investing in the healthcare sectors**
- **156 firm responses = 60% response rate = 92% of NVCA invested capital (2008-2010)**
- **Survey respondents accounted for \$10 billion of VC investment in healthcare companies in the past 3 years.**

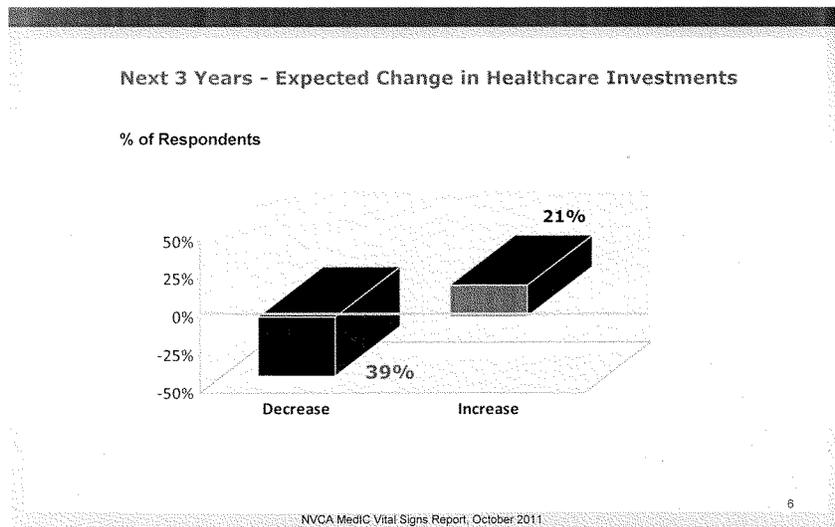
The Cycle of Innovation



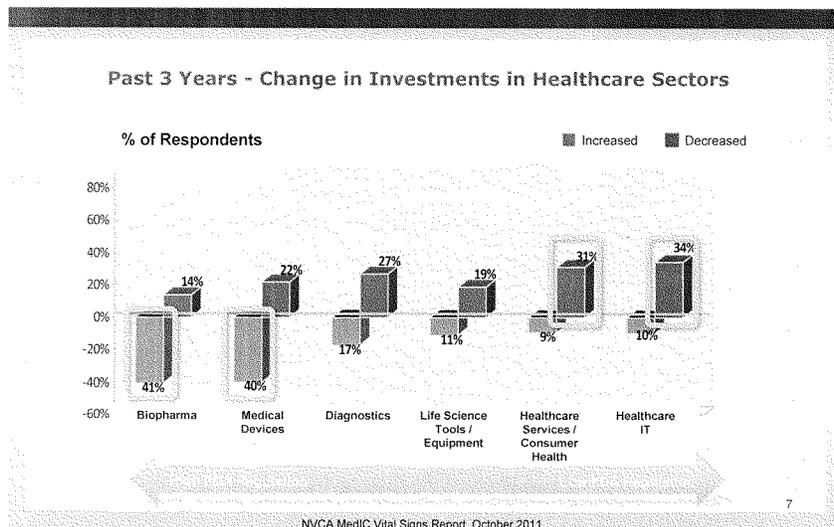
39% of VC firms reported decreases in their healthcare investment in the past 3 years.



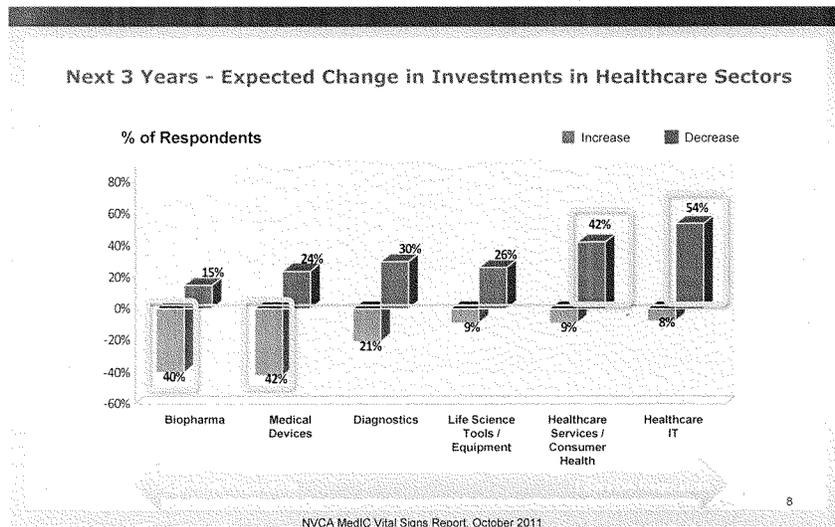
Nearly twice as many VC firms expect to decrease their healthcare investment in the next 3 years.



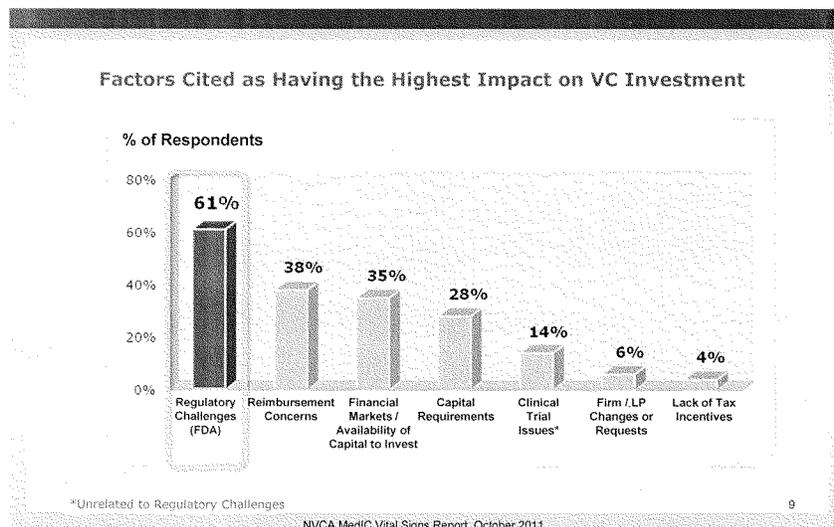
Within healthcare, venture investment has already shifted away from Biopharma and Medical Devices.



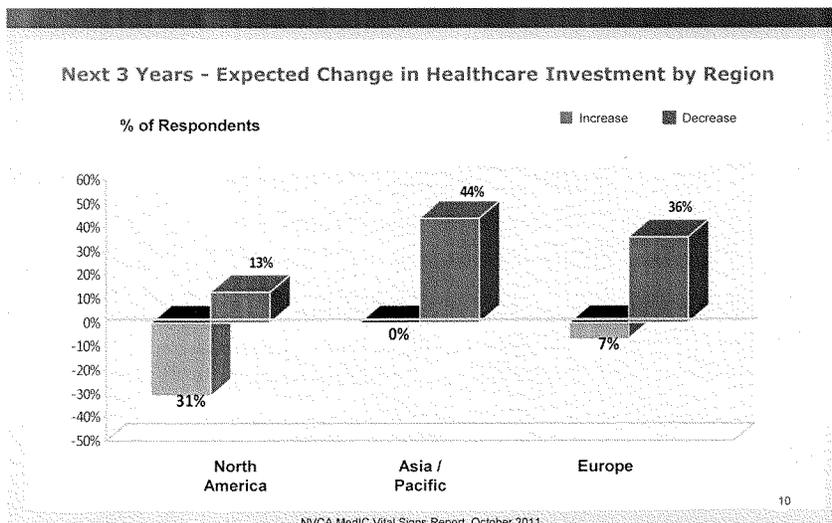
VC investment in Biopharma and Medical Devices is expected to continue to suffer.



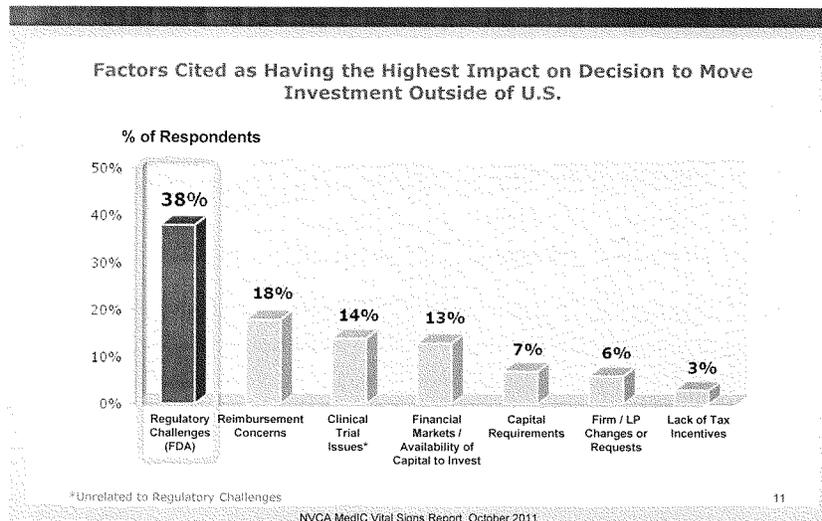
FDA regulatory challenges are having the greatest impact on VC investment decisions.



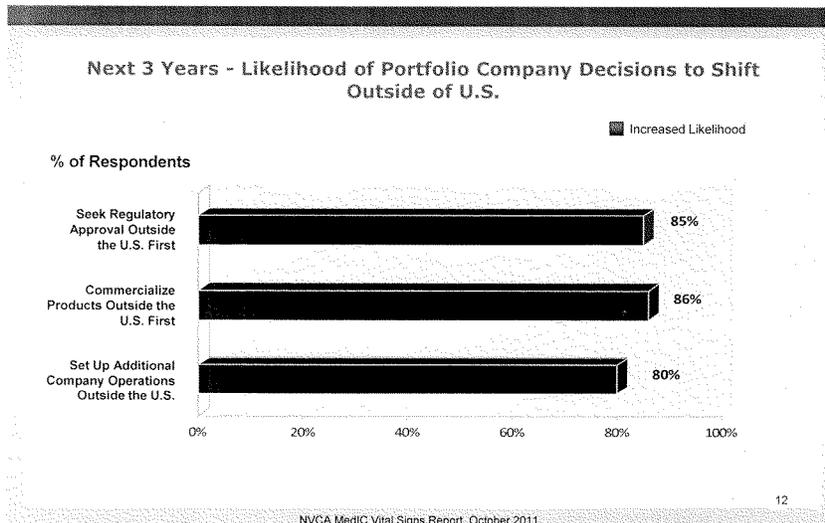
VCs expect to decrease healthcare investment in the U.S. in favor of Asia and Europe.



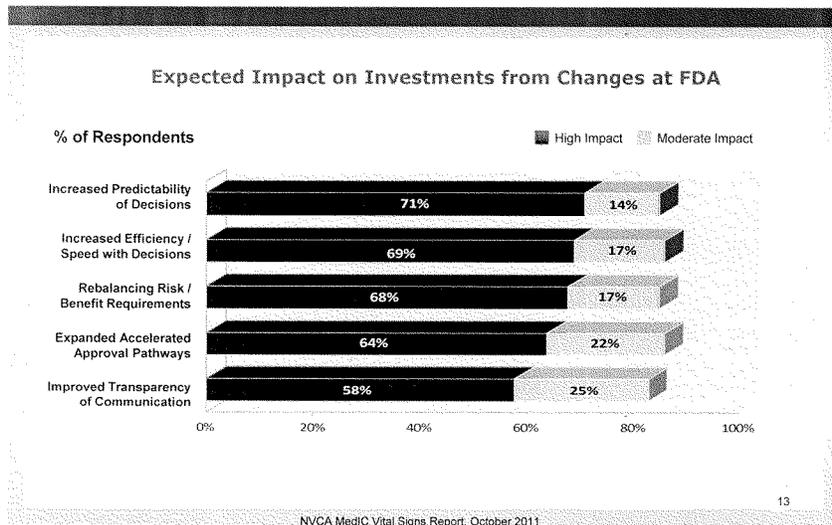
FDA regulatory challenges have the highest impact on VC firm decisions to shift investment overseas.



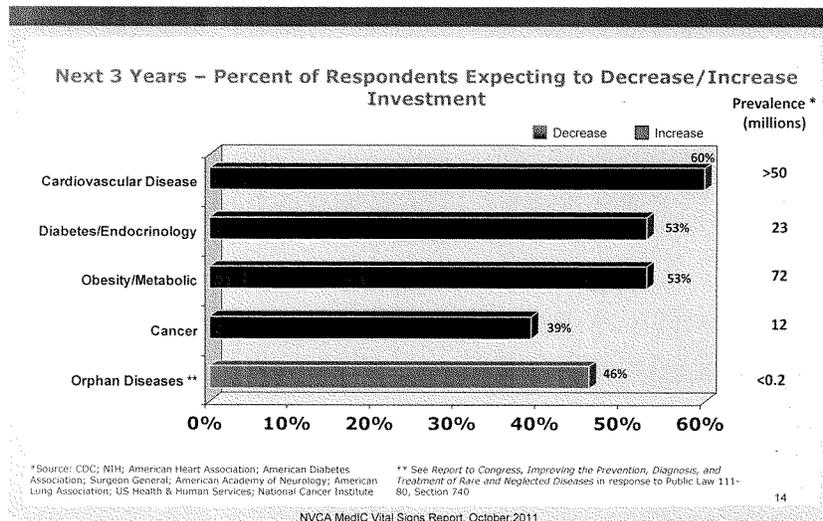
VC-backed companies are expected to increase operations outside the U.S.



Meaningful FDA reform is critical to reversing these trends.



Significant investment decreases in highly prevalent diseases with increases in orphan diseases expected.



Implications

If the current situation is left unaddressed, the implications to U.S. patients and the economy are significant:

- **Many promising medical therapies and technologies will not be funded and therefore will not reach the patients that need them.**
- **Those that are funded may not be brought to market in the United States first, or at all.**
- **An estimated funding loss of half a billion dollars over the next three years will cost America jobs at a time when we desperately need employment growth.**
- **The U.S. leadership position in medical innovation will be placed in further danger and economic growth will suffer.**

Call To Action

MedIC priorities include the following:

- **Rebalancing benefit-risk assessments in the drug and device approval processes to appropriately reflect the value of new therapies to patients in need;**
- **Expanding the accelerated approval pathway into a progressive approval system for drugs, diagnostics and medical devices;**
- **Ensuring conflict-of-interest policies are not hindering patient access to new treatments; and**
- **Ensuring FDA is well resourced and endowed with state-of-the-art scientific tools, clinical input, processes and procedures**

Mr. PITTS. The Chair thanks the gentleman, and Dr. Kesselheim, you are recognized for 5 minutes for an opening statement.

STATEMENT OF AARON S. KESSELHEIM

Mr. KESSELHEIM. Chairman Pitts, Ranking Member Pallone and members of the Subcommittee on Health, thank you very much for the chance to share my thoughts with you today about the regulation of medical devices. I am Assistant Professor of Medicine at Brigham and Women's Hospital and Harvard Medical School in the Division of Pharmacoepidemiology and Pharmacoeconomics.

One essential question being addressed in today's hearing is whether requiring the FDA to loosen its standards for medical device regulation would encourage innovation and help patients. Some offer the European Union as a model because high-risk devices generally make it to market sooner and more easily there. The main reason is that E.U. device approval usually only requires studies in small numbers of patients showing the device appears to be safe and performs as expected. Such evidence could include demonstrating that a new stent expands appropriately in the coronary artery. There are no requirements in the E.U. that companies demonstrate that their devices benefit patients. By contrast, the FDA requires more robust evidence of safety and effectiveness for many of these implantable or high-risk devices. Thus, approval for the same coronary stent might require showing fewer cardiac events or the need for another invasive procedure.

The current E.U. system for approving medical devices recalls the U.S. prescription drug market before 1962 when the FDA only required limited studies of purity or safety before a drug could be marketed, but after the thalidomide public health crisis, legislation gave the FDA authority to compel reasonable safety and efficacy data before a new drug could be sold. This reform was almost derailed by accusations that it would threaten the viability of the pharmaceutical industry, but what happened instead was that the U.S. pharmaceutical industry grew into one of the most profitable in the world. Why? FDA validation meant that physicians could prescribe drugs confident that a neutral expert body had certified their efficacy and safety. Requiring companies to demonstrate that their products were effective also created incentives for manufacturers to impose a higher standard on their product evaluation, leading to their developing some of the most important medications we have, and today, nobody seriously advocates returning to a time when we essentially let any drug on the market and then figure out afterwards which ones were useful or dangerous based on haphazard patient experience.

But this is indeed what is happening in the E.U. for approval of even the highest-risk medical devices. For example, the French company PIP is now under criminal investigation for using non-medical-grade silicone in breast implants. PIP's silicone implants were never submitted for marketing in the United States. Or take the case of the PleuraSeal lung sealant system, which was approved in the E.U. in 2007 to treat air leaks after pulmonary resection surgery. A clinical study conducted as part of an FDA pre-market approval application showed in 2011 that it had triple the rate of adverse events compared to standard techniques. As a re-

sult, the device was rejected by the FDA and a worldwide recall was initiated. Or the CorCap cardiac support device, a harness for patients with heart failure to improve their cardiac output. The device was granted E.U. approval in 2000 but a pivotal U.S. premarket trial conducted by 2004 showed no change in mortality, had numerous irregularities including missing data for about 40 percent of patients, and it was not approved by the FDA. Thus, the FDA requirement for premarket testing helped identify unsafe or ineffective devices or prevented companies from introducing sub-standard products, sparing U.S. patients from being exposed to them.

But the FDA approval process is not perfect. Rigorous premarket testing cannot identify all safety concerns, and the FDA must use a least-burdensome approach in working with manufacturers to decide what clinical data will be required. In addition, experts have identified the clearance of high-risk devices through pathways designed for low-risk devices as an important inconsistency between the FDA's mandate and practice. Thus, patient safety also requires enhanced postmarket testing of new devices.

In the drug world, one of the lessons from the Vioxx episode was that safety surveillance cannot be dependent on the receipt of adverse-event reports alone. More active postmarket device surveillance would include development of national registries with mandatory reporting of all implanted devices along with automatic review of clinical experiences for certain devices after a period of years to ensure that they are producing the expected benefits. With today's advances in informatics and epidemiological surveillance techniques, this would not be problematic in terms of either cost or regulatory burden.

In summary, patients and physicians do not want access to any latest drug or device. Rather, they want access to products that have meaningful clinical benefits with reasonable assurance of safety. The Medical Device User Fee Act should bolster this essential role of the FDA by increasing funding for inspections of manufacturers, hiring of more reviewers or safety experts, and by providing for more rigorous postmarket surveillance so that devices proven to be effective and safe can be used confidently by physicians for the benefit of their patients.

Thank you very much.

[The prepared statement of Mr. Kesselheim follows:]

HARVARD MEDICAL SCHOOL

Aaron S. Kesselheim, M.D., J.D., M.P.H.
Assistant Professor of Medicine



BRIGHAM AND WOMEN'S HOSPITAL

*Division of Pharmacoepidemiology
and Pharmacoeconomics*



Testimony of:

Aaron S. Kesselheim, M.D., J.D.

Assistant Professor of Medicine, Harvard Medical School

Division of Pharmacoepidemiology and Pharmacoeconomics

Brigham and Women's Hospital

Boston, MA

**United States House of Representatives
Committee on Energy and Commerce
Subcommittee on Health
February 15, 2012
Washington, D.C.**

HARVARD MEDICAL SCHOOL

Aaron S. Kesselheim, M.D., J.D., M.P.H.
Assistant Professor of Medicine

BRIGHAM AND WOMEN'S HOSPITAL

Division of Pharmacoepidemiology
and Pharmacoeconomics**Summary of major points**

- Approval of high-risk medical devices by the FDA can take longer than in the European Union when the FDA requires proof of safety and efficacy for clinical outcomes. In the EU devices, are usually tested to ensure safety and basic performance.
- The EU device approval framework resembles the pre-1962 US prescription drug market, when the FDA did not require companies to show that the drug had any clinical benefit for patients, so whether a drug worked was determined based on haphazard patient experience after the product was marketed.
- Legislation in 1962 requiring proof of efficacy for new prescription drugs helped spur the expansion of the pharmaceutical industry because physicians and patients could be more confident in drugs validated by the FDA, and companies were incentivized to develop useful new drugs to meet those standards.
- There are numerous examples of European patients being exposed to high risk devices later found to be ineffective, unsafe, or both, after clinical testing required by the FDA. US patients were spared from these bad outcomes.
- Even the most rigorous premarket testing by the FDA cannot identify all potential safety concerns, so active post-market surveillance of high-risk devices is essential.
- Patients and physicians want access to products that provide meaningful clinical benefits with a reasonable assurance of safety, and MDUFA should bolster the FDA's ability to meet these expectations by increasing funding for its essential functions and giving the FDA greater latitude to require and oversee rigorous post-market surveillance.

HARVARD MEDICAL SCHOOL

Aaron S. Kesselheim, M.D., J.D., M.P.H.
Assistant Professor of Medicine

BRIGHAM AND WOMEN'S HOSPITAL

Division of Pharmacoepidemiology
and Pharmacoeconomics**Chairman Pitts, Ranking Member Pallone, and Members of the Subcommittee on Health:**

My name is Aaron Kesselheim. I am an internal medicine physician in the Division of Pharmacoepidemiology and Pharmacoeconomics at Brigham & Women's Hospital in Boston and an Assistant Professor of Medicine at Harvard Medical School. I am also an attorney trained in patent law. My research focuses on legal and regulatory issues that affect use of prescription drugs and devices. It is an honor to have the opportunity to share my thoughts with you about the regulation of medical devices.

The essential question being addressed in today's hearing is whether requiring the FDA to loosen its standards for medical device approval and regulation would encourage innovation and provide patients with easier access to the latest technology. Some manufacturers, policymakers, and physicians offer the European Union as a model, providing statistics showing that high-risk devices generally make it to the market sooner and more easily in the EU.

The main reason for this disparity is that the EU device approval organizations, called Notified Bodies, usually require only studies in small numbers of patients showing the device appears to be safe and performs as expected. For example, such evidence could include demonstrating that a new stent expands appropriately in the coronary artery, or that a device for a left atrial appendage exclusion can be deployed as intended. There are no requirements in the EU that companies demonstrate that their devices benefit patients. By contrast, the FDA requires more robust evidence of safety and effectiveness for many of these implantable or high-risk devices. Thus, approval for this same coronary stent might require showing that it reduced cardiac events such as heart attack or the need for another invasive cardiac procedure. FDA

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approval of the left atrial appendage exclusion might require demonstration that the device not only be safely implanted, but reduces risk of stroke—the main reason for its use in the first place.

The current EU system for approving medical devices recalls the US prescription drug market before 1962, when the FDA only required limited studies of purity or safety before a drug could be marketed, and did not require companies to show that the drug had any real clinical benefit for patients. But after the thalidomide public health crisis, legislation gave the FDA authority to compel reasonable efficacy and safety data before a new drug could be sold. This reform was almost derailed by accusations that it would threaten the viability of the pharmaceutical industry.¹ But what happened instead was that the US pharmaceutical industry grew over the next decades into one of the most profitable in the world.

Why? A key contributor was the validation that the FDA now provided. Physicians could prescribe and patients could use drugs approved after 1962 with the confidence that a neutral, expert body had certified their efficacy and safety. Requiring companies to demonstrate that their products were effective also created an incentive for manufacturers to subject their product evaluation to a higher standard, leading to their developing some of the most important medications on the market worldwide. Today, no reasonable policymaker or drug manufacturer advocates returning the US prescription drug market to a time when we essentially let any product on the market and then figured out afterwards which ones were useful or dangerous based on haphazard patient experience.

But this is indeed what is happening now in the EU for approval of even the highest-risk medical devices. For example, the French company PIP is now under criminal investigation for using nonmedical grade silicone in its breast implants, and tens of thousands of women in the EU

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have been advised to have their implants removed.² PIP's silicone breast implants were never submitted or approved for marketing in the US. In an article published online yesterday by the New England Journal of Medicine, Daniel Kramer, Steve Xu and I describe some other cases in which EU patients were exposed to devices later shown in clinical trials to be ineffective, to cause substantial harm, or both, including³:

- The PleuraSeal lung sealant system, which was developed for the treatment of air leaks after pulmonary resection surgery. The PleuraSeal technology was approved in the EU in 2007. However, a clinical study conducted as part of an FDA premarket approval application showed in 2011 that the new technology had triple the rate of adverse events compared to standard techniques used to seal surgical incisions. As a result, the device was rejected by the FDA, and on the basis of these data, a worldwide recall was initiated.⁴
- The Acorn CorCap cardiac support device, a harness for patients with heart failure to improve their cardiac output. The device was granted EU approval in 2000, but subject to a pivotal premarket trial by the FDA. The approximately 300-person trial, completed by 2004, showed no change in mortality, and had numerous irregularities, including missing data for about 40% of patients. It was not approved by FDA.⁵

In these cases, FDA-required premarket testing helped identify unsafe or ineffective devices. But as more recent public health crises in the drug and device markets have shown,^{6 7 8} the FDA approval process is not perfect. Even the most rigorous premarket testing cannot identify all potential safety concerns, and the FDA must use a "least burdensome" approach in

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working with manufacturers to decide what clinical data will be required, which places statutory limits on the extent of premarket device testing. The clinical trials submitted to FDA to support approved devices do not always use high quality methods, such as blinding, randomization, or robust endpoint definition.^{9 10} In addition, other experts have identified clearance of high-risk devices through pathways designed for lower-risk devices as an important inconsistency between the FDA's mandate and its practice;¹¹ the FDA is currently working to correct these situations.¹²

Thus, patient safety also mandates enhanced post-market testing of new devices. In the drug world, one of the lessons from the Vioxx episode was that safety surveillance cannot be dependent on the receipt of adverse event reports alone.¹³ More active post-market device surveillance could include development of national registries with mandatory reporting of all implanted devices, along with automatic review of clinical experiences with certain devices after a period of years to ensure that they are producing the expected benefits. With today's advanced informatics and epidemiological surveillance techniques, this would not be a problematic requirement in terms of either cost or regulatory burden.

In summary, patients and physicians do not want access to *any* latest drug or device; rather, they want access to products that provide meaningful clinical benefits with a reasonable assurance of safety. This is what FDA approval ideally provides. Congress should use the Medical Device User Fee Act to bolster this essential role of the FDA—for example, by increasing funding for better inspections of manufacturers, hiring of more reviewers or safety experts, and by providing for more rigorous post-market surveillance—so that devices proven to be effective and safe can be used confidently by physicians for the benefit of their patients.

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Mr. PITTS. The Chair thanks the gentleman, and Dr. Sedrakyan, you are recognized for 5 minutes for an opening statement.

STATEMENT OF ART SEDRAKYAN

Mr. SEDRAKYAN. Thank you very much, Chairman Pitts and Ranking Member Pallone and members of the subcommittee. It is a pleasure to talk today. I am Art Sedrakyan. I am an Associate Professor at Weill Cornell Medical College, and I am directing the Patient-Centered Comparative Effectiveness Research Program that is focusing on safety and effectiveness of devices. In my career, I have been exposed to regulatory, academic and manufacturing perspectives.

In the past decade, we have seen a lot of groundbreaking devices that will change the practice of medicine. However, at the same time, we have seen a number of high-profile failures of approved medical devices. Many of these failures occurred through these pathways which was called substantial equivalency pathway, which was 510(k) pathway.

The mere presence of this pathway creates an environment that is making people prone to committing errors. The absence of funding for robust postmarket surveillance is an even more important issue that we need to consider. The Centers for Devices and Radiological Health recognized the limitations of postmarket surveillance infrastructure today and they set up a program called Medical Device Epidemiology Network, and it also created a new entity that will look for a specific example, an orthopedic device. It is called International Consortium of Orthopedic Registries that is planning to bring together 15-plus nations and registries from around the world to create an infrastructure that will enhance postmarket surveillance in the area of orthopedic devices. However, there is limited funding to sustain and replicate this effort in many other areas.

The absence of robust postmarket infrastructure system, in the absence of that, we need to make only gradual adjustment to the balance of pre- and postmarket evaluation. It is important for us to build these large comprehensive registries and registry consortia and also advance the registry science. The process will be through evidence-based innovation and will protect manufacturers as well. Only after we build this strong postmarket surveillance infrastructure will we accumulate evidence of device performance in a variety of device performance in a real-world setting. We can make those adjustments at the premarket threshold.

Let me discuss the issue that shows the limitations for both premarket and postmarket infrastructure and the investment we have to make to ensure that we don't get disasters in the future. There are over 270,000 hip replacement devices used in the country, and this is a very safe operation. There are some devices that are very successful and have 95 percent success rate over a 10-year period. Even in this environment where there are very successful devices on the market, through the 510(k) pathway new devices were introduced, so-called metal-on-metal devices, and a specific example is the ASR device. The device has been approved through the path of substantial equivalency and used a predicate device of the same company that if you look closely does not really resemble the origi-

nal predicate device. It has undergone substantial transformation. Over the iterative cycle, I was able to—these products entered the market because you could—that if you use one predicate as a predicate for another device and then so forth encourages vicious cycle for bringing device that might be dissimilar to the previous device that has been approved.

Without any evidence, these metal-on-metal devices were quickly adopted by surgeons and registries around the world reported really disastrous outcomes with this particular implant. DePuy recalled 93,000 of these devices out of the market, and the evidence has been summarized in our paper and also well covered by Barry Meyer at New York Times. Interestingly, there would be more than 50,000 patients that will undergo this serious revision surgery in the next 10 years, and this is going to cost American taxpayers billions of dollars of additional costs, and this has—I am not aware of any discussion between CMS and manufacturers to cover side effects related to faulty medical products.

So I have some graphic pictures in my testimony that show that these revision surgeries that are happening are not really trivial problems. People have substantial suffering related to these procedures.

I have to also note that even though European registries were the first and Australian registries were the first to see these problems, they are not necessarily the best registries that we have today in the world and we should build much more robust infrastructure system in this country and sometimes multinational infrastructure to be able to prevent this happening in the future, and one of the most important ways that we can do that is through public-private partnership, and a public-private partnership that can be led by FDA and involve stakeholders in partnership with manufacturers and insurers.

Thank you very much.

[The prepared statement of Mr. Sedrakyan follows:]

TESTIMONY

OF

Art Sedrakyan, MD, PhD

Associate Professor,

Director, Patient-Centered Comparative Effectiveness Program

Weill Cornell Medical College and New York Presbyterian Hospital

ON

**'REAUTHORIZATION OF MDUFA: WHAT IT MEANS FOR JOBS, INNOVATION AND
PATIENTS'**

BEFORE THE COMMITTEE ON ENERGY AND COMMERCE

SUBCOMMITTEE ON HEALTH

UNITED STATES HOUSE OF REPRESENTATIVES

February 15, 2012

SUMMARY OF THE TESTIMONY

- Many innovative and groundbreaking medical devices entered into the healthcare market in the past 20 years offering new diagnostic and therapeutic options to patients and clinicians
- However, there is also evidence of substantial limitations in the current pathway for regulatory approval. The low threshold of approval led to adoption of inferior devices that failed with disastrous consequences for the health and well being of Americans
- The metal on metal implants (e.g. DePuy ASR device) are bright examples of problem with 510(k) regulatory pathway that allows approval of devices based on 'substantial equivalency' when they are not. The failure of ASR device and emerging evidence of failure of other metal on metal devices has serious consequences for the public health. Tens of thousands of additional patients are expected to undergo complicated and costly major surgeries with high chance of complications and disability. In addition, these failures will cost billions of dollars to American taxpayers over the next 10 years
- The Institute of Medicine recommended elimination of 510(k) pathway. While complete elimination might not be possible it must undergo complete transformation with changes such as; (1) considered only in clinical settings where there is a room for substantial improvement in health outcomes, (2) ideally not applied to implants unless it is applied in limited group of innovative devices to correct their well known limitations, (3) there should be thorough pre-clinical testing in all circumstances
- The ASR and metal on metal examples in general show that availability of some registry data alone as a post-market infrastructure is not a substitute for faulty pre-market approval. The failures sometimes take long time to develop and large number of faulty products (e.g. implants) enter into the market with consequences for public health and well being of Americans. The ASR evidence also illustrates often more serious limitations of European regulatory process that often approves devices without any clinical evidence. In some instances there are good quality European registries jointly funded by the governments, manufacturers and physicians that can help reveal safety concerns early. However, they have limitation of their own and can only function in country specific health delivery environment
- A robust post-market infrastructure can certainly help prevent disasters or remove failing devices out of the market expeditiously. The post-market infrastructure is currently weak and needs very substantial funding. Device registries seem to be the best ways to build the post-market infrastructure. However, the registries that we have in the US today might not be suitable for building post-market infrastructure unless they provide FDA access to data, have detailed device information and based on mandatory reporting of device use and outcomes. In most instances it is more efficient to empower and provide funds to FDA to initiate registries or consortia of registries through Public Private Partnership (PPP) including participation of manufacturers, payers and hospitals. One example of this potential is the International Consortium of orthopedic Registries (ICOR) initiated by FDA. The PPPs led by FDA might be the best way to match or advance the success story of some well known European or Australian registries that are hailed as models for post-market evaluations
- We need only gradual change in pre vs post market balance and it needs to be linked to the process of building a robust post-market infrastructure/advancement of registry science. This process will ensure evidence based innovation. Only after we build a strong post-market infrastructure, accumulate evidence on device performance in real world settings we can provide recommendations on how to adjust the threshold for pre-market approval

Chairman Pitts, Ranking Member Pallone, and members of the subcommittee. I would like to thank you for the opportunity to speak today on 'reauthorization of MDUFA: what it means for jobs, innovation and patients'. Its an honor to provide this testimony today.

I am Art Sedrakyan, Associate Professor at Weill Cornell Medical College and Director of Patient-centered Comparative Research Program that focuses on safety and effectiveness of medical devices and procedures used in orthopedics and cardiovascular care; two most serious and costly public health settings in the country. I devoted my career to advancing device and surgery safety and effectiveness assessment and in the past 14 years had a chance to get exposed to worldwide academic, regulatory and manufacturing perspectives.

The FDA plays a key role in protecting the health and safety of Americans and the mission of the FDA Center for Devices and Radiological Health (CDRH) is to ensure the safety and effectiveness of medical devices.

In the past decade medical device market have been steadily increasing and became substantial portion of nation's healthcare expenditures. The devices become smaller and smarter and many innovative and groundbreaking medical devices entered into the healthcare market offering new diagnostic and therapeutic options to patients and clinicians. However, we also witnessed number of recent high profile failures of approved devices with disastrous consequences for the health and well being of Americans. While FDA leadership and tireless employees do their best to protect Americans, the mere presence of outdated regulatory pathways (low threshold) and legal loopholes associated with it create an environment that make them vulnerable to errors (overworked and understaffed), particularly when external pressures are exerted. The absence of funding for robust post-market device evaluation infrastructure is another and possibly even more important gap that is at least partially related to these failures.

Briefly about device approval: Based on the complexity and intended use the FDA determines the type and the depth of the premarket data necessary for approval. Hence devices are classified into three regulatory classes. Class I devices such as bandages, gloves or surgical instruments present minimal potential for harm to the patient and no data is required. Class II devices such as infusion pumps or ultrasound machines require special controls/standards and sometimes require clinical testing. Finally, devices with the highest level of risk are categorized as class III and include implants such as metal on metal hip prostheses, hip resurfacing systems or coronary stents). The effectiveness and safety of class III devices have to be based on a valid scientific evidence defined as *'evidence from well controlled investigations, partially controlled studies, studies and objective trials without matched controls, well documented case histories, by qualified experts, and reports of significant human experience from a marketed device'*. As you can see this is rather wide definition which allows the use of both well known pathways for regulatory approval: the Pre-market approval(PMA) and so called 'substantial equivalency' path commonly known as 510(k) pathway. While the PMA mechanism requires valid scientific evidence based clinical studies that establish the safety and effectiveness, the 510(k) path only requires that sponsor demonstrate that the device is 'substantially equivalent' to a device on the market which is called a 'predicate' device. The definition of 'equivalency' is based on intended use and technological characteristics hence open to many interpretations. Moreover, once one the market the new device can serve as a 'predicate' for another device and create vicious iterative cycle that can lead to a situation that the new device is very different than the earlier 'predicate' devices and approved without any clinical evidence or testing.

Let me support my statements based on the well known example of metal on metal hip replacement devices with a particular emphasis on DePuy ASR device. There are over 270,000 hip replacements performed in the country. While hip replacement is a very successful operation and addresses a great public health burden, some patients require revision surgery within 10 years to replace the implant due

to dislocation, wear, instability, loosening, or other mechanical failures. The bearing/articulating surface is designed to endure the contact stress and naturally is one of the key design factors to reduce the chance of revision. Hip implants with metal femoral heads with polyethylene cups were used as articulating surfaces with low revision occurrence. For example, the risk of revision in Sweden is about 5% at 10 years. On the other hand, metal on metal devices were re-introduced into the market to further reduce implant wear and subsequently the time to revision surgery. They also allow use of larger femoral heads (>32 mm vs. < 32 mm) that supposedly reduces the risk of dislocation. These devices were quickly adopted by surgeons and often used even in the elderly; one out of three elderly patients undergoing hip surgery received metal-on-metal hip implant.

These devices are approved using 510(k) path for a joint replacement despite being implantable devices. An outstanding example is the DePuy ASR metal on metal device that has been approved in August 2005 based on a 'predicate' large size Depuy 'Pinnacle' metal on metal device. When reviewing these two designs the only similarity seems to be the metal on metal bearing. The devices are otherwise not similar as evidenced by monoblock vs modular design, metal liner and neck combinations or positioning of the metal head in the socket/shell that might lead to much higher wear of the implant (Figure 1). Interestingly the ASR device was designed with the aim to allow more mobility and reduced wear.

In late 2010 United Kingdom regulatory agency (MHRA) alerted the public about severe cases of metallosis (accumulation of metal ions in the tissues) related to metal ion release from the implants. The information came from the National Joint Registry (NJR) of England and Wales. The Australian National Registry of joint implants also reported unacceptably higher implant revision occurrence related to ASR and subsequently all metal on metal implants larger than 32mm size. Furthermore, DePuy recalled over 93,000 ASR implants in August 2010. The implant recall and suffering of patients received widespread coverage in the NY Times and the scientific evidence related to metal on metal as well as other hip bearings has been summarized in our British Medical Journal (BMJ) publication. Based on the estimates

of ASR failure as well as failure rate related to other metal on metal implants we estimate that more than 50,000 American patients will undergo additional revision surgeries in the next decade. Half of the patients are elderly and covered by Medicare. The costs for taxpayers are likely to exceed billions of dollars. Aside from costs there are serious consequences for the health and well being of American patients that are yet to be fully investigated. The Figures 2-6 show that revision surgery and local adverse events suffered by patients are not trivial. These figures show only local tissue, muscle, bone death and fluid accumulation. Systemic effects of elevated metal ion levels related to metal on metal implants are in a process of being investigated.

ASR and metal on metal examples also show that availability of registry data alone is not a substitute for good pre-market approval process. While being very informative they are powerless when the failures take long time to develop. Large number of faulty products (e.g. implants) enter into the market before safety evidence becomes available with consequences for public health and well being of people. In the case of the ASR, it took about 4-5 years before evidence was accumulated, reported and product taken out of the market. This example also exposes the gaps in European system where the threshold for approval is much lower than that used by FDA. In Europe entities called notified bodies are used to perform compliance assessment. The devices are often approved without any clinical evidence. In addition, the notified bodies are fully funded by manufacturers. The system essentially relies on availability of national registry data to reveal safety concerns in post-market settings. Certainly in some instances there are good quality European registries jointly funded by the governments, manufacturers and physicians that can help reveal safety concerns early. However, these registries are not always available, have limitation of their own and can only function in a country specific health delivery environment that is not easily applicable to US setting. We certainly need much **more robust and larger registries or multinational registry consortia** to have sufficient power for safety evaluation in real world/practice settings and determine safety concerns in a timely fashion.

The Center for Devices and Radiologic Health (CDRH) at FDA has both mandatory and voluntary reporting to monitor post-market device adverse events and product problems. While manufacturers are required to directly report deaths, injuries, and malfunctions to the FDA, the device users are required to report these events to the manufacturers and only deaths to FDA. The voluntary reporting systems such as the MedWatch program, MAUDE database and Medical Product Safety (MedSun) enhanced surveillance network provide national medical device surveillance in the USA. However, these reporting systems have important weaknesses, such as incomplete, inaccurate, or unvalidated data, reporting biases related to event severity, concerns about adverse publicity or litigation, and general underreporting of events. Most importantly, denominator data are missing, which makes evaluation of safety event incidence or prevalence impossible. **Registries** are certainly the best way forward to fill the evidence gap and address the limitations of existing systems in immediate future. **Large registries or consortia of registries** capturing a variety of devices are particularly important for comparative outcomes evaluation and active surveillance. Often only large, longitudinal or even multinational registries we can provide denominator data for adverse events related to specific implants and allow proper conduct of safety and effectiveness studies particularly for rare endpoints. One evolving successful example is the FDA funded important initiative called 'International Consortium of Orthopedic Registries' (ICOR) that aims to build the foundations for a worldwide research consortium of orthopedic registries. The consortium represents 15+ nations that have existing registries with a mission to improve the safety and effectiveness of orthopedic devices and procedures through collaboration. Currently, these international registries combine to more than 3,500,000 orthopedic surgeries capturing all implantable devices on the market.

Finally, the registries that we have in the US today might not be suitable for building post-market infrastructure. Some well known professional society registries are broad, contain clinically important

data but are seriously limited in several respects. First, participation is voluntary so that findings are applicable only to those institutions desiring to improve their care quality. Second, due to the voluntary nature of participation, data validation through audit is very limited, if at all attempted. Many new technologies are adopted by enthusiasts who do not necessarily share all of the data (particularly when at the learning stage) with their societies. Third, while professional societies have strong interests in improving the delivery and quality of care, they can sometimes be conflicted when comparing device and treatment strategies that may negatively impact their profession or stakeholder. Fourth, they lack long-term follow up. Unless these registries provide FDA access to data, have detailed device information, long-term follow up and implement mandatory reporting of device use and outcomes these registries will not be the robust infrastructure that FDA needs. **In most instances it is more efficient to empower and provide funds to FDA** to initiate registries or consortia of registries through Public Private Partnership (PPP) including participation of manufacturers, payers and hospitals. The PPPs led by FDA might be the best way to match or advance the success story of some well known European or Australian registries that are hailed as models for post-market evaluations.

In the absence of robust post-market infrastructure we also need to be careful and make only gradual changes to pre vs post market balance for device approval. The changes need to be linked to the process of building large, comprehensive device registries and registry consortia and advancement of registry science. This process will ensure evidence based innovation. Only after we build a strong post-market infrastructure, accumulate evidence on device performance in real world settings we can provide recommendations on how to adjust the threshold for pre-market approval and ensure that disasters similar to metal on metal will not happen.

Mr. PITTS. The Chair thanks the gentleman and recognizes Ms. Swirsky for 5 minutes for an opening statement.

STATEMENT OF LISA SWIRSKY

Ms. SWIRSKY. Good afternoon. My name is Lisa Swirsky and I am a Senior Health Policy Analyst at Consumers Union. Consumers Union is the publisher of Consumer Reports magazine and Best Buy Drugs. We also have a Safe Patient Project, which is a campaign to improve the safety and efficacy of devices. We are also member of the Patient Consumer and Public Health Coalition, which is a broad coalition of public interest groups interested in the safety and efficacy of drugs and devices, and some of our comments today reflect the broader interest of that community.

Consumers Union urges Congress to take a balanced approach to reauthorizing MDUFA, focusing both on the real need to keep deficient devices off the market while also providing timely access to safe and effective devices. Safety failures such as those that occurred with metal-on-metal hips and surgical mesh resulted from failures in the device regulatory system, particularly the problem 510(k) process. But we would also urge Congress to understand that behind those failures, there are real people. Lana Keaton is one such consumer. She was a previously healthy woman who was treated for what was a pretty routine condition for a middle-aged woman, incontinence. She went on for surgery for insertion of a synthetic mesh bladder sling, which is a product that was cleared through the 510(k) system. She awoke from surgery in extreme pain due to complications from the mesh, and she has had to undergo 17 surgeries, and she has another one upcoming.

CU urges Congress to remember the experiences of hundreds of thousands of people like Lana who have been injured by defect devices as it considers reauthorization of the medical device user fee program. Our priority is that these devices work and that they don't hurt people, and we believe that with proper resources, we can have a streamlined timely system without sacrificing safety.

To this end, we would ask Congress to strengthen the premarket approval process for devices. In particular, Congress should pass legislation ensuring that recalled devices cannot be used as a predicate for subsequent devices. Congress should also shore up the system for monitoring devices once they are already on the market by providing FDA with the authority to require postmarket studies when it deems necessary to ensure the safety of devices and also to improve postmarket surveillance tools such as Sentinel and the adverse event reporting system.

CU has reviewed provisions of the agreement as described in the minutes from the FDA's January 31st meeting with industry, and we offer the following comments and concerns on the outlines of the agreement in principle.

Overall, we feel that the user fee amount is inadequate. During the course of negotiations with industry, the FDA indicated it would need somewhere between \$770 million to up to \$1 billion to implement the program enhancements that it was asking for. Now, while we understand that FDA has since scaled back those proposals in light of the lower-than-expected user fee, nonetheless, a lot of those program enhancements still remain in the agreement

and we are concerned that as long as they remain in the agreement without dedicated funding, they will become an unfunded mandate on an agency that is already struggling to meet current requirements. And we would ask that if Congress thinks that these enhancements are beneficial, that they appropriate adequate funding.

We also are concerned that the agreement overemphasizes the achievement of performance goals when device applications are reviewed and processed within a reasonable time frame because the application is sound and the device is safe and effective. This is obviously a win-win for consumers and industry. However, there is no mention in the agreement that these goals are conditioned on the overall quality of the products, the complexity of the products, the benefit of the products to consumers or really any factors that may be relevant to protecting the public health. Notably, the word “safety” does not appear once in the minutes from the meeting where industry and FDA came to agreement. We consider this a striking omission, given recent notable safety lapses by the device industry.

Even more worrisome, the agreement in principle references total time to decision, goals based on calendar years in addition to the goals based on FDA days. Current performance goals stop the clock when the FDA sends an application back to a device manufacturer when the agency needs additional information. Under the agreement, the FDA is kept on the clock even when it needs to get further information. CU opposes any kind of binding of the FDA to get the information that it needs to ensure the safety and adequacy of devices.

We have further concerns about provisions in the agreement that call for incorporating the patient perspective and risk-benefit considerations. The industry has requested that groups that represent patients with a specific disease represent the patient perspective. However, in our experience, many of these patient groups are heavily funded by industry. Patient representatives used for these purposes should be held to conflict of interest standards and should be required to disclose any financial ties with industry.

Finally, as Congress considers MDUFA, we urge it to provide a direct seat at the table for consumers in future reauthorization negotiations. While the stakeholder meetings that FDA conducted with consumer groups was an advancement over prior authorization processes, they still kept consumers at arm’s length from negotiations that have significant implications for the public health.

Thank you.

[The prepared statement of Ms. Swirsky follows:]



Statement of

Lisa Swirsky

Senior Policy Analyst

before the

United States House of Representatives

Committee on Energy and Commerce

on

**Reauthorization of MDUFA:
What It Means for Jobs, Innovation and Patients**

February 15, 2012

My name is Lisa Swirsky, and I am a Senior Health Policy Analyst at Consumers Union. Consumers Union (CU) is the policy and advocacy arm of Consumer Reports, the nonprofit publisher of *Consumer Reports* magazine and *Best Buy Drugs*. Consumers Union's Safe Patient Project, which has successfully organized consumers on patient safety issues such as hospital-acquired infections over the past eight years, has recently launched a campaign to improve medical device safety. CU is a member of the Patient, Consumer and Public Health Coalition, which represents a broad group of academics, think tanks, scientific integrity organizations and consumer groups concerned about the safety and efficacy of drugs and devices. Many of the concerns we have with the draft agreement between FDA and the industry on medical device legislation reflect the concerns of a broader community of public interest organizations committed to changing the Medical Device User Fee Act (MDUFA) so it will provide timely access to safe and effective medical devices.

Medical devices, like eyeglasses and contact lenses, are a part of our everyday lives and are a growing part of the health care we receive. Complex devices like artificial hip joints, surgical mesh, and cardiovascular stents, are permanently implanted and can be essential for sustaining life. These high-risk devices can cause serious harm if they break, leak, stop functioning or disintegrate. When an implanted device is recalled or removed from the market, patients cannot simply stop using them. Removal of the device requires surgery, sometimes multiple surgeries, and it may take months or years to repair the damage done by the device. Many patients are permanently disabled due to complications from a device. Even low-risk devices, like contact lens solution and alcohol swabs have recently caused patients harm that could have been prevented.

Unlike prescription drugs, most devices do not require proof that they have been tested on humans and found to be safe and effective prior to being cleared by the FDA for distribution or sale. Further, the system for monitoring and tracking what happens with devices once they are on the market is weak and does not adequately protect people using them.

Any reauthorization of MUDFA should improve safety and the current pathways followed to bring devices onto the market and improve the system of monitoring devices after being implanted in patients or sold to consumers. For example two specific policies that Congress should consider are: (1) legislation ensuring that devices that have proven faulty can not be used as the basis for clearing other subsequent devices; and (2) legislation providing FDA authority to require post market studies when it deems necessary to ensure the safety of devices.

Our priority is that these devices work and don't hurt people. With proper resources, we can have a streamlined, timely system without sacrificing safety.

Contrary to public perception, the device industry is far less regulated than the drug industry. Consumers Union urges Congress to take a balanced approach to reauthorizing the Medical Device User Fee program, focusing on the real need to keep deficient and dangerous devices off the market while providing timely access to safe and effective devices. Safety failures resulting from failures in the device regulatory system, particularly the problematic 510(k) process, have caused serious harm to real consumers.

Consider the case of Lana Keaton, a healthy woman who was treated for incontinence, a common condition for middle aged women. She went in for surgery for insertion of a synthetic mesh bladder sling, a product cleared through the 510(k) system. She awoke from surgery in extreme pain. The synthetic mesh used in her surgery has caused severe complications and pain that has required her to undergo 17 additional surgeries. CU urges Congress to remember the experiences of hundreds of thousands of people like Lana who have been injured by defective devices as it considers reauthorization of the medical device user fee program.

CU has reviewed provisions of the agreement as described in the minutes from the FDA's January 31st meeting with industry. We anticipate having the opportunity to publicly comment on a more detailed description of the agreement. Nevertheless, Consumers Union offers the following comments and concerns on what we know now.

User Fee Adequacy

The fees paid by medical device makers are currently so modest, that even doubling of the fees is a small price to pay when considering that these devices may make companies millions to billions of dollars. In 2012, the fees should be increased to reflect the level of work required by FDA to review and ensure the long-term safety of complex devices.

During the course of negotiations with industry, the FDA indicated that it needed resources of between \$770 million to \$ 1.15 billion to implement the performance goals desired by industry.¹ The \$595 million allocated under the agreement falls far short of FDA's requests. FDA has said it will scale back its commitments to industry-requested enhancements in light of the lower than requested user fee.² However some of these process improvements, such as additional pre-submission steps, remain in the agreement without any dedicated funding and will have to be paid for with base resources. Without adequate funding, we are concerned that FDA will be pressured to take on new tasks for the industry, leaving fewer resources available to fulfill its current responsibilities and to ensure the safety of medical devices. To the extent that Congress decides to require the FDA to meet these new industry-requested responsibilities that are not paid for by user fees, it must provide dedicated funding to the agency for these tasks.

Performance Goals

We remain concerned about the implied quid pro quo created by the user fee system which, in exchange for industry fees, places an emphasis on speedier review times as an end to itself without ensuring that the safety and effectiveness of devices aren't sacrificed. When device applications are reviewed and processed within a reasonable timeframe because the application is sound and the device is safe and effective that is a win for both consumers and industry. But speeding the introduction of devices to market only makes sense in the context of a system that assures that these devices are safe and work in a way that advances the public health.

¹ Food and Drug Administration, Minutes from Negotiation Meeting on MDUFA III Reauthorization, October 31, 2011.

² Food and Drug Administration, Minutes from Negotiation Meeting on MDUFA III Reauthorization, January 31, 2012.

Currently the 510 (k) process, through which 90 percent of regulated devices are currently cleared, merely tests whether or not a device is substantially equivalent to something on the market.

The chart below shows the emphasis in the agreement on speedy review of medical devices. For all three of the device approval tracks the agreement commits FDA to at least a 90 percent approval rate in five years. Absent from the agreement is any commensurate commitment to ensuring that these goals be met without compromising safety or efficacy.

MDUFA III Goals for Percent of Applications Approved as Agreed to by Industry and FDA			
	Goals for Pre Market Approval of devices that go to panel (320 FDA days)	Goals for Pre Market Approval that don't go to panel (180 FDA days)	510(k) Clearance
FY 13	50%	70%	91%
FY 14	70%	80%	93%
FY 15	80%	80%	95%
FY 16	90%	90%	95%
FY 17	90%	90%	95%

Source: FDA minutes from January 31, 2012 meeting with industry to negotiate MDUFA agreement.

The agreement in principle reached by the FDA and industry illustrates this inherent problem with a user fee structure. At a time when the device industry has seen large scale safety failures of some of its products, such as surgical mesh and metal-on-metal hips, it is troubling that the main focus of conversations between industry and the agency that regulates it is on speeding up review times. Instead, the focus should be on improving the review process to ensure that it provides timely access to high quality devices that improve the public health while assuring safety. The word "safety" does not appear once in the minutes from the meeting where industry and FDA came to agreement. This is a striking omission given recent notable safety lapses by the device industry.³

There is no mention in the agreement that these time goals are conditioned on the overall quality of the products, the complexity of the products, the benefit of the product to consumers, or any other factors that may be relevant to protecting the public health.

Even more worrisome, the agreement in principle references total time to decision goals (see chart below) based on calendar years in addition to the goals based on FDA days. This

³ Food and Drug Administration, Minutes from Negotiation Meeting on MDUFA III Reauthorization, January 31, 2012.

additional metric raises troubling safety and efficacy concerns for consumers. Current performance goals stop the clock when the FDA sends an application back to a device manufacturer when the agency needs additional information. Under the agreement, the FDA and industry agree to total time to decision goals based on calendar years. This construct keeps FDA on the clock even when it has to send back an incomplete application to the manufacturer. This places constraints on the ability of the FDA to seek additional information with respect to safety and efficacy once a completed application has been submitted. CU opposes any provision that would limit FDA's ability to ask for more information when needed to ensure the safety and efficacy of devices.

MDUFA III Shared Outcome Goals for Total Time to Decision as Agreed to by FDA and Industry		
	PMA	510(k)
FY 13	395 calendar days	135 calendar days
FY 14	395 calendar days	135 calendar days
FY 15	390 calendar days	130 calendar days
FY 16	390 calendar days	130 calendar days
FY 17	385 calendar days	124 calendar days
Source: FDA minutes from January 31, 2012 meeting with industry to negotiate MDUFA agreement.		

Benefit Risk Determinations

We have further concerns about provisions in the agreement that call for incorporating the patient perspective into risk benefit considerations. The industry wants groups that represent patients with a specific disease to represent the patient perspective. However, many of these patient groups are heavily funded by industry and could misrepresent the public perspective. The FDA must commit to finding patient voices free from conflicts with industry to inform risk benefit considerations. Patient representatives used for these purposes should be held to conflict of interest standards and should be required to disclose any financial ties with industry.

Pre-submission Process

The FDA and industry have agreed to administrative improvements to the pre-submission process in order to bring greater consistency to the process and to provide industry with greater clarity about the FDA's expectations prior to submitting a device application. In principle, we agree that improving the quality of submissions is an appropriate way to reduce review times.⁴

During negotiations with industry the FDA proposed specific timelines and goals for different steps in the pre-submission process. The agency also proposed publishing guidance

⁴ Food and Drug Administration, Minutes from Negotiation Meeting on MDUFA III Reauthorization, January 31, 2012.

clarifying submission acceptance criteria, so that the agency is only reviewing completed submissions. In patient and consumer group stakeholder meetings, the FDA indicated that the clock will start running with respect to time goals only after it receives a completed submission. The details of the formal agreement are not yet available, but in principle we support this provision of the agreement. This is consistent with FDA's focus on a shared commitment with industry to reduce review times that includes industry responsibility to improve the quality of submissions, as well as administrative efficiencies by the FDA.

We are supportive of efforts by the FDA to improve the quality of submissions and provide greater clarity to the industry, but we are disappointed in the lack of designated user fees to fund pre-submission meetings. Without new resources for these improvements, this amounts to an unfunded mandate on an agency already struggling to meet its current responsibilities. Unfortunately, the industry has not agreed to additional user fees to pay for improvements to the pre-submission process. As a result, the agency states that it has scaled back plans for improvements to the pre-submission process to reflect the level of user fees the industry is willing to pay. Specifically, FDA has removed specific timelines and goals for different steps in the process. However, the agency still commits to improving the pre-submission process using its base resources.

Involving Consumers in the Process

As Congress considers reauthorization of the Medical Device User Fee Act, we urge it to provide a direct seat at the table for consumers in future reauthorization negotiations. While these parallel stakeholder meetings with patient and consumer groups were an advancement over previous reauthorization processes, they still keep consumers at arm's length from negotiations that have significant implications for the public health. Despite the participation of consumer groups in stakeholder meetings with FDA, concerns raised in these meetings do not appear to have impacted any of the provisions in the agreement in principle.

The FDA and Congress have an opportunity to fix a system that is currently flawed because it allows too many unsafe medical devices to enter the market. In the next five years, the use of medical devices – especially implants – will increase significantly more than in the past five years. Yet, our system of review fails to ensure safety up front and there is no workable early warning system to adequately identify problems with devices after they have been implanted in patients. Americans are counting on their representatives to strengthen the law to ensure that patient safety isn't sacrificed in the drive to speed up the approval of new medical devices.

Mr. PITTS. The Chair thanks the gentlelady and now recognizes Mr. Shull for 5 minutes for an opening statement.

STATEMENT OF JAMES SHULL

Mr. SHULL. My name is Jim Shull. I am from Browns Mills, New Jersey. I would like to thank the committee for allowing me to speak here today.

My story goes back to 2005 when I was told I had a hernia. I woke in the recovery room from the surgery in excruciating pain. Two days later, I was in such pain that I couldn't stand up straight or barely walk. I called my surgeon's office and he told me to meet him at the emergency room. He took me into an examination room, looked at the surgical site and told me that it was very infected. He prescribed an antibiotic, and morphine for the pain, but nothing seemed to help. The infection was so bad that I had streaks running down my groin.

I continued to call the surgeon over the next 2 weeks only for him to tell me that I am a slow healer. At my 6-week follow-up I explained again to my surgeon that I was in unbearable pain, so, he decided to inject my groin with Novocain right through the incision and sent me back to work.

The pain I was feeling was as if there was a sharp object left inside of me. After continuously going back to the surgeon he decided to send me to pain management, where over the course of 6 weeks the pain doctor injected my groin upwards of 70 times.

Nothing would help the pain so I decided to investigate myself. I went back to the surgeon and explained to him what I had found. Only then did he tell me that he had put a synthetic mesh inside of me and told me that it was not the mesh, because the mesh is inert and my problem has to do with the nerves in my groin. I tried to go back to work because I couldn't afford not getting a paycheck, but the pain was so unbearable that I ended up in the ER. The doctor in the ER did a CT scan only to find nothing. That is because the mesh is transparent and cannot be seen on X-rays. The doctor in the ER told me that I probably had diverticulitis and that I needed to follow up with a GI specialist. Those tests came back negative also.

I decided to get a second opinion from another surgeon and asked if he could remove the mesh from inside of me. He told me that he couldn't remove the mesh but could do an exploratory surgery to see if the nerves were stitched up. This surgeon did cut and tie off one of the nerves in my groin and thought that it would ease my suffering. After returning to him for 6 weeks in unbearable pain, he told me that there was nothing else he could do for me. So I was on my own.

I finally did find a surgeon in another State and he agreed to see me. When he examined me he told me that he knew exactly what was wrong with me but to be sure he sent me to have an MRI. I went back to this surgeon and he showed me the problem. There it was: a hardened piece of synthetic mesh inside of me. So finally after almost 2 years of unbearable pain, I found someone who could give me some answers. The surgery to remove the mesh took 3-1/2 hours. When I awoke in the recovery room, the surgeon was at my bedside. He told me that he was sorry and that I would be in

pain for the rest of my life. The surgeon explained to me that he had removed a balled-up piece of concrete from my groin, that the mesh had hardened and balled up, and had encapsulated the other two main nerves in my groin. In order to get the mesh out, the nerves had to be severed. He explained to me that the mesh was so hard, that when I moved it was acting like a saw and cutting into the surrounding tissue. I had a 3-inch gash in my pelvic floor along with hundreds of smaller cuts and tears.

In 2008 I was diagnosed with a degenerative nerve condition. The pain that I suffer through on a daily basis consists of constant burning and sharp pains in my groin and upper thigh. My groin and upper thigh are purple and brown color because of the nerve condition I now have. I must take three strong medications—OxyContin, Percocet and Tramadol—just for the pain alone. Every 6 months I have to have radio frequency ablation done at the spinal level where the nerve roots are located. It is very uncomfortable for me to sleep at night without the help of medication. Because of this product I am no longer able to work as a printer.

When I was a teenager, I had a hernia. That hernia was not repaired with mesh, but was stitched back together. Thirty-four years later and I still have no problems with that repair. The mesh that was put inside of me caused so much damage that none of the nerves will ever be able to be repaired and will never grow back. I live a life of pain because of a product that never had any kind of clinical testing and slipped through the back door of what you know as the 510(k) process based on the use of predicate devices. I am left disabled because the FDA considered surgical mesh equivalent to that of sutures and allowed it to be implanted in patients like me.

After years of people reporting problems and investigations into synthetic mesh, the FDA published a public health warning. Unfortunately, the warning was only for synthetic transvaginal meshes that are used in woman. There was no public health notification for hernia meshes, which are just as tragic and cause horrible complications for men and women alike. Failing to address the hernia mesh issue puts too many people in danger. I think synthetic mesh should not be on the market because it is unsafe and I have proudly taken the challenge to work to prevent this from continuing to happen to others.

In closing, I would like to say that I am only one face in thousands of people that this has happened to, and the sad part of it all is that I feel that I may be one of the lucky ones. This committee can change the laws to improve the safety of medical devices and put patients first. Surgical mesh and other medical devices should be tested for safety before they are allowed to be implanted into people like myself. We also need a national system to track what happens to patients like me after devices are implanted, to catch these problems as soon as possible.

Thank you.

[The prepared statement of Mr. Shull follows:]

Testimony of James Shull
U.S House Committee on Energy and Commerce/Subcommittee on Health
February 15, 2012

My name is Jim Shull and I am from Browns Mills, New Jersey. I would like to thank you for allowing me the opportunity to speak here today.

My story goes back to 2005 when I was told I had a hernia. I was told that I was young and would recover quickly. I was told I would be walking up stairs in 3 days and back to work in 2 weeks.

I awoke in the recovery room from the surgery in excruciating pain, the nurses gave me some pain medication and told me I would be fine and sent me home. Two days later I was in such pain that I couldn't stand up straight or barely walk. I called my surgeon's office and he told me to meet him at the hospital Emergency Room. He took me in to an examination room, looked at the surgical site and told me that it was very infected. He prescribed an anti-biotic and Morphine for the pain but, nothing seemed to help. The infection was so bad that I had streaks running down my groin; I was still very swollen, bruised and in severe pain.

I continued to call the surgeon over the next 2 weeks only for him to tell me that I am just a slow healer. Quite a difference from walking up stairs in 3 days, like he told me before the surgery. As time went on I was still in unbearable pain. At my 6 week follow up I explained again to my surgeon that the pain was unbearable, so, he decided to inject my groin with Novocain, right thru the incision and sent me back to work.

The pain I was feeling, was as if there was a sharp object left inside of me. My boss told me that I couldn't be at work if I couldn't stand up straight and walk, so, he sent me home. After continuously going back to the surgeon he decided to send me to Pain Management, where over the course of 6 weeks the pain doctor injected my groin upwards of 70 times with steroids and Novocain.

Nothing would help the pain so I decided to investigate myself. The internet is a wonderful tool to launch an investigation. I googled complications from hernia surgery and was amazed at what I found.

It was only then that I figured out that a Hernia Mesh kit must have been put inside of me. I went back to the surgeon and explained what I found. Only then did he tell me that he had put a Synthetic Mesh inside of me and told me that, it was not the mesh,

because the mesh is inert and my problem has to do with the nerves in my groin. I tried to go back to work because I couldn't afford not getting a paycheck, but the pain was so unbearable that I ended up in the ER. The doctor in the ER did a CT scan only to find nothing. That is because the mesh is transparent and cannot be seen on X-rays. The doctor in the ER told me that I probably had Diverticulitis and that I needed to follow up with a GI specialist. That test came back negative also.

I decided to get a second opinion from another surgeon and asked if he could remove the mesh from inside of me. He told me that he couldn't remove the mesh but could do an exploratory surgery to see if the nerves were stitched up. This surgeon did cut and tie off one of the nerves in my groin and thought that it would ease my suffering. After returning to him for 6 weeks in unbearable pain he told me that there was nothing else he could do for me. So I was on my own. I continued to be in unbearable pain and still tried to work. I continued to try to find a surgeon who knew what was happening to me.

I finally did find a surgeon in another state and he agreed to see me. When he examined me he told me that he knew exactly what was wrong with me but to be sure sent me to have an MRI. I went back to this surgeon and he showed me the problem. There it was a hardened synthetic mesh. This surgeon told me that he has been removing these products for 20 years because of problems similar to mine.

So finally after almost 2 years of unbearable pain I found someone who could give me some answers. The surgery to remove the mesh took 3 ½ hours. When I awoke in the recovery room, the surgeon was at my bedside. He told me that he was sorry and that I would be in pain for the rest of my life.

The surgeon explained to me that he had removed a balled up piece of concrete from my groin, that the mesh had hardened and balled up, and had encapsulated the other 2 main nerves in my groin. In order to get the mesh out the nerves had to be severed. He explained to me that the mesh was so hard, that when I moved it was acting like a saw and cutting into the surrounding tissue. I had a 3 inch gash in my pelvic floor along with hundreds of smaller cuts and tears.

In 2008 I was diagnosed with a degenerative nerve condition, which I believe was caused by the mesh. The pain that I suffer through on a daily basis consists of constant burning and sharp pains in my groin and upper thigh. My groin and upper thigh are a purple and brown color because of the nerve condition I now have. It is a constant battle every day. I must take three strong medications Oxycontin, Percocet, and Tramadol just for the pain alone. Every 6 months I have to have radio frequency ablation done at the spinal level where the nerve roots are located. This just to relieves 50 percent of the burning. It is very uncomfortable for me to sleep at night without the help of medication.

Because of this product I am no longer able to work as a printer. I loved my job; where else can you take 12 different components and put them all together and make what I considered art. I am now on New Jersey State Disability, which is about to run out. I have applied for Social Security Disability but have not heard back from them yet.

When I was a teenager, I had a hernia. That hernia was not repaired with mesh, but was stitched back together – 34 years later and I still have no problems with that repair, while the repair that I had when I was 42 went bad immediately and I now face a lifetime of pain and struggles because of it.

All of this I have to go thru because of a piece of hernia mesh that was supposed to be inert and not cause any problems. The mesh that was put inside of me caused so much damage that none of the nerves will ever be able to be repaired and will never grow back. I live a life of pain because of a product that never had any kind of clinical trials and slipped through the back door of what you know as the 510K process based on the use of predicate devices. Did you know that the mesh that was inside of me used only sutures as a predicate device? I am left disabled because the FDA considered surgical mesh equivalent to sutures and allowed it to be implanted in patients like me.

After years of people reporting problems and investigations in to synthetic meshes, the FDA published a Public Health Warning. Unfortunately, the warning was only for Synthetic Trans-vaginal meshes that are used in woman for Pelvic Organ Prolapse, Incontinence and Bladder Slings, which have caused problems every bit as terrible as mine.

There was no Public Health Notification for the Hernia Meshes. Which are just as tragic and cause horrible complications for men and woman alike. In my research I found that in the United States alone there are 750 thousand to 1 million hernia surgeries each year. Failing to address the hernia mesh issue puts too many people in danger. I think synthetic mesh should not be on the market because it is unsafe and I have proudly taken the challenge to work to prevent this from continuing to happen to others.

In closing I would just like to say that I am only one face in thousands of people that this has happened to and the sad part of it all is that I feel that I may be one of the lucky ones. This committee can change the laws to improve the safety of medical devices and put patients first. Surgical mesh and other medical devices should be tested for safety before they are allowed to be implanted into people like myself. We also need a national system to track what happens to patients like me after devices are implanted, to catch these problems as soon as possible.

Thank you.

Mr. PITTS. The Chair thanks the gentleman and thanks to all the panel for your testimony, and we will now begin questioning, and I will recognize myself for 5 minutes for that purpose.

Dr. Jaffe, you presented some very compelling data in your testimony, and it reiterates what we have been hearing from medical device innovators who have testified before this committee and those we speak with back in our home districts. PWC reports show that in 2007, 116 medical device startups had \$720 million in funding, and that last year, 55 companies received under \$200 million. This reflects more than a half-billion-drop in funding of medical device startups. Can you explain the impact of this alarming drop in funding, the impact on patients and jobs?

Mr. JAFFE. Thank you, Chairman Pitts. Let me start with the jobs issues first. Clearly, each of these companies may only have five to ten employees who start up funding, but if they are successful, they will grow, and many successful medical device companies we are involved with have hundreds of employees. We also know from data that for every one job we create in a company, there are three or four created in the community to support to those jobs, so clearly there is an economic impact.

The more important issue, though, is really the impact on patients and potential technologies for those patients. I have an unusual job in the sense that I invest in things I hope I never have to use personally and I hope none of you or your loved ones ever need any one of the products we develop. But if you are someone with the issue that our technologies address, you will be very grateful they were developed. And the sad part of all this is that there are many technologies that I mentioned earlier that I see every day that deserve development but I can't pursue because the time and capital requirements would be too great to allow me to make returns I need to satisfy my investors' requirements, and it is the challenge of the system we all need to work on.

Mr. PITTS. Thank you.

Mr. Perez, can you give us an example of difficulties your company has had with the FDA? Have you experienced an increase in how long it takes to get through the FDA process, and why do you believe that doubling the amount you pay in user fees is going to solve what is partly a management issue?

Mr. PEREZ. Well, I think the performance metrics that are specifically addressed in the MDUFA agreement go back to some of the issues that we have had with the FDA. I will give you an example. We had a pre-submission hearing with the FDA on a technology, and then we went almost 14 months before we heard back from the FDA, and a lot of that had to do with the fact that there was not agreement within the FDA on how to go forward with the approval process of a product like this, and this specific MDUFA agreement addresses that where we have a pre-submission meeting, there has to be agreements and those agreements can't be changed. We had another example where we had an agreement with the FDA on a clinical trial. We moved forward on the clinical trial. We got about halfway through the clinical trial and the requirements of that trial were changed.

So once again, I think some of the things that we are trying to address regarding predictability and accountability are specifically

addressed in this MDUFA agreement, and I think some of the challenges that we have, I am not saying they are all going to go away but I think some of the specific challenges that we have had will be addressed with this new agreement.

Mr. PITTS. Ms. George, how does the proposed user fee agreement improve predictability and consistency with respect to FDA's review of medical devices, if you can be specific?

Ms. GEORGE. I believe that there are a couple of areas that it does that. First off, that through the pre-submissions process, as was stated by Mr. Perez, there would be agreement as to what the requirements are ahead of time, early, prior to submission, so that the manufacturer when they submit their 510(k) it includes the requirements up front so that it can flow through the process more quickly. I also think that the interaction requirement that we have put into the agreement of having earlier interaction with the FDA so that we know what the questions might be if they are going to have them, that will support it, and then the added management as through the resources that are going to be added, that will ensure consistency in how they make those determinations so that a reviewer by themselves doesn't have to make that decision.

Mr. PITTS. Professor Hall, from what I understand, FDA has extensive postmarket authority for medical devices. Would you walk us through that authority, please?

Mr. HALL. There are a number of authorities the agency currently has. They include obtaining information through medical device reports, so-called MDRs, the MedSun process, which is an active postmarket surveillance system linking about 350 hospitals. There is a 522 order process. You have special controls that specifically include the statutory authority for postmarket surveillance obligations, patient registries and other tools. In the PMA world, you have conditions of approval. The QSR systems include postmarket surveillance. We call them CAPA, corrective and preventive action, processes that, for example, require product trending, root-cause analysis, etc. So those are just a number of the statutory systems that are currently in place.

Mr. PITTS. Thank you. My time is expired. The Chair recognizes the ranking member, Mr. Pallone, for 5 minutes for questions.

Mr. PALLONE. Thank you, Mr. Chairman.

I wanted to ask Ms. Swirsky and Ms. George, only because of time limitations, because of these advisory committees and conflict of interest. As you know, industry and some patient groups have focused on removing limits on how many experts with financial conflicts of interest may serve on the committees. Many consumer groups are concerned that for FDA and the public to be confident in the objectivity of the advice FDA receives, every effort must be made to minimize the number of conflicted experts that serve on these committees. I would like to ask Ms. Swirsky, if you could suggest ways that FDA could broaden its pool of experts. Let me start with that and then I will go to Ms. George. How would you suggest the FDA could broaden its pool of experts?

Ms. SWIRSKY. I want to say first off, I think the FDA has already suggested that those caps on the waivers, which I think are the subject of many of the bills in the House and some in the Senate, haven't really been at issue. They are not using the existing caps.

Mr. PALLONE. Right. She mentioned that when we had the Commissioner here last week.

Ms. SWIRSKY. So that suggests to us that there is some broader problems.

Mr. PALLONE. Right. Just give me your suggestions, because I don't have a lot of time.

Ms. SWIRSKY. I am sorry. So some of our suggestions, we would hope that the FDA would be ripe for a task force to bring in stakeholders, various stakeholders, consumer groups and industry to sort of come together to look at some of the barriers and identify some solutions. But some of the solutions I think we and other consumer groups have thought about is first of all, creating better awareness of advisory panels. I think right now there isn't great awareness of it, and so what you have now are self-selected folks who sign up for these advisory panels, and some ideas include trying to work with medical schools to make this a part of their curriculum so we can create more prestige around the advisory panels. Obviously we can pay them more, which is probably not in the cards for the short term. But also I think there is a lot of evidence that about 50 percent of academic researchers aren't conflicted at all so we need to tap into that pool, and research suggests that academic medical centers have fewer conflicted members, and so bringing them into the process and getting their input in how we can make it more attractive to them.

Mr. PALLONE. Thank you.

Ms. George, first I wanted to thank you for coming to that FDA roundtable we had at Rutgers with the Commissioner, but would explain why elimination of the caps on waivers would be helpful, given as Ms. Swirsky said, that the FDA hasn't come anywhere near reaching its cap to date? Do you think it would be helpful? And if you want to comment on broadening the pools also but—

Ms. GEORGE. One of the challenges—

Mr. PALLONE. Quickly because I have one more question.

Ms. GEORGE. One of the challenges I think that does occur with the panels is, anything that goes to panels is innovative. It is new technology. It is new clinical science and there are not a lot of available people out there to actually come in to be those experts, to come in and answer the questions, to be able to ask industry the questions. So one of the challenges that we have as a manufacturer if we bring something to panel is, we have probably already tapped a lot of those people to help us in the development and in the creation of the technology or science and so the FDA has limited people available that they could use, so that does cause some aspect of conflict.

Mr. PALLONE. Let me ask Mr. Perez, I have one more question. I have about a minute left. You know, I understand the negotiation over the medical device agreement wasn't easy, but we have heard from the drugs and biologics trade associations that they are committed to a clean PDUFA, and while they may have some additional legislation they would be happy to see enacted as part of the UFA legislation package, they don't want anything that would slow down or jeopardize the passage of that package. So I just wanted to ask you, are you committed to seeing that nothing slows down

or stands in the way of passage of MDUFA as part of the package of FDA legislation? I am asking you to take the same pledge.

Mr. PEREZ. I think we share a common goal here, that we want to get this done in a very timely manner. We know many members have already introduced some legislation all in an effort to improve and help the FDA be more successful but I think right now we need to make sure that we balance those efforts with trying to get the MDUFA passed in a very timely manner. So we would like to work with the members of the committee, to listen to them, and I think it is very, very important to get this done. Dr. Shuren outlined a timetable and I hope we can stick to it.

Mr. PALLONE. All right. Thank you so much.

Mr. PITTS. The Chair thanks the gentleman and recognizes the vice chairman of the committee, Dr. Burgess, for 5 minutes for questioning.

Mr. BURGESS. Thank you, Mr. Chairman.

Mr. Perez, a valid point, what a lot of people don't realize about the user fee agreements is when they expire on September 30, this is not like the typical Congressional action where we can say the dog ate my homework so I am going to give myself an IOU for the next couple of months. These are voluntary funds that are provided by the industry, and without the user fee agreement and in force, those monies simply stop on October 1st. Is that correct?

Mr. PEREZ. That is correct.

Mr. BURGESS. So this timeline that we are looking at now is one with a great deal more severity than the usual Congressional timelines. I mean, I forget, we had, what, 35 different temporary patches to the FAA reauthorization in the last 10 years. We can't do this.

Mr. PEREZ. I agree. We have to get it done.

Mr. BURGESS. We have to get it done, and so I appreciate all of you being here and Dr. Shuren being here because I think this is—you know, we may disagree about some parts of this but we all understand how important it is to get this done.

Dr. Jaffe and Dr. Kesselheim, let me just take advantage of the fact that you two are sitting next to each other and you seem to have vastly different views of the world. You both heard each other's testimony. Is there any common ground between you or are we left with this rather stark definition on either side of what an ideal user fee agreement would look like?

Mr. JAFFE. Well, I don't know where the differences are between us on the user fee agreement. I certainly didn't hear any concerns about the need for more resources for the FDA and for process improvements.

Mr. KESSELHEIM. I would agree with that. I mean, I think that the need for greater funding for a lot of the essential work that the FDA does is essential and it would be my preference to see that money come directly from Congress, but since that is not going to happen, I think that the user fee agreement is essential and a lot of the issues we will deal with by improving the—

Mr. BURGESS. Let me interrupt you in the interest of time because they just called a vote. Dr. Jaffe, you describe a world in which the risk-averse nature of the agency charged with protecting

the public interest, the risk-averse nature has damaged your business model. Is that correct? Did I misinterpret that?

Mr. JAFFE. Yes, Dr. Burgess.

Mr. BURGESS. And Dr. Kesselheim, your view seemed to be that it doesn't matter about the damage because these companies are out there trying to push products out on the American public, the unsuspecting American public that are bad products and the FDA has to stand as the last bastion of defense against the industry and these bad products. Did I miss something in the testimony of two individuals?

Mr. KESSELHEIM. Well, so I would first say that for many products in the 510(k) clearance process, for 95 percent of products the time to market in the United States and the European Union is not different, that what we are talking about are the highest risk products that arrive at the E.U. market sooner, and I think as I said before, the essential reason for that is that they are just not being tested for efficacy and for—

Mr. BURGESS. Dr. Jaffe, do you agree with that?

Mr. JAFFE. I don't fully agree with that, I must say. You know, we do go to Europe early because there is a more straightforward path but we do test products in Europe. They do have to have data to get approved. We have a company selling in Europe a leadless cardiac defibrillator which could be a major improvement over the problems we have had with leads here in the United States. That product has been on the market for 3 years in Europe and it will probably be several more years before it is approved here.

Mr. BURGESS. Now, let me ask you something. Do they have a postmarket surveillance program in Europe?

Mr. JAFFE. The company has continued to do studies but I am not sure—I am not directly involved in it. I don't know if they are required to but the company has continued to do studies of that product both in Europe and it has completed a clinical trial here in the United States which is submitted.

Mr. BURGESS. Now, will that company be able to use any of that data when it goes to the FDA to present its case?

Mr. JAFFE. I do not know the answer to that question. I am not directly involved.

Mr. BURGESS. Mr. Hall, do you know?

Mr. HALL. It is possible, assuming that it meets the U.S. criteria for informed consent, data, validity, etc., but there are many situations where data can be used.

Mr. BURGESS. Now, I have got a list of a number of things where the postmarketing authority exists in the device world and is missing from the drug world. Now, there are some things where drugs and devices share some postmarketing authority, things like adulteration, misbranding, manufacturer changes both drugs and devices are required to report but you look at things like classification based on risk, devices have it, drugs don't; user reporting, devices have it, drugs don't; reports of removals or corrections, devices have it, drugs don't; tracking, devices have it, drugs don't. I mean, it looks like the Food and Drug Administration is already applying many of these standards in the device world maybe even a little bit more stringently than the drug world. Do you agree with that, Mr. Hall?

Mr. HALL. There are obviously a number of differences between drugs and devices. The agency has a plethora of postmarket authorities in the device world. Some of them do not exist in the drug world. In part, that is because of the differences between drugs and devices. You don't have an implantable drug, you know, as a general rule.

Mr. BURGESS. You do for some hormonal agents.

Mr. HALL. As a general rule, is what I am trying to say.

Mr. PITTS. The Chair thanks the gentleman and recognizes the ranking member emeritus—I mean ranking member of the full committee, Mr. Waxman, for 5 minutes.

Mr. WAXMAN. Thank you. I will be emeritus when we get the control back and then I will be chairman, but thank you very much for calling on me and I thank this panel for their testimony. I had a chance to review some of the testimony, and I have had my staff here throughout your presentation.

Dr. Kesselheim, I must express alarm over your article describing the harms caused by the devices approved in Europe first and then later found to be ineffective or, worse, harmful to patients. This is important information for us to have given that so many in the device industry have complained that FDA is depriving Americans of the innovative devices patients in the E.U. get so early. Obviously as you have shown, this is not always such a good thing. Your New England Journal article also describes what are some critical fundamental differences between the E.U. and the U.S. systems. You say that “the E.U. system is a part of a framework for commerce which originated as a means of streamlining trade and coordinating manufacturing, safety, and environmental standards” in the E.U. Your article also states that so-called notified bodies, which are for-profit independent companies that specialize in evaluating many products, not just medical devices, are not “designed to work as public health agencies,” and the approval standards in the E.U. are quite different from ours. Device manufacturers have only to prove that the device works as intended, not that it is effective at treating or curing the particular indicated condition.

So yet in recent months, many have argued that we should reformulate our device regulatory system so that it more closely resembles the E.U. Let me ask you, based on what you have learned from your study, do you agree that we should look to the European system as a model for how we regulate devices in the United States?

Mr. KESSELHEIM. Absolutely not. You know, there is no evidence that I have found in all the places that I have looked that suggests that the model for device approval in the E.U. in any way benefits patients overall as compared to the U.S. system, and indeed these notified bodies have major problems with conflicts of interest and their independence, and in fact, they only evaluate devices for approval whereas the competent authorities in the E.U. are the ones charged with safety evaluations. So the safety and the approval evaluations in the E.U. are separate and that is just not the way to effectively protect the public health.

Mr. WAXMAN. Some of the bills that are being proposed change FDA device regulation to make our system look a lot more like the

E.U. system. Let me ask you about one of them that would expand the device center's so-called third-party review program. Currently, that program permits third parties to review certain 510(k) applications and provide recommendations to FDA on whether the agency should clear a particular device. FDA has 30 days in which to make a final decision, but it is FDA that has the final say. That is existing law. One bill has an alteration of the scheme to make the third party's recommendation binding on FDA if FDA fails to respond in 30 days. The bill would also expand the types of devices that these third parties are permitted to review to include "permanently implantable or life-sustaining or supporting devices." These outside reviewers are not currently allowed to review these devices.

Dr. Kesselheim, as an expert on the U.S. and E.U. systems of medical device oversight, do you believe this legislation is a move in the right direction? Would you be concerned about these kinds of changes to the program?

Mr. KESSELHEIM. Yes, I believe this is definitely a move in the wrong direction, and I would be concerned about these types of changes. First of all, there is plenty of peer-reviewed evidence showing in the drug realm that decisions made at the end of a fixed regulatory period end up more likely leading to drugs that have safety problems later on down the road, so imposing this 30-day fixed time limit on the FDA in terms of devices is bad policy, and I also think that increasing the role of these independent agents into the evaluation of the most highest-risk devices would again move us more towards the E.U. equivalent, notified bodies, and it would be bad policy, and there is very little individual oversight of what these notified bodies are able to do. Manufacturers are able to game the system in a way and select which notified bodies they want to based on which are known to provide a faster path to approval, and I just think it would be a bad idea.

Mr. WAXMAN. It is ironic that Governor Romney is attacking President Obama saying he wants us to be more like the Europeans. That may or may not be right, but in this case, we don't want to be more like the Europeans. The FDA gives a seal of approval that is respected all around the world for our drugs and devices and we are better able to protect the public health with our present system.

Mr. KESSELHEIM. Indeed, I do, and in fact, a lot of the European authorities rely on the studies done for FDA approval in order to make decisions about payments and use of the devices there. So indeed, you know, authorities around the world rely on the FDA system.

Mr. WAXMAN. Thank you, Mr. Chairman.

Mr. PITTS. The Chair thanks the gentleman. We are going to try to wrap this up. We are in the middle of a vote. Dr. Cassidy, 5 minutes for questions.

Mr. CASSIDY. So Mr. Hall and Dr. Jaffe, just to be on record, are you all in favor of this bill, the number three, if you will?

Mr. JAFFE. The MDUFA reauthorization? Yes.

Mr. CASSIDY. And Mr. Hall, are you?

Mr. HALL. The agency needs adequate resources. I am Don Quijote on this. I prefer the funding to be from public sources. I recognize the practical aspects and problems with that right now.

Mr. CASSIDY. OK. That sounds good.

Now, Dr. Kesselheim, I think William Moser said let us use our drugs while they still work, and that was obviously way back when, when there was poor regulation. You suggest it still may be true in Europe of medical devices. And Dr. Jaffe, obviously there is tension there that was earlier alluded to. I am way out of field. I am a gastroenterologist. But don't I recall something—I was looking at but I couldn't find it—that there was an artificial disc that was being used by maybe orthopods or spine surgeons that had been implanted in lots of folks and turned out not to be efficacious?

Mr. KESSELHEIM. As far as I am concerned, yes, there have been examples of those sorts of orthopedic spine devices that turn out later to have been unsafe or not work, yes.

Mr. CASSIDY. Now, Dr. Jaffe, how would you—understanding there has to be a kind of movement towards innovation but understanding that there are these instances where things are not efficacious, that they are approved and they are put in a lot of people and they cost a lot of money. How would you balance that tension?

Mr. JAFFE. Congressman, I just wanted to say clearly that we have not advocated for any type of European system here in the United States, and we still believe in the importance of good clinical safety and efficacy studies. The challenges we have with the FDA are less around those standards than they are about the unpredictability and the delays and the difficulty in getting decisions made that cost our companies millions that stretch time frames in a great distance.

Mr. CASSIDY. So you are not so concerned with the paradigm that they use, rather how they implement it, if you will?

Mr. JAFFE. Exactly. It is more their internal management. That is why these guidance documents that Dr. Shuren referred to are so important, making the clinical risk-benefit determination much more transparent and clear and accountable so we can review over time, make sure that we are in agreement to start and we are in agreement at the end of the process using the same standards because we have seen standards change as reviewers change. We have seen delays in getting to decisions. We see—

Mr. CASSIDY. I have limited time, so Dr. Kesselheim, again, I am just kind of curious about this, and again, I am trying to dig from the recesses of my memory, so if I say something stupid, it won't be the first time. Somebody has pointed out to me that some of the things that are approved, maybe certain types of stents for cardiac disease, turn out not to be efficacious but there is no vested interest in terms of learning efficacy in terms of your outcome data is—if your outcome data is mortality, it is a long study, very expensive, etc. Surrogates may not be adequate markers for the ultimate outcome. And Dr. Sedrakyan, I think I saw you nodding your head. Would you all comment on that? Because again, I am trying to understand this issue. I am not challenging anybody. I am just trying to understand.

Mr. SEDRAKYAN. I can answer that. In many situations, it is possible that a device will take time until side effects will develop, and a large number of products will be already on the market with consequences for public health. Now, the best answer to that kind of

problem is to have a worldwide network that will help us determine the side effects early.

Mr. CASSIDY. But side effects is lack of clinical efficacy. It may decrease angina, for example, but it may not prolong life. Do we need 10,000 people and 5,000 get a stent and 5,000 don't? Do you see what I am saying? Can we use surrogate markers?

Mr. KESSELHEIM. I mean, I think that there are surrogate markers that have been validated as relatively well predicting final outcomes, and in those cases, surrogate markers are useful. There are also, you know, new techniques for doing randomized trials in detecting efficacy so that they can be done in a more expedited way, and I am also more in favor of promoting an efficient and predictable FDA regulatory process as well, but I think that at the end of the day—

Mr. CASSIDY. Let me cut you off because I told my colleague I would give him the remainder of my time, because I think I got your point.

Mr. BURGESS. I thank the gentleman for yielding.

Dr. Kesselheim, if I could just ask you very quickly, are you currently involved either with the plaintiff or defense in any of the product liability lawsuits involving, say, the artificial hip?

Mr. KESSELHEIM. No.

Mr. BURGESS. And the same question to you, Dr. Sedrakyan?

Mr. SEDRAKYAN. No.

Mr. BURGESS. Mr. Shull, let me just ask you, your story is very compelling. Certainly at some point there has been a lawsuit involved, I would assume.

Mr. SHULL. Yes.

Mr. BURGESS. And currently your lawsuit is against whom?

Mr. SHULL. It has settled.

Mr. BURGESS. With whom did you settle?

Mr. SHULL. That would be the doctor.

Mr. BURGESS. Was the product you referenced in your case, was that product ultimately recalled from the market?

Mr. SHULL. No, it was never recalled.

Mr. BURGESS. Did you file suit against the company?

Mr. SHULL. I did, but the product was deemed used off label and—

Mr. BURGESS. So it was the physician involved, not the company?

Mr. SHULL. The company exchanged testimony for me to drop the suit against them.

Mr. BURGESS. All right. I thank you for that.

I will yield back, Mr. Chairman.

Mr. PITTS. The Chair thanks the gentleman. We have a unanimous consent request.

Mr. PALLONE. Mr. Chairman, I would ask unanimous consent to enter into the record first the testimony from Public Citizen; second, testimony from American Congress of Obstetricians and Gynecologists; and third, two New England Journal of Medicine articles, one, "Postmarketing Surveillance of Medical Devices—Filling in the Gaps," and second, "Regulation of Medical Devices in the United States and European Union."

Mr. PITTS. Have you shared that with us?

Mr. PALLONE. Yes.

Mr. PITTS. Without objection, so ordered.
[The information follows:]



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**Statement of Michael A. Carome, M.D., Deputy Director, and
Sidney M. Wolfe, M.D., Director
Public Citizen's Health Research Group**

**Hearing on Reauthorization of MDUFA:
What It Means for Jobs, Innovation and Patients
Subcommittee on Health of the House Energy and Commerce Committee
February 15, 2012**

On behalf of Public Citizen's more than 250,000 members and supporters nationwide, we thank the Subcommittee on Health of the House Energy and Commerce Committee for the opportunity to share our views on the regulatory oversight of medical devices by the Food and Drug Administration (FDA). For 35 years, Public Citizen's Health Research Group has been involved in research-based consumer advocacy work related to medical device safety.

As the debate on the reauthorization of the Medical Device User Fee Act (MDUFA) has approached, members of Congress have introduced more than a dozen bills, most of which aim to ease the approval and clearance processes for medical devices, often by weakening measures intended to ensure patient safety. The bills reflect the medical device industry's concerted lobbying campaign to expedite medical devices' path to the marketplace during a time in which the debate over MDUFA is shining a spotlight on issues surrounding the FDA. Specifically, the bills aim to accelerate approval and clearance times by such means as:

- further lowering the already weak standards for clearing and approving medical devices;
- substantially weakening the "conflict of interest" prohibition for serving on the FDA advisory committee that oversees device approvals. This would allow more people to review applications for which they have a vested financial interest related to the medical devices under review by the committee;
- expanding the pool of third-party companies that can review device applications to include those with significant financial relationships with the device industry;
- requiring the FDA to rule on third-party reviews of a device within 30 days or grant automatic approval of the device on the 31st day, which would result in the elimination of independent oversight by FDA officials for many devices;
- prohibiting the FDA from disapproving of the methods used in any type of clinical trial conducted by a medical device company. This would include clinical trials conducted on human subjects.

Recent history is replete with examples of devices that were approved or cleared for marketing by the FDA without adequate premarket testing and subsequently caused serious harm to

hundreds or thousands of patients, with some cases resulting in death. Some of these devices have subsequently been recalled, others have not. Furthermore, the history of FDA's postmarket surveillance and enforcement activities for marketed medical devices reveals a consistent pattern of failure to adequately monitor and analyze adverse events related to devices and to remove devices from the market after serious safety signals have become readily apparent. Passage of many of the bills related to medical devices recently introduced in Congress, with few exceptions, would undoubtedly accelerate the rate of patient casualties resulting from unsafe and ineffective medical devices.

We urge subcommittee members to support alternative bills, such as H.R. 3847, the Safety of Untested and New Devices Act (the SOUND Devices Act) of 2012, that would improve patient safety — rather than threaten it. In particular, further legislation is needed requiring the FDA to promulgate new regulations for the premarket approval of medical devices that include mandates for appropriate premarket clinical testing for safety and effectiveness for all moderate- to high-risk medical devices, especially those that are intended to be life-sustaining, life-supporting, or permanently implanted. These are requirements we have advocated for the past 35 years.

I. Major Deficiencies Regarding Current Medical Device Oversight

A. Problems with the premarket approval (PMA) process

Medical devices reviewed by the FDA under the current PMA process generally present the highest level of risk among devices proposed for marketing, many of which are life-sustaining, life-supporting, or permanently implanted. For many such devices, the risks are at least equivalent to, and in many cases significantly greater than, the risks associated with many new drugs. Nevertheless, the current statutory standard for approving or clearing any medical device is “a reasonable assurance of . . . safety and effectiveness,” which is significantly lower than the statutory standard required for approval of a new drug: “substantial evidence” of effectiveness based on “adequate and well-controlled investigations, including clinical investigations” and evidence of safety based on “adequate tests by all methods reasonably applicable to show . . . [that] such drug is safe for use” (21 U.S.C. § 355[d]). In practice, for most new drugs, at least two well-designed, randomized, controlled, phase 3 clinical trials are required. In contrast, for most medical devices approved under the PMA process, only one controlled study is required by the FDA, and in many cases, the quality of the design of such device studies is subject to a lower standard than that for most clinical trials for drugs (e.g., many are not randomized and use retrospective control groups).

The current low standard for PMA approvals already puts patients at risk by allowing approvals based on poorly designed, uncontrolled trials. In a paper recently published in a peer-reviewed scientific journal, researchers with Public Citizen's Health Research Group described one example of how the FDA's current lower standard for approving medical devices via the PMA process allowed an ineffective, high-risk, implanted medical device to be approved for marketing:¹

Consider the vagus nerve stimulator (VNS), a surgically implanted device for treatment-resistant depression. In the only randomized controlled trial (RCT), the device did not

demonstrate a statistically significant benefit on the primary measure of depression at ten weeks ($p = 0.25$). However, in its PMA application, the company relied on follow-up data at one year in which treated patients were claimed to have improved more than a non-randomized, unblinded, non-concurrent control group ($p < 0.001$); both groups were also permitted co-interventions. A psychopharmacology expert in the FDA's drug center advised [the Center for Devices and Radiological Health (CDRH)] that, with similar data for an antidepressant drug, the center would not have permitted the filing of [a new drug application], adding, "it is artificial to us to consider one study for a device (that is negative on face) as sufficient to provide evidence for regulatory efficacy when we require positive studies for a drug." While CDRH initially issued a non-approvable letter, the director of CDRH reversed this decision and approved the device, overruling more than 20 FDA scientists and officials.

Subsequently, the Centers for Medicare and Medicaid Services determined that VNS was not "reasonable and necessary," the standard for reimbursement under Medicare. Moreover, it did "not believe there is a treatment benefit directly attributable to VNS." Other third-party payers have also denied coverage for this expensive device.

Recently introduced legislation would seriously undermine standards for PMA approval that are already too weak by explicitly encouraging the FDA to approve PMA applications based on data from studies other than randomized, controlled clinical trials.

From a medical perspective, there is no reasonable substitute for well-designed, randomized, controlled clinical trials in human subjects for assessing the safety, effectiveness, and long-term durability of high-risk medical devices. Pre-clinical bench and animal testing, although important, are insufficient for determining how such devices will perform in human patients. Indeed, the necessity for well-controlled clinical studies has increased over the past few decades as medical devices have become increasingly complex.

Recent experience with metal-on-metal hip implants, such as the DePuy (Johnson & Johnson) ASR XL Acetabular System (ASR), shows the threat to patients when devices are approved without appropriate premarket clinical testing. Metal-on-metal hip implants are devices whose ball-and-socket joints are made solely from metals like cobalt and chromium, in contrast to older hip implants made of other materials, such as metal and plastic. While the FDA could potentially require PMA applications for these high-risk, permanently implanted devices, a current regulatory loophole allows them to be approved through the 510(k) premarket clearance process, which, as discussed below, does not require well-designed, randomized, controlled clinical trials in human subjects. Although these devices appeared to be safe in bench tests, when placed in the human body, the devices can quickly begin to wear, depositing metallic debris in the surrounding tissues that causes severe soft tissue and bone damage.² For example, the DePuy ASR hip implant was cleared for marketing in 2005 under the 510(k) process without undergoing any clinical testing. After being permanently implanted in nearly 100,000 patients, the device was recalled in 2010 because of serious problems related to premature failure of the device due to erosion of the metal joint surface and migration of metallic particles into the surrounding tissues and blood-stream.^{3,4} The end result has been characterized by some leading academic physicians as a "public health nightmare."⁴ To prevent such public health disasters, all implanted hip

devices should undergo testing in well-designed, randomized, controlled clinical trials to assess their safety, effectiveness, and long-term durability.

Likewise, the history of the FDA's approval and the subsequent marketing of the Wingspan Stent System with Gateway PTA Balloon Catheter (the Wingspan Stent System) provides another dramatic example of the serious harms that can occur in patients when a high-risk medical device that normally would require approval under the PMA process is instead approved under even lower standards, without adequate premarket clinical testing. On August 3, 2005, the FDA approved the humanitarian device exemption (HDE) application for the Wingspan Stent System for the treatment of patients having 50% or greater stenosis (narrowing) of intracranial arteries (blood vessels that supply blood to the brain) due to atherosclerosis and refractory to medical therapy.⁵ Under an HDE application, the sponsor was exempt from the effectiveness requirements of a PMA.⁶ In this case, the only clinical data provided to FDA prior to approving the Wingspan Stent System was derived from one uncontrolled, single-arm study involving 44 patients who underwent treatment with the device.⁷ Such a study was woefully insufficient for establishing a reasonable assurance that this high-risk device was safe, let alone effective.

Although approval of the Wingspan Stent System under an HDE application may have been appropriate, the subsequent history of this device demonstrates the type of dangers that may result if Congress passes legislation allowing high-risk devices to be approved under the PMA process without adequate premarket testing through well-designed, randomized, controlled clinical trials. Results recently published in the *New England Journal of Medicine* from a well-designed, randomized, controlled, multicenter study funded by the National Institute of Neurological Disorders and Stroke demonstrated that the Wingspan Stent System is neither safe nor effective.⁸ In this study, patients who had 70-99% narrowing of intracranial arteries and were at high risk of stroke were randomized to receive interventions with aggressive medical therapy plus the Wingspan Stent System or aggressive medical therapy alone. Subjects randomized to the Wingspan Stent System group had a more than two fold-higher incidence of stroke or death in comparison to subjects receiving aggressive medical therapy alone (14.7% versus 5.8%) — a contrast so striking the researchers were forced to stop enrollment in the trial for ethical reasons. Had data from such a study been submitted to the FDA prior to the agency's approval of the Wingspan Stent System, the FDA almost certainly would not have found reasonable assurance that the device was safe and effective and would have denied approval for this unsafe device. Because of the failure to conduct such a well-designed study prior to marketing, it is certain that many patients suffered from strokes and died because they were treated with this inadequately tested device.

Furthermore, the language of some of the recently introduced bills is also flawed because they encourage "the use of surrogate endpoints" as an alternative to "randomized, controlled trials," whereas the use of surrogate endpoints is, in fact, a frequently used method for measuring endpoints in such clinical trials. We note, however, that for most high-risk devices approved under the PMA process, surrogate endpoints would not be reasonable clinical trial markers for assessing safety and efficacy. Direct, clinically relevant endpoints such as mortality and morbidity endpoints (e.g., strokes in subjects undergoing a carotid artery stent procedure) would be more appropriate for most clinical trials of high-risk devices.

Finally, the assessment of the safety and effectiveness of today's complex, high-risk medical devices demands significant time and effort by FDA review staff. Statutory requirements that pressure the agency to carry out reviews more quickly, such as those proposed in some of the recently introduced legislation, will likely result in short-cuts being taken by FDA staff. Inevitably, patients would be harmed by increased exposure to unsafe and ineffective devices.

B. Problems with the 510(k) premarket clearance process and the determination of substantial equivalence

The 510(k) premarket clearance process is the pathway by which approximately 94% of moderate-risk and many high-risk medical devices — including many that are life-sustaining, life-supporting, or permanently implanted — reach the U.S. market.⁹ Under the current 510(k) process, the proposed device must be found to be “substantially equivalent” to a predicate device already on the market. Substantial equivalence is evaluated according to the intended use of the device and its technological characteristics (21 U.S.C. § 360c[i][1]).

For most medical devices cleared under the 510(k) process, no clinical trials assessing the safety or effectiveness of the devices in humans are conducted prior to clearance for marketing. Furthermore, once a device had been cleared through the 510(k) process, it may serve as a predicate device for subsequent 510(k) submissions, even if the predicate device has subsequently been withdrawn from the market because it was shown to be dangerous or ineffective.

Again, recently introduced legislation would further weaken the 510(k) process by not only retaining the grossly inadequate legal standard — substantial equivalence to a predicate device already on the market — used by the FDA for clearing medical devices under the 510(k) process, but also by constraining the agency's authority to consider important information relevant to the safety and effectiveness of medical devices and by pressuring the agency to take shortcuts to meet the demands for an accelerated review process for increasingly complex medical devices.

The highly respected Institute of Medicine (IOM) in its recently issued report *Medical Devices and the Public's Health: The FDA 510(k) Clearance Process at 35 Years*,⁹ criticized the major underpinnings of the 510(k) premarket clearance process more broadly. After extensive, careful study, the IOM concluded that the FDA's 510(k) process for clearing medical devices is fatally flawed and cannot be fixed. In particular, the IOM found the following:

The 510(k) clearance process is not intended to evaluate the safety and effectiveness of medical devices with some exceptions. 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. [emphasis in original]

The IOM fully articulated a compelling and irrefutable rationale for this conclusion. To address its primary conclusion, the IOM recommended the following:

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. [emphasis in original]

Public Citizen strongly agrees with the IOM.

The fundamental failure of the 510(k) process to protect the American public from dangerous and ineffective medical devices has been demonstrated again and again, as numerous devices approved under the 510(k) process have resulted in large-scale harms to patients and many had to be recalled because of their dangers.

For example, over the past decade, multiple synthetic, non-absorbable surgical mesh products designed for transvaginal surgical repair of pelvic organ prolapse (POP) have been cleared by the FDA under the 510(k) process, based on the standard of substantial equivalence to predicate devices. Randomized, controlled studies done after these devices were cleared for marketing under the 510(k) process have shown that while transvaginal POP repair with mesh appears to result in less prolapse being detected on pelvic examination following surgery in comparison to non-mesh repair procedures, the use of mesh does not provide any better outcomes in terms of relief of symptoms and quality of life measures, which ultimately are the clinically significant indicators for measuring treatment success for this condition.¹⁰ Moreover, with respect to safety, a review of the scientific literature demonstrates that use of the non-absorbable, synthetic mesh products for transvaginal surgical repair of POP leads to a high rate of serious complications, many of which require additional surgical intervention and some of which are not amenable to surgical correction and result in permanent life-altering harm to women.¹¹

The experience with non-absorbable surgical mesh products for transvaginal POP repair exposes the fundamental failure of the 510(k) premarket notification process to protect the public's health and welfare. Multiple mesh devices specifically designed for transvaginal POP repair were allowed by the FDA to come onto the U.S. market, based only on in vitro and animal-testing data and a determination of substantial equivalence to other surgical mesh products already on the market. Despite a complete lack of clinical data demonstrating that any of these invasive mesh devices was reasonably safe and effective for transvaginal repair of POP, these devices have been heavily promoted by industry and its well-compensated physician consultants. As a result, thousands of women have been seriously harmed, many permanently. Had appropriate premarket clinical trials, like those conducted in the postmarket period, been conducted before the FDA cleared these products for marketing under the 510(k) process, serious harms to these women could have been prevented.

C. Problems with the FDA's postmarket surveillance and enforcement activities

In addition to allowing too many dangerous devices to reach the market, the FDA has also proven inadequate at mitigating the damage from dangerous devices that are in use after evidence of serious adverse events caused by marketed devices becomes apparent.

The current state of postmarket surveillance is ineffective and wasteful. The agency must depend on manufacturers and users such as hospitals to report events of injury or death related to the use of their devices. Manufacturers, in turn, are often unable to locate patients who have been implanted with dangerous devices because they generally do not track which patients have been implanted with their products.

For its part, the FDA has been criticized for making poor use of the data it receives from device manufacturers concerning recalled products. It lacks an internal system to analyze recall trends, which it might otherwise use in future decisions when reviewing a device for PMA approval or 510(k) clearance.

The FDA also has been criticized for failing to take enforcement actions when evidence of unacceptable harm caused by a device becomes apparent or manufacturers violate the law. The IOM, for example, concluded: "When the FDA discovers violations of the law or products that pose unacceptable risks to consumers, it has a wide variety of authorities (or tools) available to try to remedy the situation and to sanction the violators. The committee found that the agency uses those authorities sparingly."¹¹

Finally, the prospect of product-safety litigation is theoretically a deterrent to selling unsafe or faulty products. But, in the realm of medical devices, manufacturers enjoy an enormous liability shield. The Medical Device Amendments of 1976 prevent states from establishing "any requirement" that is "different from, or in addition to" requirements in the federal statute that relate "to the safety or effectiveness of the device."¹² In 2008, in *Riegel v. Medtronic*, the Supreme Court cited the 1976 Medical Device Amendments and ruled that federal law preempts all state civil court claims arising from allegedly defective devices, as long as the device in question was approved under the PMA process and the manufacturer followed proper procedure in its application. The result: if the FDA approves a dangerous or defective device through the PMA process, federal law generally prevents consumers harmed by the device from seeking redress in court.

II. Proposals for Improving Medical Device Safety

Ensuring that the medical devices used to treat patients in the U.S. are safe and effective should be the paramount goal of any new medical-device legislation. Patients in the U.S. deserve legislation that improves the review of the safety and efficacy of these devices, instead of weakening it.

The dangers and weaknesses of the existing flawed systems for both premarket review and post-market surveillance of medical devices are readily apparent. On one hand, the current premarket regulation of devices has repeatedly failed to prevent unsafe devices from reaching the market

and injuring and killing patients. On the other hand, devices unequivocally shown to be unsafe after being cleared or approved by the FDA are not being removed from the market in a timely and efficient manner by the agency. Strengthening of applicable Federal statutes and the FDA's policies and practices for reviewing and monitoring devices needs to occur in order to increase the agency's ability to protect the public.

A. Premarket Review Processes

Replace the 510(k) process (long-term action). Congress should mandate, in accordance with the IOM's recommendation, that the FDA obtain the necessary information to design a new medical device approval process to replace the 510(k) process. No future medical device premarket review system should rely on "substantial equivalence" to a device already on the market as evidence of safety and effectiveness. Instead, moderate- to high-risk devices, particularly those intended to be life-sustaining, life-supporting, or permanently implanted, should be subject to the same regulatory scrutiny as drugs. Review decisions should rely on "substantial evidence" to support a device's safety and effectiveness.

Modify the 510(k) process (interim, short-term action). Recognizing that replacing the current 510(k) system will take several years to implement, the following revisions to the process should be implemented immediately to improve the safety of medical devices:

- When a device cleared through the 510(k) device is recalled or removed from the market due to safety or effectiveness problems, that device should automatically be removed from the list of devices that can serve as a predicate for a proposed class II device.
- Require manufacturers to provide the FDA with information not just about the immediate predicate device on which a 510(k) clearance request is based, but about the full lineage of predicates.
- To facilitate efficient and effective tracking of the status of marketed devices that a manufacturer might use as a predicate for a proposed device, require the FDA to maintain an up-to-date and easily searchable database of eligible predicates.
- Require the FDA to reevaluate the safety and effectiveness of devices previously cleared under the 510(k) process whenever a device that served as the predicate for those 510(k) clearances is withdrawn from the market due to safety or effectiveness problems. This reevaluation should include any device cleared under the 510(k) process that can be traced back through a chain of 510(k) clearances to the predicate device no longer on the market. This requirement should be imposed retroactively on all devices previously cleared under the 510(k) process.
- Prohibit the clearance of any class III device under the 510(k) process.
- Provide the FDA with authority to require postmarketing surveillance studies, including clinical studies, as a condition of clearance of a device under the 510(k) process

Revise the PMA process. The standard for approving any class III device under the PMA process should be changed to "substantial evidence" of safety and effectiveness. Device submissions reviewed under the PMA process should provide data from at least two well-designed, randomized, controlled, clinical trials conducted by qualified experts that can evaluate the true safety and effectiveness of that device. The current low standard threatens patient safety

when data from poorly designed and uncontrolled clinical trials are considered to be acceptable evidence for establishing the safety and effectiveness of a device during the review process.

Drop the least-burdensome requirement. For all submissions, the requirement that the FDA evaluate devices in a manner that is “least burdensome” upon manufacturers should be eliminated. It is in the best interests of patients for the FDA to make its judgments based on all necessary information.

B. Post-Market Surveillance

Improve device tracking to patients. At present, when a device is recalled because it poses a hazard, no reliable system exists to locate affected patients because, unlike drugs and most other consumer products, medical devices in most cases are not given unique identifier codes that would allow for efficient and effective tracking. Under the current system, most companies only track devices to distributors or user-facilities. Without unique device identifiers, reliable tracking of devices to entities beyond the distributors and to patients is difficult, if not impossible. There are more efficient tracking systems in place for appliances, automobile parts and even pet food today, than there are for medical devices. Under the Food and Drug Administration Amendments Act of 2007, Congress mandated that the FDA establish a unique identification system for medical devices. In the almost five years since the Amendments became law, the FDA has failed to issue regulations implementing this system. Congress should set a deadline in the near future for the FDA to implement such regulations for all devices that pose a moderate- to high-risk to the patients intended to use them.

Improve adverse-event reporting. The FDA should require more thorough standards for reporting adverse events, similar to those used for pharmaceuticals. At present, manufacturers tend to under-report and user-facilities tend to over-report adverse events, but with insufficient specificity. Higher quality mandatory reporting would give the FDA a better database of adverse event information to analyze.

FDA should assert authority in policing unsafe devices. At present, the FDA typically relies on manufacturers to report problems with devices. The FDA often, as in the case of the Wingspan Stent System, has failed to act in the face of convincing evidence that proves certain devices to be unsafe. The agency should utilize more often and more promptly its authority to order recalls of medical devices when the agency deems them to compromise patient safety. All too often, the agency relies on device manufacturers to take action voluntarily, resulting in substantial delays in removing dangerous and ineffective devices from the market.

A recall should be a recall. When a manufacturer does initiate a voluntary recall, the recall must mean the removal of the suspected defective device from market. Communications to customers or user-facilities, like sending warning letters to hospitals, should not be classified as a recall.

Systematically analyze and track recalls. The FDA should be required to systematically collect and assess data regarding all medical device recalls, whether mandated by the agency or voluntarily implemented by manufacturers. As part of this analysis, the agency should determine whether recalls were implemented in an effective and timely manner in order to ensure patient

safety. The FDA also should document the basis for any termination of a recall ordered by the agency. All such information regarding the analysis and tracking of recalls should be maintained in a publicly accessible database on the agency's website.

Restore patients' legal rights. Finally, Congress should pass legislation to restore injured patients' ability to bring claims for injuries caused by defective medical devices. A 2008 Supreme Court decision, *Riegel v. Medtronic*, had held that pre-market approval of a medical device by the FDA preempted most state tort law claims against the device manufacturer. The decision removed a vital and long-standing component of the consumer safety net for medical devices. As a result, patients harmed by unsafe devices are often deprived of their only avenue for seeking compensation for their injuries.

The mechanisms of public safety are failing to protect the public from dangerous devices and instead are protecting device manufacturers' pocketbooks from both proper FDA regulation and from being held accountable in court.

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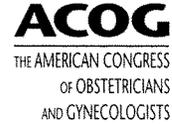
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Written Statement

**On Behalf of the American Urogynecologic Society and
the American Congress of Obstetricians and Gynecologists**

House Energy and Commerce Committee, Subcommittee on Health

**Hearing: Reauthorization of Medical Device User Fee and Modernization Act MDUFA: What It Means
for Jobs, Innovation and Patients**

February 15, 2012

The American Urogynecologic Society (AUGS) and the American Congress of Obstetricians and Gynecologists (ACOG) thank the Subcommittee for the opportunity to submit comments for the record regarding the re-authorization of MDUFA and the impact on women given the recent actions by the Food and Drug Administration with regard to the safety and effectiveness of transvaginal surgical mesh used for repair of pelvic organ prolapse and stress urinary incontinence.

Founded in 1979, the American Urogynecologic Society (AUGS) is a professional organization of 1,400 physicians and allied health professionals who are dedicated to caring for women with pelvic floor disorders that include pelvic organ prolapse (POP) and stress urinary incontinence (SUI).

The American Congress of Obstetricians and Gynecologists (ACOG) is a national medical organization representing over 57,000 members dedicated to the advancement of women's health care through continuing medical education, practice, research and advocacy.

Pelvic Organ Prolapse (POP) is a prevalent condition that can substantially affect a woman's quality of life. A woman's lifetime risk of surgery for POP is approximately 7%, and over 300,000 prolapse surgeries are performed annually in the USA.^(1,2) Of those who receive surgery, an estimated 13% will require a repeat operation within 5 years, and as many as 29% will undergo another surgery for genital prolapse or a related condition at some point during their life.^(2,3) Prolapse of the anterior vaginal wall, or cystocele, is the most common form of pelvic organ prolapse and the most likely to recur after surgery.^(1,2) Reinforcement of vaginal repairs with synthetic mesh has been widely employed in the hope of improving the effectiveness and durability of vaginal prolapse repairs, with almost one-quarter of all prolapse repairs currently involving the placement of transvaginal mesh.

Urinary incontinence affects up to a third of US women. Stress urinary incontinence (SUI) is the most common type of urinary incontinence in women under 60 and accounts for at least half of incontinence in all women. Surgery is an important and effective treatment for SUI in women, with over 210,000 women receiving surgery for this indication each year.⁽⁴⁾ Midurethral slings using synthetic mesh, placed via either a retropubic or transobturator approach, represent the current standard of care for the surgical treatment of SUI.

More information on SUI, POP and transvaginal mesh can be found at www.voicesforpfd.org.

As the largest professional organizations dedicated to caring for women with pelvic floor disorders including pelvic organ prolapse (POP) and stress urinary incontinence (SUI), AUGS and ACOG make the following recommendations to the Health Subcommittee regarding the re-authorization of MDUFA and the resources,

expertise, and authority needed at the Food and Drug Administration to ensure the safe and effective use of transvaginal mesh for POP and SUI.

More Resources Needed at the FDA:

Ensuring the safe and effective use of transvaginal mesh for POP and SUI is a complicated and time and expertise intensive undertaking. It is imperative that the FDA have staff with particular expertise and adequate resources to work closely and effectively with medical societies in order to determine the appropriate pathways for clearance of synthetic mesh products. These crucial decisions are based both on the indications and methods of use proposed by the company.

For example, clinical experience and research of synthetic mid-urethral slings for SUI is significantly more mature and provides a more favorable risk-benefit ratio than synthetic mesh for POP. Synthetic mid-urethral slings represent a considerable advance over more traditional non-mesh incontinence surgeries. The safety and efficacy of midurethral slings using synthetic mesh is supported by 15 years of clinical experience and over 40 randomized clinical trials.⁽³⁾ While at the same time, new data suggests that complications from transvaginally placed mesh for POP are more common (10%) and more complex compared to mesh complications associated with mid-urethral slings (1-2%) and abdominally placed mesh for POP (abdominal sacral colpopexy (ASC) (3-4%).

This prompted ACOG, along with AUGS, the Society for Female Urology and Urodynamics (SUFU) and the Society for Gynecologic Surgeons (SGS), to write a letter on December 21, 2010 recommending that the FDA revisit the issue of vaginal mesh complications to further support the development of a registry and consider a new Public Health Notification to increase awareness of this issue with patients and providers. The FDA released its Safety Communication on July 13, 2011 addressing increasing concerns from the public and health care providers as well as advocates for patient safety.

In looking at the method for use, AUGS and ACOG agree that as with synthetic mesh mid-urethral slings the safety and effectiveness of surgical mesh indicated for abdominal sacrocolpopexy (ASC) is well-established and that reclassification of this group of devices is not necessary. Any new products related to mid-urethral slings or ASC can be adequately evaluated using the 510(k) premarket notification.

However, AUGS and ACOG support mandatory clinical studies for transvaginal mesh for POP. Specifically, we support a requirement that premarket notifications (or premarket approval applications) for *transvaginal* mesh for POP include clinical studies that use patient-centered outcomes and which include long-term patient follow up to capture long-term results. We recommend well-designed prospective, cohort studies that include an assessment of clinically-relevant functional, quality of life, and anatomic outcomes, as well as an assessment of adverse events. We also recommend that the clinical trials include a minimum of 1 year follow-up prior to market clearance or approval, with an additional 2-4 years of mandatory patient follow-up and FDA reporting following device clearance, for new vaginal prolapse mesh devices or for significant modifications of existing devices. Randomized, controlled trials may be appropriate in certain cases. Robust comparative effectiveness premarket research studies would hopefully reduce device recalls, poor patient outcomes, and litigation.

This is just one example where the FDA needs the expertise and significant resources to work with companies in determining the appropriate pathway for clearance. For devices where there are numerous methods for clinical use, FDA needs to have the authority to mandate clinical trials where there is a higher level of risk to the patient and higher probability of adverse events.

On a broader scale, AUGS and ACOG support the FDA's interest in reassessing the 510(k) process. The FDA's letter to the IOM in January 2011 in which the agency proposed to seek greater authority to require postmarket surveillance as a condition of clearance for some devices, develop class IIB definitions, and clarify

when a device may no longer be used as a predicate is consistent with the goals of ensuring safe and effective devices for use in caring for women.

Mandatory Postmarket Registry Needed for All Vaginal Mesh Placed for Prolapse:

Surgeons and patients both agree that surgical procedures should be safe and effective. Post-market surveillance currently is voluntary in nature and is not inclusive of all vaginal mesh placed for treatment of prolapse. Without post-market surveillance that includes an assessment of the denominator, or total procedures performed, the risks of vaginal mesh repair of prolapse cannot accurately be determined. **AUGS and ACOG recommend that Congress support FDA in invoking its power under section 522 of the Act to require postmarket surveillance for existing and future transvaginal mesh devices for POP repair.**

In particular, AUGS and ACOG would support a postmarket registry and/or national database for all users of vaginally placed mesh for prolapse, to comprehensively track all outcomes, both positive and negative. This registry should include patient characteristics, intraoperative data-points, device information and post-operative outcomes – both anatomic and subjective at specific time points to assess for both short- and long-term complications. Standardized outcome measures must be determined to allow meaningful comparisons. Until such a registry is created, AUGS and ACOG encourage all surgeons to track their outcomes so that information is available to hospital credentialing committees and insurers. AUGS and ACOG have enthusiastically offered their expertise to the FDA and other regulatory agencies to assist with the development of any such registry including appropriate baseline and outcome measures as well as the timing and nature of assessments.

Support Needed for Increased Research Regarding Vaginal Mesh Procedures:

More research is needed to determine patient selection and patient factors that contribute both to complications and successes of vaginal mesh procedures, as well as the effect of surgeon experience, volume, and technique on outcomes.

Neither native tissue nor vaginal mesh repairs have 100% success rates and neither is free of complications. Associated complications, including dyspareunia, vaginal shortening, and injury to nearby organs, recurrence of prolapse, nerve injury, and bleeding can occur with any pelvic reconstructive surgical treatment, with or without mesh, whether it is conducted abdominally, vaginally, robotically or laparoscopically. No surgery is ever free of all risks and no surgeon, even the most experienced, operates without any complications.

To further determine the risk/benefit ratio of vaginal mesh procedures, quality data are needed. More investigation is needed to explore the mechanisms, through bench research, that underlie the causes of POP; this research should include the effects and results of mesh in the vaginal walls and should evaluate the root causes of mesh erosion and shrinkage. **AUGS and ACOG are supportive of the FDA's call for better data upon which to determine whether or not mesh devices are a safe and effective adjunct device to treat vaginal prolapse. The establishment of a mesh registry/ post-surveillance database will be an important first step in this process.**

In addition, AUGS and ACOG encourage industry, researchers and providers to voluntarily begin comparative effectiveness trials with longer-term patient outcomes on previously-cleared, currently-available devices. Recommendations for comparative effectiveness trials with patient centered outcomes are aligned with the AHRQ's initiatives for development of comparative effectiveness research (CER) and the patient centered outcomes research institute (PCORI).

In conclusion, ensuring patient safety, while still allowing for diagnostic and treatment innovations with an acceptable risk/benefit ratio, is our ultimate goal. We cannot achieve this without all stakeholders, including Congress, our regulatory agencies, health care professionals, and industry, taking an active role. Regarding

the use of transvaginal mesh for the treatment of POP, **the establishment of a national mesh registry/ post-surveillance database will be an important first step in this process.**

Thank you.

For more information: Please contact Matthew Barber, MD, AUGS President at barberm2@ccf.org or (216) 445-0439.

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Perspective

Postmarketing Surveillance of Medical Devices — Filling in the Gaps

Frederic S. Resnic, M.D., and Sharon-Lise T. Normand, Ph.D.

Failures of implantable medical devices, although rare, can carry a substantial risk of serious injury. From 2000 through 2011, more than 150 new high-risk medical devices were approved by the

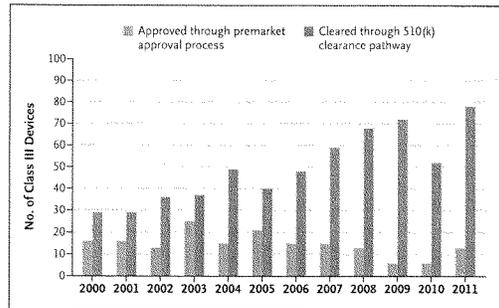
Food and Drug Administration (FDA) through the premarket approval (known as PMA) process, and an additional 600 devices were cleared through the less demanding 510(k) process, in four medical specialty areas (cardiovascular care, neurology, obstetrics and gynecology, and orthopedics; see graph). The problem that Hauser describes (10.1056/NEJMp1114695) — the erosion of the insulation in St. Jude Medical's Riata leads for implantable cardioverter-defibrillators — highlights the fact that medical devices are complex assemblies of multiple components, and the failure of any single com-

ponent can lead to unexpected and serious safety problems. Because it is impossible to design an implantable medical device with zero risk of failure, effective systems for monitoring safety after a device is on the market are essential for protecting the public health. Moreover, since incremental changes are made in medical devices throughout their life cycles, it is impractical to prospectively study each change comprehensively before marketing. Balancing the need for robust postmarketing safety monitoring with the need to avoid the stifling of innovation is a prime responsibility of the Center

for Devices and Radiological Health (CDRH) at the FDA.

The FDA's safety-surveillance strategy has relied on physicians, health care institutions, manufacturers, and patients to report medical device failures and complications through the Medical Device Reporting system. This system can identify unanticipated medical device failures and complications but requires extensive analytic review and has important limitations.¹ Although the CDRH receives more than 100,000 reports annually, the proportion of medical device failures that are registered is estimated to be less than 0.5%; this low reporting rate greatly limits the information available regarding the balance of risk and health improvement associated with a given medical device.²

Several FDA initiatives have



Numbers of High-Risk (Class III) Medical Devices Approved or Cleared by the FDA in Cardiovascular Care, Neurology, Obstetrics and Gynecology, and Orthopedics, 2000–2011.

The proportion of class III devices introduced through the 510(k) clearance pathway, which generally requires little clinical premarketing testing, has increased significantly during the past decade. Therefore, effective and efficient postmarketing surveillance has become ever more important. Data are from the FDA.

been launched to fill the gaps in the passive event-reporting system. In 2002, the CDRH established the Medical Product Safety Network, which represents more than 300 health care institutions that collaborate to identify and investigate trends in device failures and adverse events. In 2007, the FDA was given the regulatory authority to mandate follow-up safety studies after initial market approval (the Section 522 rule) — a change that improves the agency's flexibility to investigate potential safety concerns. In 2009, the FDA launched the Sentinel initiative, a program to integrate the electronic health records of large, representative U.S. populations for postmarketing safety analysis. However, despite great success in linking nearly 100 million claims-based health records, Sentinel projects have thus far focused only on medications — at least in part because of the very limited information about medical devices currently available in billing claims data.

In contrast to drugs, medical devices suffer from a major impediment to safety monitoring: the lack of unique device identifiers (UDIs). To address this limitation, the FDA Amendments Act of 2007 authorized the agency to develop a comprehensive UDI system, which is currently under review within the Office of Management and Budget. As a UDI system is integrated with administrative and claims databases, it will become possible to identify patients who have been exposed to specific devices. However, the complex interplay among device design, the procedural safety of implantation, the learning curve associated with medical devices, and the risks to individual patients will continue to make it difficult to conduct effective and reliable safety surveillance using only billing data.

There are important opportunities to leverage large, disease-specific clinical registries for monitoring device safety. In many countries, such registries are a mandatory component of the

health care system and required for all implantations of high-risk devices. In the United States, there is no national system to ensure that registries exist for high-risk medical devices. Nevertheless, several nonprofit professional medical organizations in the United States have recognized the critical need for medical device registries and have spearheaded their development in an effort to monitor and improve the quality of care. The American College of Cardiology, in conjunction with several partner organizations, has established detailed clinical registries covering many high-risk cardiovascular devices, including coronary stents, implantable defibrillators, and defibrillator leads, which together contain information on approximately 4 million implantation procedures. The recently developed transcatheter heart-valve registry will provide early postmarketing information about the safety of this revolutionary treatment for patients with high-risk aortic-valve stenosis. Clinical registries in cardiac surgery already exist, and newer efforts by professional societies related to orthopedics, ophthalmology, and other fields are under way.

Perhaps the most successful example of a coordinated effort to study newly introduced devices has been the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS), established to capture detailed clinical data on all patients receiving implantable ventricular assist pumps in the United States. Its success is related to the requirement by the Centers for Medicare and Medicaid Services (CMS) that patient information be entered into an audited national registry as a condition of reimbursement. INTERMACS now

serves as a ready infrastructure to support the postapproval study of every new generation of mechanical cardiac support device, saving manufacturers substantial time and resources that they would otherwise have to invest in establishing new systems of data collection, auditing, and analysis.³

Creating and maintaining these detailed clinical registries is challenging and expensive. Many registries are supported by voluntary submissions from health care providers, so hospitals must bear the costs of collecting and submitting information. Emerging standards for electronic health records, including "meaningful use" regulations, will provide unprecedented opportunities for securely mapping clinical information to distributed clinical registries.

But having reliable and complete clinical data is not enough. The development of sound methods and practical tools for monitoring safety over a product's life cycle is essential. We have advocated a strategy of automated prospective surveillance of high-risk implantable devices, using database monitoring tools to support continuous surveillance of clinical registries.⁴ Such tools are capable of monitoring hundreds of high-risk medical devices simultaneously, to maximize efficiency in detecting unrecognized safety problems. Automated surveillance systems constantly watch a growing database of clinical experience and trigger an alert when the rate of a de-

vice failure or complication rises above threshold levels. Automated monitoring tools must incorporate the best available statistical methods to account for the complexity of the surveillance of device safety, including risk differences among patients, effects of physicians' learning curves, and interactions between the device and medications; they must also balance specificity and sensitivity in the detection of safety signals to permit efficient epidemiologic exploration of such alerts.

The complexity of device-safety surveillance requires the use of complementary approaches in an organized, prospective strategy. A comprehensive national safety surveillance system must include several key elements, beginning with the adoption of the proposed UDI system. We recommend expedited review and finalization of the UDI rule to permit implementation as soon as possible. Next, the FDA, together with the CMS, should require that detailed information regarding the use of high-risk devices and clinical outcomes be submitted to selected national registries operated by independent academic or professional medical organizations. We recommend that the FDA retain full rights of access to the data for additional analysis as needed. Third, the FDA should redirect a portion of the resources currently spent by the medical device industry on underpowered condition-of-approval studies to support the national device-safety

registries. Fourth, automated safety-surveillance tools should be applied to device registries to prospectively monitor for the most severe and the most common device failures and complications. Finally, methods for linking information across premarketing studies, the new registries, and existing FDA surveillance systems to provide valid safety estimates require further development.

Complementing existing event-reporting systems with enhanced prospective surveillance of high-quality registries will permit the FDA to efficiently monitor the safety of increasingly complex and widely used medical devices.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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HEALTH LAW, ETHICS, AND HUMAN RIGHTS

Regulation of Medical Devices in the United States and European Union

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Millions of patients worldwide depend on an ever-widening array of medical devices for the diagnosis and management of disease. In the United States, the Food and Drug Administration (FDA) requires manufacturers of high-risk devices such as heart valves and intraocular lens implants to demonstrate safety and effectiveness before the devices can be marketed. However, some policymakers and device manufacturers have characterized U.S. device regulation as slow, risk-averse, and expensive.^{1,2} Other experts, such as those at the Institute of Medicine, have suggested that current premarketing procedures may not be comprehensive enough and may be particularly dangerous for devices that have been cleared by the FDA on the basis of substantial similarity to an already marketed device.³

A frequent point of comparison for device regulation in the United States is regulation in the European Union.⁴⁻⁶ Reports suggest that European patients have access to some high-risk medical devices, such as coronary stents and replacement joints, earlier than American patients. This system has been touted as being better for patient care,⁷ as well as supporting good-paying jobs and a positive trade balance.⁸ However, the E.U. system has drawn criticism for conflicts of interest in its evaluation process,⁹ and a recent recall of a popular silicone breast implant that was approved only in the European Union has reinforced European concerns about the clinical evaluation of high-risk devices.¹⁰⁻¹²

As policymakers in the United States and Europe weigh these critiques, it is an opportune time to compare the two systems and consider what evidence exists on the performance of each device-approval system.

APPROVAL SYSTEMS FOR MEDICAL DEVICES

UNITED STATES

The Medical Device Amendments of 1976 gave the FDA primary authority to regulate medical devices and required the FDA to obtain “reasonable assurance of safety and effectiveness” before marketing.¹³ This legislation has been updated several times, including the Medical Device User Fee and Modernization Act of 2002, which established sponsor user fees for application reviews and set performance targets for review times.¹⁴

Each device type is assigned by the FDA into one of three regulatory classes on the basis of its risk and the evaluation necessary to demonstrate safety and effectiveness.¹⁵⁻¹⁶ Most class I devices (e.g., stethoscopes) are low-risk and subject only to “general controls,” such as tests of sterility. Class II devices (e.g., computed tomographic scanners) meet general controls as well as “special controls,” such as additional labeling requirements. These moderate-risk devices generally pass through the 510(k) review pathway, which refers to the section of the Food, Drug, and Cosmetic Act dealing with premarket notification. In this process, the FDA and the manufacturer rely on similarities between the device at issue and a previously cleared device. If a manufacturer can show that its device is “substantially equivalent,” additional clinical data are usually not required, although requirements for performance standards and postmarketing surveillance may be imposed. Class III products (e.g., deep-brain stimulators and implantable cardioverter-defibrillators) require clinical studies evaluating the safety and effectiveness of the device, called a

Premarket Approval (PMA) application.¹⁷ However, class III devices that arise from changes to previously PMA-approved devices may not need additional clinical studies.^{18,19} In addition, some older class III devices for which the FDA has not specifically called for PMAs can receive clearance through the 510(k) pathway.¹⁷ Devices that treat rare disorders (fewer than 4000 patients annually) may receive a Humanitarian Device Exemption and be approved on the basis of “probable” benefits, a more flexible standard that recognizes the difficulty of studying patient populations with small numbers and limited treatment options.²⁰

Sites where cleared or approved devices are used must report related serious adverse events to the FDA and the manufacturer.^{21,22} These reports are stored in a searchable, publicly available database called Manufacturer and User Facility Device Experience. In addition, the FDA may conduct inspections, require manufacturers of high-risk devices to conduct postapproval studies, and initiate recalls.

EUROPEAN UNION

Until the 1990s, each country had its own approach to device evaluation.⁶ To regulate an uneven and complex market, E.U. directives that outlined requirements under which a medical device (as well as other commercial goods) could be marketed across all E.U. member states after earning a *Conformité Européenne* (CE) mark in any one member country.^{23,24} These directives categorize devices into four classes (I, IIa, IIb, and III) on the basis of increasing risks associated with their intended use.^{25,26}

Device approval in each E.U. country is overseen by a governmental body called a Competent Authority, such as the Medicines and Healthcare Products Regulatory Agency in the United Kingdom and the French Agency for the Safety of Health Products. The lowest-risk devices are declared to the Competent Authority, which may conduct inspections to confirm manufacturing standards and review the technical file for the device. Approval for more complex devices is directly handled by Notified Bodies, independent companies that specialize in evaluating many products, including medical devices, for CE marks and are designated by Competent Authorities to cover certain types of devices. First, a manufacturer of a device selects a properly des-

ignated Notified Body in a country of the manufacturer's choosing. For approval by a Notified Body, devices are subject to performance and reliability testing linked to the risks of their intended use.²⁷ For most devices, the standard is met if the device successfully performs as intended in a manner in which benefits outweigh expected risks.^{23,28} The specific requirements for premarketing clinical studies are vague, and details of trials are typically not made available to the public. Although clinical data are required for high-risk devices, guidelines for the nature of these studies are not binding on manufacturers or Notified Bodies.²⁹

In the postmarketing phase, manufacturers are required to report all serious adverse events to the Competent Authorities. Since 1998, each Competent Authority (but not the public) has had access to the European Databank on Medical Devices (EUDAMED). This database stores information on manufacturers, data related to approvals and clinical studies, and details on postmarket events. Manufacturers have been required to directly report events to EUDAMED since May 2011. However, coordination and analysis of postmarketing reports are highly variable, and EUDAMED has limited utility even to Competent Authorities. A few E.U. member states provide the majority of adverse-event reports and field-safety notices, which are public notifications of device-related safety concerns.³⁰ In 2004, the guidelines published by the European Commission urged manufacturers to include both general and device-specific follow-up as part of their quality-assurance programs.³¹ These programs, which the guidance document suggests might include registries or more formal prospective postmarketing studies, are left to the discretion of manufacturers.

PROMINENT DIFFERENCES BETWEEN THE SYSTEMS

MANDATE

Emerging from a public outcry over adverse events, the FDA was given a mandate to provide reasonable assurance of the safety and effectiveness of medical devices^{32,33} (Table 1). Thus, the FDA may consider the severity of the disease and available alternatives when evaluating high-risk devices. For example, a new system for catheter ablation of atrial fibrillation, which had been

Table 1. Prominent Points of Comparison between the United States and European Union for Approval of Medical Devices.^a

System Feature	United States	European Union	Potential Implications
Mandate	Oversight of public health	Device safety (overseen through Competent Authorities), device approval (through Notified Bodies), and facilitation of trade	May influence dealings with industry clients, and attention paid to balance between effectiveness and risk of safety concerns
Centralization	Oversight of all device regulation by the FDA	Directives outline processes carried out by Competent Authorities and Notified Bodies	Standardization and coordination of premarketing and postmarketing evaluation are theoretically simpler and easier to enforce in the United States
Data requirements	Reasonable assurance of safety and effectiveness for approval of high-risk devices, "substantial equivalence" for 510(k) clearance	Generally performance-based analysis, requiring proof that device works as intended	E.U. assessment made by manufacturers and Notified Bodies; provides less insight into clinical end points for high-risk devices
Transparency	Proprietary limits with public reporting of premarketing review of approved devices, recalls, and adverse events	Review of Notified Bodies not made public; postmarketing data shared among Competent Authorities but not with the public	Greater public access to evidence in the United States
Funding	Combination of federal appropriations (80%) and user fees (<20%)	Funding of Competent Authorities variable among countries; Notified Bodies paid directly by sponsors	Notified Bodies may be vulnerable to conflict of interest with industry client; the FDA may be influenced by changes in federal funding and political climate
Access	Clinical premarketing testing of high-risk devices delays patient access to these devices (no differences for low- and moderate-risk devices)	E.U. patients may have access to certain high-risk devices sooner than in the United States, subject to limitations by payers	E.U. patients have faster access to certain devices, but these products are marketed with less rigorous proof of effectiveness and may have a greater chance of later-identified adverse events

* FDA denotes Food and Drug Administration.

marketed in the European Union since 2006 on the basis of pilot data, was presented to the FDA in 2011 on the basis of a clinical trial involving 210 patients.³⁴ An FDA advisory panel recommended against approval owing to safety questions raised by the study, the existence of established alternatives, and the fact that the treatment largely targeted quality of life rather than survival.

By contrast, the E.U. system is part of a framework for commerce, which originated as a means of streamlining trade and coordinating manufacturing, safety, and environmental standards within the European Union.^{35,36} Notified Bodies are not designed to work as public health agencies. The most important public health role in the system is played by Competent Authorities, which primarily oversee device safety, although the composition, funding, and responsibilities of Competent Authorities vary widely among member states. These features in part explain why proof that the device works as intended may be sufficient to permit marketing of even high-risk

medical devices.²³ For example, a distal protection system for coronary-artery interventions received a CE mark after a single-group study involving 22 subjects showed that the device worked as intended.^{37,38} In the United States, FDA approval came several years later on the basis of a randomized study involving 800 subjects, in which a clinical end point of major adverse cardiac events was used.³⁹

CENTRALIZATION

Central coordination in the United States allows postmarket phenomena in one generation of devices to inform later applications and study designs. For example, specific criteria for trial design and end points have been developed to standardize the development of artificial heart valves⁴⁰ and devices to treat congenital heart disease.⁴¹⁻⁴² These criteria also informed novel methods and statistical approaches to studying devices.⁴³ A central registration system also provides publicly searchable listings and databases of adverse events

and postmarketing reports, which are useful to independent researchers evaluating specific devices.⁴⁴⁻⁴⁶

Directives and guidance documents provide an overview of the evaluation process in the European Union, but the system defers significant authority to Competent Authorities and even more to nongovernmental Notified Bodies. Though individual Notified Bodies may be motivated to provide a predictable and streamlined approach to attract customers, there may be inconsistency in the process for approving similar devices among Notified Bodies.⁴⁷ Such differences in interpreting and applying European directives may allow manufacturers to identify the most conducive path toward earning the CE mark. Decentralization also hinders collection and analysis of safety data and does not aggregate large numbers of patients to help identify potential rare but life-threatening adverse events.^{9,48}

DATA REQUIREMENTS

In the United States and the European Union, data requirements for high-risk devices can differ substantially. For example, a device for left atrial appendage exclusion for prevention of stroke in atrial fibrillation received a CE mark in 2009 on the basis of pilot data but was rejected by the FDA on the basis of safety concerns, including procedural complications and high rates of stroke, emerging from a 700-patient study conducted as part of a PMA.⁴⁹⁻⁵¹ Notably, researchers have criticized the data that have been collected in some PMAs.^{46,52} One group showed that about two thirds of the PMA applications were approved on the basis of a single study and that trials were rarely randomized or blinded.⁵² Trials may lack sufficient representation of women⁵³ and have inconsistencies in the way they report data.⁵⁴

Differences in data requirements between the United States and the European Union are less stark for devices that do not require a PMA. Devices that are cleared through the 510(k) process in the United States generally do not require clinical trials, which remains a point of substantial controversy. For example, one study investigating a cohort of high-risk recalls in the United States showed that 71% of such devices had previously been cleared through the 510(k) process and another 7% had been exempt from review.⁵⁵ In another report, approximately 25% of high-risk device submissions during a 4-year period were found to be inappropriately evaluated through the

510(k) pathway,¹⁸ although the FDA has a stated goal of correcting these cases by the end of 2012.⁵⁶ Studies in the European Union regarding the pre-market features of devices that are subject to recalls have proved impossible to conduct.⁵⁷

TRANSPARENCY

The FDA has several mechanisms for making its decision-making process accessible, even though much of a sponsor's application for a new device may remain proprietary. Open presentations to advisory committees describe particularly novel, complex, or high-risk devices, and committee panelists can publish their views.^{58,59} At the time of approval of high-risk devices, a "Summary of Safety and Effectiveness Data" provides the justification for approval as well as discussion of adverse events. Public postmarket data have been used in the United States to quantify the risks for several devices, including implantable cardioverter-defibrillator leads⁴⁴ and generators⁶⁰ and cardiac septal-closure devices.⁴⁵ In contrast, in the European Union, Notified Bodies have no obligation to publish their decision-making process or the evidence provided by sponsors.^{9,47,61}

FUNDING

In the United States, user fees account for less than 20% of the budget for the medical-device approval process, and the government supplies the remainder.⁶² Relying on centralized funding subjects the FDA to resource limitations, particularly in postmarketing surveillance.^{63,64} However, public funding also promotes the independence of regulators. In the European Union, the funding of Competent Authorities varies with different combinations of public support and fees levied on manufacturers or Notified Bodies, and this variability may exacerbate differences among the resources focused on device safety in each country. The system of Notified Bodies is for-profit, with funds derived from the review fees. This sets up a dynamic in which Notified Bodies view manufacturers as clients or customers and compete with one another for business. As one Notified Body writes in its advertising brochure, "Our aim is to provide a high quality, fast, reliable and stress-free service to meet your deadlines."⁶⁵

ACCESS

Patients in the European Union have access to some new, complex technologies earlier than patients in the United States (in some cases, sev-

eral years earlier), though precise estimates vary among reports.^{66,67} The timing of approval of low- and moderate-risk devices, which account for more than 95% of devices reviewed by the FDA, is generally equivalent.⁶⁷ For devices in which clinical data ultimately prove favorable, E.U. patients will have enjoyed these options before similar patients in the United States. For example, two devices for transcatheter aortic-valve implantation (TAVI) have had CE marks since 2007.⁶⁸ Later, in a study involving patients with inoperable severe aortic stenosis, TAVI was shown to reduce mortality in absolute terms by 20 percentage points at 1 year, as compared with standard therapy,⁶⁹ with a favorable effect on quality of life.⁷⁰ On the basis of these data, the FDA approved one TAVI model in late 2011. In the United States, truly new but high-risk devices may be available at an early stage only through a humanitarian exception or as part of a clinical trial, and in both cases conditions of use include oversight by institutional review boards and typically postapproval studies evaluating outcomes.

However, differences in timing are related to the need in the United States to conduct clinical trials for high-risk devices. Although E.U. patients may have earlier access to some devices, they also face the risk that subsequent studies will show no benefit to the new device or reveal important harms from adverse events that did not emerge from the premarket review. For example, the PleuraSeal Lung Sealant System for the treatment of air leaks after pulmonary resection was approved for the E.U. market from 2007 through 2011 but was withdrawn after an FDA-required study showed a higher complication rate than with standard care.⁷¹ Approval of a device in the European Union does not necessarily guarantee earlier access for patients, since insurance coverage and payers' decisions vary widely.⁷²

RECOMMENDATIONS

This review of device approval in the United States and Europe shows that both systems are facing problems requiring policy changes. Much attention has been focused on the time to approval and regulatory barriers in the United States,⁷³ but we found numerous examples of high-risk devices that were first approved in the European Union but showed no benefit or demonstrated substantial safety risk in subsequent

testing. There is some irony in criticizing the FDA for delayed approval of technology, such as TAVI, in which the effectiveness has been shown only in the studies performed to meet the FDA's safety and effectiveness requirements. One essential question that remains unanswered is whether speedier access to some newer technologies in the European Union has improved public health. Or does the more deliberative posture taken for some high-risk devices by the FDA better serve patients overall? Certainly, swifter approval helps generate revenue for manufacturers, and physicians may benefit from having more tools at their disposal. But the primary goal of bringing new devices to market should be to improve the treatment of specific diseases, and no current studies address this outcome.

The few studies that have evaluated the performance of regulatory systems have relied on unconvincing outcomes such as recall rates. Because recalls require a number of unpredictable steps (including device-malfunction recognition, reporting, aggregation with other events, and regulatory action), low rates of recalls do not show an optimally functioning system, and high rates do not necessarily translate into patient harm or identify regulatory flaws.

One way to address unresolved questions about the effectiveness of the two approaches to device regulation would be to perform more comparative-effectiveness studies of device technology or disease management in which outcomes with new therapeutics could be compared with alternative approaches or devices. Yet the FDA and Competent Authorities have limited power to require these sorts of studies. Comparative technology assessment in the European Union is currently handled by other government bodies or private organizations in an unsystematic manner, whereas policymakers' attention to comparative-effectiveness research for devices in the United States remains in its infancy. More government resources in the two settings need to be applied to address both the effectiveness and cost-effectiveness of new device technology.

In our view, the greatest challenge facing U.S. device regulation is the evaluation of high-risk devices through pathways intended for lower-risk devices, such as the 510(k) process. Although it is worrisome that many PMA approvals in the United States result from unblinded studies or other features of high-quality clinical trials, these study elements may be impossible in trials of

some of the highest-risk implantable devices. In such cases, one solution is reliance on postmarket surveillance to ensure that devices are closely monitored when they are approved, perhaps with automatic review of clinical experiences after a period of years to ensure that the devices are operating as intended and producing the expected benefits. However, calls for more drastic increases in requirements or the adoption of a more lenient and outsourced “European” system lack any legitimate empirical basis in the literature.

By contrast, the E.U. system may be improved with better coordination and centralization to ensure consistent interpretation of directives at the level of a Notified Body and to assist understaffed Competent Authorities in monitoring device safety. Key problems in the European Union are the near-total lack of empirical evidence regarding the performance of its system and the lack of public access to either premarket or postmarket data. Data transparency also promotes improved knowledge about device performance and would facilitate more precise comparisons of regulatory decisions among regions. Adopting these characteristics would promote more rapid identification of postmarket safety signals and allow for a coordinated response to adverse events, as has been possible at times in the United States.

CONCLUSIONS

Systems for approving new medical devices must provide pathways to market for important innovations while also ensuring that patients are adequately protected. To achieve these goals, the United States and European Union use a combination of premarket testing and postmarket vigilance but with some marked contrasts in their approaches. Features of both environments require reform, as well as continuing research to assess policy changes.

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Mr. PITTS. That concludes the second panel. I would like to thank the witnesses and members for participating in today's hearing. I remind the members that they have 10 business days to submit questions for the record, and I ask the witnesses to respond promptly to the questions. Members should submit their questions by the close of business on Thursday, March 1. Without objection, the subcommittee is adjourned.

[Whereupon, at 1:57 p.m., the subcommittee was adjourned.]

[Material submitted for inclusion in the record follows:]

Opening Statement
Chairman Fred Upton
Subcommittee on Health Hearing
Wednesday, February 15, 2012

(As Prepared for Delivery)

Encouraging a well-run FDA and promoting innovation has been a focal point of the Energy and Commerce Committee. During this Congress, the committee has held three hearings and hosted a jobs forum where we heard from entrepreneurs, inventors, and small business owners in the medical device industry. Directly and indirectly, these businesses employ about 2 million people. In my home state of Michigan, the medical device industry—led by great American companies such as Stryker—employs approximately 9,000 people. However, these companies told the committee that the lack of predictability at FDA is forcing American companies to move jobs to Europe.

The lack of predictability is also harming American patients. Last July, Marti Conger testified before our committee that she had to deplete her life savings and travel to England to benefit from a device developed and manufactured by a company located forty miles from her house in California.

To address these concerns, members of the committee and a medical device champion on the Ways and Means Committee, Congressman Paulsen, introduced legislation designed to bring predictability, consistency, and transparency to FDA regulation.

Ultimately, the goal of these reforms is to save patients, promote innovation, and create jobs without sacrificing quality or safety. A goal that, I believe, is bipartisan and consistent with the goal of Commissioner Hamburg and the FDA.

Finally, I understand that FDA and the device industry have come to a proposed user fee agreement. That is welcome news, but, in order for the committee to complete its work on the user fees on schedule, we need to get the proposed user fee agreement as soon as possible. I ask FDA and the administration to do all that they can to make that happen.

FRED UPTON, MICHIGAN
CHAIRMAN

HENRY A. WAXMAN, CALIFORNIA
RANKING MEMBER

ONE HUNDRED TWELFTH CONGRESS
Congress of the United States
House of Representatives
COMMITTEE ON ENERGY AND COMMERCE
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April 4, 2012

Dr. Jeffrey E. Shuren
Director
Center for Devices and Radiological Health
U.S. Food and Drug Administration
10903 New Hampshire Avenue
W066-5429
Silver Spring, MD 20993

Dear Dr. Shuren:

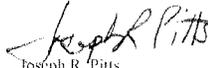
Thank you for appearing before the Subcommittee on Health hearing entitled "Reauthorization of MDUFA: What It Means for Jobs, Innovation and Patients" on February 15, 2012.

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for 10 business days to permit Members to submit additional questions to witnesses, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your answer to that question in plain text.

To facilitate the printing of the hearing record, please e-mail your responses, in Word or PDF format, to early_mcwilliams@mail.house.gov by the close of business on Tuesday, April 17, 2012.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,


Joseph R. Pitts
Chairman
Subcommittee on Health

cc: The Honorable Frank Pallone, Jr., Ranking Member, Subcommittee on Health

Attachment



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

The Honorable Joseph R. Pitts
Chairman
Subcommittee on Health
Committee on Energy and Commerce
House of Representatives
Washington, D.C. 20515-6115

OCT 18 2012

Dear Mr. Chairman:

Thank you for providing the opportunity for the Food and Drug Administration (FDA or the Agency) to testify at the February 15, 2012, hearing before the Subcommittee on Health, Committee on Energy and Commerce, entitled "Reauthorization of MDUFA: What It Means for Jobs, Innovation and Patients." This letter provides responses for the record to questions posed by certain Members of the Subcommittee, which we received on April 4, 2012.

If you have further questions, please let us know.

Sincerely,

A handwritten signature in cursive script that reads "Ireland".

Jeanne Ireland
Associate Commissioner
for Legislation

cc: The Honorable Frank Pallone, Jr.
Ranking Member
Subcommittee on Health
Committee on Energy and Commerce

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We have restated each Member's questions below in bold, followed by our responses.

The Honorable Joe Barton

- 1. Dr. Shuren testified that he feels real world use of a device is "critically important" to device evaluation. At the February 10, 2012 Neurological Devices Panel meeting, the Petitioner manufacturers of Cranial Electrotherapy Stimulation (CES) devices provided CDRH and the Panel with testimony and letters from many practitioners who use the devices within their field of expertise, including military practitioners who use the device in their practices, but CDRH discounted all such information provided as "anecdotal." For a device that has been on the market, legally cleared by FDA, for over 30 years, how can the opinions and findings of those in the field be so grossly discounted and overlooked, and treated as absolutely meaningless yet a Panel be treated as "experts" on the subject while none of them have had any prior dealings with CES? Should data and survey information collected by a company who has had a device on the market for over 30 years be considered by CDRH when determining a device's safety and effectiveness?**

The Food and Drug Administration's (FDA or the Agency) February 10, 2012, Neurological Devices Advisory Panel meeting was held to discuss, and make recommendations regarding, the possible reclassification of Cranial Electrotherapy Stimulator (CES) devices. The issues you raise about this meeting have been raised in three Citizen Petitions,¹ which FDA is currently reviewing. It is, therefore, premature for the Agency to address your specific questions prior to responding to the Citizen Petitions.

FDA's advisory committees play an essential role in the protection and promotion of public health by providing independent expert advice and recommendations to the Agency on scientific, technical, and policy matters related to human and animal drugs, biological products, medical devices, foods, and tobacco products.² Advisory committees enhance FDA's ability to protect and promote public health by ensuring that FDA has access to such advice through the public hearing process as provided in existing laws and regulations.

¹ See Docket No. FDA-2012-P-0260. "Request that the ("Commissioner") investigate actions taken by the Center for Devices and Radiological Health ("CDRH") related to the August 8, 2011, proposed rule," available at

<http://www.regulations.gov/#/docketDetail;dc=FR%252BPR%252BN%252BO%252BSR;ipp=25;po=0;D=FDA-2012-P-0260>; Docket No. FDA-2012-P-0270. "Petition Concerning Actions as They Pertain to Conduct of The Neurological Review Panel Held February 10, 2012. Regarding the Reclassification for the Cranial Electrotherapy Stimulator," available at

<http://www.regulations.gov/#/docketDetail;dc=FR%252BPR%252BN%252BO%252BSR;ipp=25;po=0;D=FDA-2012-P-0270>; Docket No. FDA-2012-P-0493. "Request to Reclassify Cranial Electrotherapy Stimulator From Class III to Class II," available at

<http://www.regulations.gov/#/docketDetail;dc=FR%252BPR%252BN%252BO%252BSR;ipp=25;po=0;D=FDA-2012-P-0493>.

² FDA's regulations governing advisory committees are in Title 21, Part 14 of the *Code of Federal Regulations* (21 CFR Part 14).

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Although advisory committees provide recommendations to FDA, FDA makes the final decisions on any matters considered by an advisory committee.³

The primary role of an advisory committee is to provide independent advice that will contribute to the quality of the Agency's regulatory decision-making and lend credibility to the product review process. In this way, FDA can make sound decisions about new medical products and other public health issues.

FDA encourages participation from all public stakeholders in its decision-making processes. Every advisory committee meeting includes an open public hearing session, during which interested persons may present relevant information or views orally or in writing. To ensure the transparency and impartiality of the committee process, FDA advisory committees are governed both by the Federal Advisory Committee Act and Agency-established regulations.⁴

Membership in FDA advisory committees is balanced fairly in terms of the points of view represented in light of the functions to be performed. Although proportional representation is not required, advisory committee members are selected without regard to race, color, national origin, religion, age, or sex.⁵ FDA also insists on getting industry and public perspectives, and nearly all advisory committees include industry and consumer representation. Industry representatives address global concerns for industry. Consumers are represented on advisory committees by technically qualified professionals who have specific links with consumer advocacy groups. In addition, some FDA advisory committees include patient representatives. These individuals present "real world" concerns of the patient who is to be the potential recipient of the new medical product.

Advisory committees typically are asked to comment on whether adequate data support approval, clearance, or licensing of a medical product for marketing. Advisory committees also may recommend that FDA request additional studies or suggest changes to a product's labeling. Their recommendations are just that—advice—and do not bind FDA to any decision. While advisory committee discussions and final votes are very important to the Agency, the final regulatory decision rests with FDA.⁶

In accordance with section 515 of the Federal Food, Drug, and Cosmetic Act (FD&C Act), on August 8, 2011, FDA issued a proposed rule in the *Federal Register*⁷ to require the filing of a premarket approval (PMA) or a notice of completion of a product development protocol (PDP) for CES devices. In the proposed rule, the Agency summarized its findings regarding the degree of risk of illness or injury designed to be eliminated or reduced by requiring this device to meet the statute's approval requirements and the benefits to the public from use of

³ See 21 CFR 14.5(b), providing that FDA "has sole discretion concerning action to be taken and policy to be expressed on any matter considered by an advisory committee."

⁴ See 21 CFR Part 14.

⁵ See 21 CFR 14.40(f)(2).

⁶ See 21 CFR 14.5(b).

⁷ FDA, "Proposed Rule: Effective Date of Requirement for Premarket Approval for Cranial Electrotherapy Stimulator," Docket No. FDA-2011-N-0504, 76 *Fed. Reg.* 48062 (Aug. 8, 2011), available at <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/NeurologicalDevicesPanel/UCM290788.pdf>.

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the device. In addition, FDA announced the opportunity for interested persons to request that the Agency change the classification of CES devices based on new information, and invited interested persons to submit comments to the docket for review. In response, FDA received several Citizen Petitions requesting a change in classification. The docket remained open until November 7, 2011.

In accordance with statute, FDA convened a meeting of the Neurological Devices Panel (the Panel) of the Medical Devices Advisory Committee. On February 10, 2012, the Panel discussed and made recommendations regarding the possible reclassification of CES devices.⁸ The Panel discussion included review of comments received in response to the August 8, 2011, proposed rule, all existing data to support CES safety and effectiveness, and whether the data would be sufficient to develop special controls to support regulation of these devices under Class II.

In light of the available scientific evidence, the Panel recommended 9-4 that the probable benefits to health from using CES devices do not outweigh the probable risks for the labeled indications of insomnia and depression, and that CES devices should remain as Class III for these indications. The Panel also recommended 8-5 that the probable benefits to health from using CES devices do not outweigh the probable risks for the labeled indication of anxiety, and that they should remain Class III for this indication. (Post-traumatic stress disorder (PTSD), it should be noted, is a form of anxiety.) In addition, it was the Panel's consensus that the available scientific evidence did not demonstrate a reasonable assurance of effectiveness for these same indications in the substance-abuse population, which is currently not within the cleared indications for use for these devices, the consideration of which had been raised by certain petitioners.

As stated above, the Panel's recommendations remain advisory in nature: all final decisions on both policy and technical matters are made by FDA. Please be assured that the Agency is carefully considering the Panel's recommendation and all public comments received before taking next steps with regard to the classification of CES devices.

2. **Dr. Shuren testified that CDRH needs more funds because it does not have the ability or expertise to currently make fully informed decisions with regards to the various forms of medical devices. If that is accurate, then why is FDA using its "Expert Panels" as a rubber-stamp to approve decisions already reached by CDRH, rather than actually seeking the expertise of medical experts in the field? An example of this would be the February 10, 2012 Neurological Devices Panel Meeting where CDRH employees went into the meeting attempting to seek validation for their opinion from the Panel, and celebrated the decision reached by the Panel, rather than actually providing the Panel with sufficient information so that it could reach an informed decision and provide CDRH with guidance.**

⁸ The complete package of meeting materials, including a brief summary of the February 10, 2012, Panel meeting, is available on FDA's website at <http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/NeurologicalDevicesPanel/ucm289361.htm>.

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The issues you raise about the February 10, 2012, Neurological Devices Advisory Panel meeting have been raised in three Citizen Petitions,⁹ which FDA is currently reviewing. It is, therefore, premature for the Agency to address your specific questions prior to responding to the Citizen Petitions. Please be assured that the Agency is carefully considering the Panel's recommendations and all public comments received before taking next steps with regard to the classification of CES devices.

At the February 15, 2012, hearing, Dr. Shuren testified that insufficient funding has been at the root of, or a contributing factor to, several of the problems identified in the Center for Devices and Radiological Health's (CDRH) premarket programs, including 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; and insufficient guidance for industry and FDA staff. User fee revenues under the Medical Device User Fee Act (MDUFA) will, among other things:

- help to reduce the ratio of review staff to front-line supervisors in the device premarket review program and enhance and supplement FDA's scientific review capacity by hiring additional device submission reviewers and leveraging the external expertise needed to assist in the review of device applications;
- support FDA in developing guidance documents, building an improved process for tracking guidance development and communicating the priority list of topics for guidance development to industry and the public; and
- result in enhanced accountability, predictability, and transparency for the medical device industry through a more structured pre-submission process, earlier interactions between FDA and device applicants, and increased communication during the review process.

FDA's advisory committees provide independent expert advice and recommendations to the Agency on scientific, technical, and policy matters related to FDA-regulated products. Advisory committees enhance FDA's ability to protect and promote public health by ensuring that FDA has access to such advice through the public hearing process as provided in existing laws and regulations. Although advisory committees provide recommendations

⁹ See Docket No. FDA-2012-P-0260, "Request that the ("Commissioner") investigate actions taken by the Center for Devices and Radiological Health ("CDRH") related to the August 8, 2011, proposed rule," available at <http://www.regulations.gov/#/docketDetail;det=FR%252BPR%252BN%252BO%252BSR;ipp=25;po=0;D=FDA-2012-P-0260>; Docket No. FDA-2012-P-0270, "Petition Concerning Actions as They Pertain to Conduct of The Neurological Review Panel Held February 10, 2012, Regarding the Reclassification for the Cranial Electrotherapy Stimulator," available at <http://www.regulations.gov/#/docketDetail;det=FR%252BPR%252BN%252BO%252BSR;ipp=25;po=0;D=FDA-2012-P-0270>; Docket No. FDA-2012-P-0493, "Request to Reclassify Cranial Electrotherapy Stimulator From Class III to Class II," available at <http://www.regulations.gov/#/docketDetail;det=FR%252BPR%252BN%252BO%252BSR;ipp=25;po=0;D=FDA-2012-P-0493>.

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to FDA, FDA makes the final decisions on any matters considered by an advisory committee.

Advisory committees typically are asked to comment on whether adequate data support approval, clearance, or licensing of a medical product for marketing. Advisory committees also may recommend that FDA request additional studies or suggest changes to a product's labeling. Their recommendations are just that—advice—and do not bind FDA to any decision. While advisory committee discussions and final votes are very important to the Agency, all final regulatory decisions rest with FDA.

The primary role of an advisory committee is to provide independent advice that will contribute to the quality of the Agency's regulatory decision-making and lend credibility to the product review process. In this way, FDA can make sound decisions about new medical products and other public health issues.

- 3. Mr. Barton and Dr. Shuren both indicated that there is a need to keep medical device jobs in the United States, but based on the CDRH's actions on and before the February 10 Neurological Devices Panel meeting, Electromedical Products International, Inc. (EPI) is taking its manufacturing out of Oklahoma and going back to manufacturing its device in China. Mr. Waxman indicated in his testimony that there were merely anecdotal examples of companies leaving, but this is a real example of the arbitrary nature of CDRH leading to jobs leaving the United States.**

The issues you raise about the February 10, 2012, Neurological Devices Advisory Panel meeting have been raised in three Citizen Petitions,¹⁰ which FDA is currently reviewing. It is, therefore, premature for the Agency to address your specific questions prior to responding to the Citizen Petitions. Please be assured that the Agency is carefully considering the Panel's recommendations and all public comments received before taking next steps with regard to the classification of CES devices.

In keeping with its mission, CDRH is responsible for protecting and promoting the public health. The Center's goal is to ensure that patients and providers have timely and continued access to safe, effective, and high-quality medical devices and safe radiation-emitting products. CDRH provides consumers, patients, their caregivers, and providers with understandable and accessible science-based information about the products that the Center

¹⁰ See Docket No. FDA-2012-P-0260, "Request that the ("Commissioner") investigate actions taken by the Center for Devices and Radiological Health ("CDRH") related to the August 8, 2011, proposed rule," available at <http://www.regulations.gov/#/docketDetail;det=FR%252BPR%252BN%252BO%252BSR;ipp=25;po=0;D=FDA-2012-P-0260>; Docket No. FDA-2012-P-0270, "Petition Concerning Actions as They Pertain to Conduct of The Neurological Review Panel Held February 10, 2012. Regarding the Reclassification for the Cranial Electrotherapy Stimulator," available at <http://www.regulations.gov/#/docketDetail;det=FR%252BPR%252BN%252BO%252BSR;ipp=25;po=0;D=FDA-2012-P-0270>; Docket No. FDA-2012-P-0493, "Request to Reclassify Cranial Electrotherapy Stimulator From Class III to Class II," available at <http://www.regulations.gov/#/docketDetail;det=FR%252BPR%252BN%252BO%252BSR;ipp=25;po=0;D=FDA-2012-P-0493>.

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oversees. CDRH also facilitates medical device innovation by advancing regulatory science, providing industry with predictable, consistent, transparent, and efficient regulatory pathways, and ensuring consumer confidence in devices marketed in the United States. For example, in 2011 alone, CDRH:

- Issued 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, and final guidance issued on March 27, 2012);
- Created 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);
- Developed 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 (draft guidance released December 1, 2011);
- Revamped 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 (December 2011);
- Improved communications between FDA and industry through enhancements to interactive review (some enhancements are already in place);
- Implemented 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 decision-making (Center Science Council established March 31, 2011);
- Created 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); and

- Instituted a mandatory Reviewer Certification Program for new reviewers (program launched September 2011).

In 2012, the Center's priorities are to fully implement a total product life-cycle approach, enhance communication and transparency, strengthen our workforce and workplace, and proactively facilitate innovation and address unmet public health needs.¹¹ We believe that these and other ongoing activities at CDRH will further the Agency's goal to ensure that safety and effectiveness and innovation are complementary, mutually supporting aspects of CDRH's mission to promote the public health.

4. **Dr. Shuren testified that there is an effort to make CDRH more transparent. If transparency is the key then wouldn't it make sense to have published criteria for what studies will be considered for determining "valid scientific evidence" rather than changing the criteria from device to device? For example, CDRH excluded many studies in reviewing CES for reasons that were not the basis for exclusion of studies when other devices were considered. Shouldn't the device review process be more transparent so that manufacturers can assist CDRH in collecting the needed data? In 31 years of business EPI has been granted one meeting with CDRH. Why is the process so adversarial? Is the adversarial nature of CDRH's handling of manufacturers truly in the patient's best interests?**

The issues you raise about the February 10, 2012, Neurological Devices Advisory Panel meeting have been raised in three Citizen Petitions,¹² which FDA is currently reviewing. It is, therefore, premature for the Agency to address your specific questions prior to responding to the Citizen Petitions. Please be assured that the Agency is carefully considering the Panel's recommendations and all public comments received before taking next steps with regard to the classification of CES devices.

It is the responsibility of the device manufacturer to ensure that adequate, valid scientific evidence exists, and to furnish such evidence to FDA to provide reasonable assurance that the device is safe and effective for its intended uses and conditions of use. Although a manufacturer may submit any form of evidence to FDA in an attempt to substantiate the safety and effectiveness of a device, the Agency relies upon only "valid scientific evidence"

¹¹ CDRH's strategic priorities for 2012 are described in greater detail on FDA's website at <http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHVisionandMission/UCM288736.pdf>.

¹² See Docket No. FDA-2012-P-0260. "Request that the ("Commissioner") investigate actions taken by the Center for Devices and Radiological Health ("CDRH") related to the August 8, 2011, proposed rule." available at

<http://www.regulations.gov/#/docketDetail;dc=FR%252BPR%252BN%252BO%252BSR;ipp=25;po=0;D=FDA-2012-P-0260>; Docket No. FDA-2012-P-0270. "Petition Concerning Actions as They Pertain to Conduct of The Neurological Review Panel Held February 10, 2012. Regarding the Reclassification for the Cranial Electrotherapy Stimulator." available at

<http://www.regulations.gov/#/docketDetail;dc=FR%252BPR%252BN%252BO%252BSR;ipp=25;po=0;D=FDA-2012-P-0270>; Docket No. FDA-2012-P-0493. "Request to Reclassify Cranial Electrotherapy Stimulator From Class III to Class II," available at

<http://www.regulations.gov/#/docketDetail;dc=FR%252BPR%252BN%252BO%252BSR;ipp=25;po=0;D=FDA-2012-P-0493>.

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to determine whether there is reasonable assurance that a medical device is safe and effective.

Only after considering the nature of the device and applicable regulations does FDA determine whether the evidence is "valid scientific evidence" for the purpose of determining the safety or effectiveness of a particular device and whether the available evidence, when taken as a whole, is adequate to support a determination that there is reasonable assurance that the device is safe and effective for its conditions of use.

According to FDA regulations, "valid scientific evidence" is defined as:

[E]vidence from well-controlled investigations, partially controlled studies, studies and objective trials without matched controls, well-documented case histories conducted by qualified experts, and reports of significant human experience with a marketed device, from which it can fairly and responsibly be concluded by qualified experts that there is reasonable assurance of the safety and effectiveness of a device under its conditions of use.

The evidence required may vary according to the characteristics of the device, its conditions of use, the existence and adequacy of warnings and other restrictions, and the extent of experience with its use.

Isolated case reports, random experience, reports lacking sufficient details to permit scientific evaluation, and unsubstantiated opinions are not regarded as valid scientific evidence to show safety or effectiveness.¹³

Since 2010, when CDRH issued the preliminary reports from the 510(k) Working Group and the Task Force on the Utilization of Science in Regulatory Decision Making, the Center has been taking concrete steps toward creating a culture change toward greater transparency, interaction, collaboration, and the appropriate balancing of benefits and risks. This culture change is occurring by means of:

- Better engagement with industry;
- Greater use of external experts;
- Implementing flexible, risk-based policies that appropriately balance benefits and risks and apply a more patient-centric approach;

¹³ See 21 CFR Sec. 860.7(c)(2), "Medical Device Classification Procedures: Determination of Safety and Effectiveness," available at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?FR=860.7>.

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- Establishing new ways of doing business that add value; and
- Setting clear expectations for CDRH staff.

By engaging more collaboratively with industry, patients, and outside experts, better explaining our thinking and decision-making, establishing the right balance between benefits and risks, setting the right expectations, and creating new internal processes and pathways that get safe and effective devices to market more quickly and efficiently, we will create a more open, interactive, and flexible culture at CDRH.

- 5. A CDRH epidemiologist was caught misleading the Neurological Devices Panel during their February 10, 2012 meeting by stating that cranial electrotherapy stimulation (CES) devices under review could cause seizures, and CDRH has been incorrectly labeling CES with the “potential risk” of seizures for decades in the public domain. When questioned by the Panel, the CDRH epidemiologist, Lauren Min, Ph.D., disclosed that the only evidence of seizures CDRH had found were from an old study (1991) using a device that was not ever in commercial distribution and occurred when two people in the study had seizures during a drug washout period before the device was used on the patients. Epidemiologists should recognize that the device must actually be used before it can be blamed for side effects. What are you doing to make sure that devices receive fair and impartial treatment from CDRH employees and the Panels enlisted by CDRH to help justify CDRH’s conclusions?**

The issues you raise about the February 10, 2012, Neurological Devices Advisory Panel meeting have been raised in three Citizen Petitions,¹⁴ which FDA is currently reviewing. It is, therefore, premature for the Agency to address your specific questions prior to responding to the Citizen Petitions. Please be assured that the Agency is carefully considering the Panel’s recommendations and all public comments received before taking next steps with regard to the classification of CES devices.

By way of background, FDA regulates medical devices and categorizes them into one of three classes (I, II or III) based on their level of risk. Class I devices are generally considered to be lower risk and are usually exempt from premarket review. Class II devices typically require FDA clearance of an application, referred to as a premarket notification (510(k)), which requires a showing of substantial equivalence to a legally marketed device

¹⁴ See Docket No. FDA-2012-P-0260, “Request that the (“Commissioner”) investigate actions taken by the Center for Devices and Radiological Health (“CDRH”) related to the August 8, 2011 proposed rule,” available at <http://www.regulations.gov/#/docketDetail,dct=FR%252BPR%252BN%252BO%252BSR,pp=25;po=0;D=FDA-2012-P-0260>; Docket No. FDA-2012-P-0270, “Petition Concerning Actions as They Pertain to Conduct of The Neurological Review Panel Held February 10, 2012, Regarding the Reclassification for the Cranial Electrotherapy Stimulator,” available at <http://www.regulations.gov/#/docketDetail,dct=FR%252BPR%252BN%252BO%252BSR,pp=25;po=0;D=FDA-2012-P-0270>; Docket No. FDA-2012-P-0493, “Request to Reclassify Cranial Electrotherapy Stimulator From Class III to Class II,” available at <http://www.regulations.gov/#/docketDetail,dct=FR%252BPR%252BN%252BO%252BSR,pp=25;po=0;D=FDA-2012-P-0493>.

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and is usually reserved for moderate and low-risk devices that exceed the criteria for exemption. Class III devices, which tend to be higher risk and/or first-of-a-kind devices, require FDA approval in the form of a premarket approval (PMA) application.

When Congress enacted the classification and premarket notification/review provisions of the Medical Device Amendments of 1976 (MDA) (P.L. 94-295), it included provisions to address devices already marketed. FDA was to classify approximately 1,700 known, marketed devices into one of the three classes described above. Approximately 140 of these fell into Class III. FDA was to regulate these "pre-amendment" Class III device types, and newly marketed devices that were "substantially equivalent" to them, through the 510(k) program, until it had followed the procedures outlined in the law and either reclassified each device type into Class I or II, or sustained the classification in Class III and required PMA applications. In some instances, FDA may allow approval through completion of a PDP.

The process for addressing the appropriate regulation for the remaining pre-amendments class III device types for which there has not been a call for PMAs is described in section 515(i)(2) of the FD&C Act. CES devices are one of the remaining 22 device types that remain in this transitional state.

- 6. Currently the Department of Defense and National Institutes of Health are investing millions of dollars in research on CES devices. Before the DOD will complete research on a device it has to have seen effectiveness in using the device. Evidence of these studies was provided to CDRH and the Neurological Devices Panel, yet it has been completely ignored. Should CDRH consider enlisting the support and knowledge gained by other governmental entities in its review of devices?**

The issues you raise about the February 10, 2012, Neurological Devices Advisory Panel meeting have been raised in three Citizen Petitions,¹⁵ which FDA is currently reviewing. It is, therefore, premature for the Agency to address your specific questions prior to responding to the Citizen Petitions. Please be assured that the Agency is carefully considering the Panel's recommendations and all public comments received before taking next steps with regard to the classification of CES devices.

¹⁵ See Docket No. FDA-2012-P-0260, "Request that the ("Commissioner") investigate actions taken by the Center for Devices and Radiological Health ("CDRH") related to the August 8, 2011, proposed rule," available at <http://www.regulations.gov/#!docketDetail;det=FR%252BPR%252BN%252BO%252BSR;ipp=25;po=0;D=FDA-2012-P-0260>; Docket No. FDA-2012-P-0270, "Petition Concerning Actions as They Pertain to Conduct of The Neurological Review Panel Held February 10, 2012, Regarding the Reclassification for the Cranial Electrotherapy Stimulator," available at <http://www.regulations.gov/#!docketDetail;det=FR%252BPR%252BN%252BO%252BSR;ipp=25;po=0;D=FDA-2012-P-0270>; Docket No. FDA-2012-P-0493, "Request to Reclassify Cranial Electrotherapy Stimulator From Class III to Class II," available at <http://www.regulations.gov/#!docketDetail;det=FR%252BPR%252BN%252BO%252BSR;ipp=25;po=0;D=FDA-2012-P-0493>.

As part of CDRH's 2012 strategic priority to proactively facilitate innovation and address unmet public health needs, the Center has committed to work with our federal government partners and external constituencies to facilitate the development of innovative, safe and effective medical devices. CDRH further plans to work collaboratively with our federal government partners and external constituencies to ensure the appropriate regulatory oversight of therapeutics and diagnostics when their safety and effectiveness are intimately tied to one another, and to advance medical device regulatory science. Additional information about CDRH's 2012 strategic priorities is available on FDA's website at <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHVisionandMission/ucm288735.htm>.

7. Since the 2002 effective date of device User Fee authorization has the CDRH/FDA undertaken any effort to seek payer evaluation of the benefit of User Fee payments for PMAs, 510(k)s, registration, or Section 513(g) inquiries? How do you measure payer satisfaction with the User Fee program?

FDA receives feedback from user fee payers regarding the benefits of, and payer satisfaction with, the MDUFA program by means of quarterly meetings with industry representatives, public meetings and workshops, and FDA-initiated industry surveys.

When MDUFA was reauthorized in 2007, FDA committed to report quarterly its progress toward meeting the quantitative medical device user fee goals; in addition, in an effort to enhance accountability and transparency, the Agency agreed to meet with representatives of industry informally to discuss issues related to MDUFA performance and expenditures and provide a qualitative update on how user fee funding is being used for the device review process, including investments in information technology and training.¹⁶ The agendas for these meetings, as well as copies of the detailed information presented at each of these meetings, are available on FDA's website at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationActMDUFMA/ucm109210.htm>.

In September 2010, FDA held a meeting to solicit public input on the medical device user fee program. This public workshop was attended by a wide variety of stakeholders, including industry payers of user fees. Stakeholders provided their assessment of the overall performance of the MDUFA program and their opinions about which aspects of the program should be retained, changed, or discontinued in order to further strengthen and improve the program. The agenda, webinar and video presentations, and transcript from that meeting (including access to the archived meeting webcast) is available on FDA's website at <http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm218250.htm#>

¹⁶ See Enclosure to Letter from Michael O. Leavitt, Secretary of Health and Human Services, to Sen. Edward M. Kennedy, Chairman, United States Senate, Committee on Health, Education, Labor and Pensions, dated Sept. 27, 2007, "MDUFA Performance Goals and Procedures" (p. 3, Section (I)(J), Quarterly Performance Reports), available at <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationActMDUFMA/UCM109102.pdf>.

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omment. In addition to the public meeting, FDA issued a notice in the Federal Register¹⁷ requesting written comments from interested persons on the medical device user fee program. Twenty-seven written comments were submitted by members of the public in response to that notice, including a number of written submissions from user fee payers.¹⁸

In March 2012, FDA held a second public workshop on the medical device user fee program, which included presentations by representatives of regulated industry. Copies of the agenda and presentations from that meeting, along with a meeting transcript, are available on FDA's website at <http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm292860.htm>; written comments received from the public, including those received from MDUFA payers, are likewise available at <http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm300782.htm>.

In addition to holding quarterly meetings with industry to report and receive feedback on the Agency's progress in achieving the goals under the device user fee program, and holding periodic public meetings soliciting input on that program, CDRH has sent out "Pre-market Industry Perception Surveys" to members of the device industry in order to obtain feedback on the medical device review process. The responses to these surveys have been used to help gauge those areas of the device review program that are working well and to identify those areas that are in need of improvement. The questions presented in these surveys have addressed areas including the timeliness of application review, review staff professionalism, reviewer knowledge, consistency of the review process, the utility of review-related CDRH websites, the usefulness of guidance for industry and FDA staff, new and emerging technologies, the conduct of review-related meetings, and device reviewer interaction, and helpfulness.

Valuable input from representatives of device user fee payers was also received via 35 meetings that were held with industry between January 2011 and February 2012 to discuss recommendations for the reauthorization of the MDUFA program. The minutes of those meetings are available on the FDA website at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationActMDUFMA/ucm236902.htm>.

8. What is the actual time it takes to process an individual registration submission and the cost to the CDRH? What is the annual allocation of CDRH personnel for this registration function and the annual income to the FDA?

In 2011, CDRH's Office of Compliance (OC) processed \$35.2 million dollars in fees associated with the registration of medical device facilities. The amount of time necessary

¹⁷ FDA, "Medical Device User Fee Act: Public Meeting; Request for Comments," 75 Fed. Reg. 49502 (Aug. 13, 2010), available at <http://www.regulations.gov/#!documentDetail;D=FDA-2010-N-0389-0001>; FDA, "Medical Device User Fees; Public Meeting; Extension of Comment Period," 75 Fed. Reg. 63845 (Oct. 18, 2010), available at <http://www.regulations.gov/#!documentDetail;D=FDA-2010-N-0389-0008>.

¹⁸ See Docket No. FDA-2010-N-0389, available at <http://www.regulations.gov/#!docketDetail;dcf=SR%252BPS:cpp=25:po=0;D=FDA-2010-N-0389>.

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to process an individual registration application may vary, based on the application's completeness and level of detail. FDA does not have data pertaining to the actual time spent on, or cost associated with, the medical device registration function. However, the revenue collected from the registration of medical device manufacturing facilities was intended to stabilize the amount of fees collected under the medical device user fee program from year to year.

9. Has the CDRH/FDA thought about limiting User Fees for the next 5 years only to the wealthiest of device manufacturers, as has been applied to the major pharmaceutical manufacturers, and relieve other manufacturers of these fees for 510(k)s, PMAs and registration as well as 513(g) inquiries? If not, why not?

MDUFA III¹⁹ represents a commitment between the U.S. medical device industry and FDA to increase the efficiency of regulatory processes in order to reduce the time it takes to bring safe and effective medical devices to the U.S. market. It is the result of more than a year of public input, discussions with industry representatives, and consultations with patient and consumer representatives. Under MDUFA III, FDA is authorized to collect user fees that will total approximately \$595 million (plus adjustments for inflation) over five years (FY 2013-2017). In exchange, FDA has committed to meet certain performance goals outlined in the Secretary of Health and Human Service's letter to Congress.²⁰

FDA and representatives from the medical device industry reached an agreement on the proposed recommendations for MDUFA III, striking a careful balance between what industry agreed to pay and what FDA can accomplish with the amount of funding proposed. The actual structure of the user fee program was, therefore, determined in consultation with representatives of the medical device industry.²¹ During the course of those meetings, the device industry participants did not propose a fee structure such as the one described in this question.

However, MDUFA III provides that small businesses may qualify for a fee waiver or for a reduced fee on certain device-related submissions.²² Specifically, a medical device

¹⁹ The Food and Drug Administration Safety and Innovation Act (FDASIA) (Public Law 112-144) includes the Medical Device User Fee Amendments of 2012, or "MDUFA III." MDUFA III will take effect on October 1, 2012, and will sunset in five years on October 1, 2017. More information about MDUFA III is available at <http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticAct/FDCA/SignificantAmendmentsToTheFDCA/EDASIA/ucm313695.htm>.

²⁰ See "MDUFA Performance Goals and Procedures" (April 18, 2012), available at <http://www.fda.gov/downloads/MedicalDevices/NewsEvents/WorkshopsConferences/UCM295454.pdf>.

²¹ The agendas for these meetings, and the detailed information presented at each of these meetings, is available on FDA's website at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationActMDUFMA/ucm109210.htm>.

²² Detailed information regarding qualifying as a "small business" for purposes of FDA's medical device user fee program is available in CDRH's "Guidance for Industry and Food and Drug Administration Staff and Foreign Governments: FY 2013 Medical Device User Fee Small Business Qualification and Certification" (Aug. 2, 2012), available at <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/Overview/MDUFAIII/UCM314389.pdf>.

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company may qualify as a “small business” entitled to reduced device-related submission fees under MDUFA if it reported \$100,000,000 or less in gross receipts or sales for a taxable year²³ in its most recent federal income tax return. If a firm has gross receipts under \$30 million, it may qualify for a waiver of the firm’s first PMA application. Small businesses make up a large proportion of the device industry, and the discounts and waivers for small entities under MDUFA help to reduce the financial impact of user fees on this critical sector of the device industry, which plays an important role in fostering innovation.

Information regarding MDUFA fees for FY 2013²⁴ appears below:

Medical Device Fees for FY 2013		
Annual Fee Type	Standard Fee	Small Business Fee
Annual fee for periodic reporting on a Class III device	\$8,680	\$2,170
Annual establishment registration fee	\$2,575	\$2,575
Application Fee Type	Standard Fee	Small Business Fee
Premarket application	\$248,000	\$62,000
Premarket report	\$248,000	\$62,000
Efficacy supplement	\$248,000	\$62,000
Panel-track supplement	\$186,000	\$46,500
180-day supplement	\$37,200	\$9,300
Real-time supplement	\$17,360	\$4,340
510(k) premarket notification submission	\$4,960	\$2,480
30-day notice	\$3,968	\$1,984
513(g) request for classification information	\$3,348	\$1,674

MDUFA user fees are substantially lower than fees assessed under the Prescription Drug User Fee Act (PDUFA). Information regarding PDUFA fees for FY 2013²⁵ appears below:

PDUFA Fee Schedule for FY 2013		
Annual Fee Category	Standard Fee	Small Business Fee
Products	\$98,380	N/A
Establishments	\$526,500	N/A
Application Fee Category	Fee Rate	Small Business Fee
Applications Requiring Clinical Data	\$1,958,800	N/A
Applications Not Requiring Clinical Data	\$979,400	N/A
Supplements Requiring Clinical Data	\$979,400	N/A

10. Has the CDRH identified the average amount of personnel resources applied to review of each 510(k) submission and PMA application during each prior fiscal

²³ Including receipts of all of the entity’s affiliates.

²⁴ Information regarding annual MDUFA user fee rates is published in the *Federal Register* on an annual basis (see FDA, “Medical Device User Fee Rates for Fiscal Year 2013” (Docket No. FDA-2012-N-0785), 77 *Fed. Reg.* 45359 (July 31, 2012), available at <http://www.gpo.gov/fdsys/pkg/FR-2012-07-31/html/2012-18647.htm>).

²⁵ For additional information regarding PDUFA user fee rates for FY 2013, see FDA, “Prescription Drug User Fee Rates for Fiscal Year 2013” (Docket No. FDA-2012-N-0007), 77 *Fed. Reg.* 45639 (July 31, 2012), available at <https://www.federalregister.gov/articles/2012/08/01/2012-18711/prescription-drug-user-fee-rates-for-fiscal-year-2013>.

year of User Fees? If yes, how has the average numerator/denominator data compared for each year?

CDRH collects data pertaining to full-time equivalent position (FTE) resources through the Center Time Reporting System (CTRS). Employees' time is collected on a quarterly basis; the CTRS is intended to capture time spent on many of the Center's core functions, including premarket notification (510(k)) and PMA application review. CTRS data for FY 2003-2011 for 510(k) and PMA application review appears below:

510(k) Submission Processing: CDRH & CBER FTE Resources									
	2003	2004	2005	2006	2007	2008	2009	2010	2011
CDRH - 510(k) Review FTEs	166	166	179	248	277	277	291	332	337
CBER - 510(k) Review FTEs	6.1	8.3	9.2	13.0	11.5	11.0	10.6	13.9	11.0

PMA Application Processing: CDRH & CBER FTE Resources									
	2003	2004	2005	2006	2007	2008	2009	2010	2011
CDRH - PMA Review FTEs	133	133	120	251	261	264	260	289	309
CBER - PMA Review FTEs	5.5	4.0	5.8	9.5	3.4	3.6	3.5	5.2	7.0
CBER - BLA Review FTEs	15.0	23.2	30.3	41.3	50.2	39.9	42.1	46.3	41.4

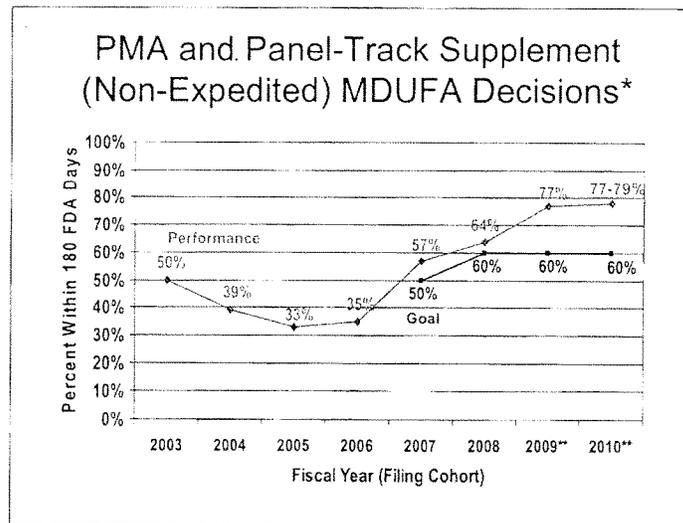
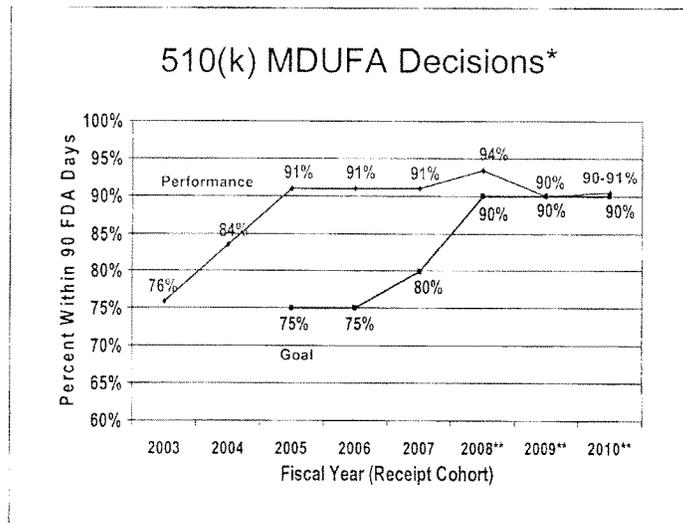
NOTE: In FY 2006, CDRH modified its time reporting categories to better account for effort on training, guidance document and standards development, and outreach initiatives. Prior to FY 2006, most of these areas had been considered part of the MDUFA process. This change allowed CDRH to better distinguish between premarket and post-market efforts.²⁶

CDRH 510(k) FTE values for FY 2006 to 2011 contain the proportional share of support activities associated with the review process; CDRH PMA FTE values for FY 2006 to 2010 contain the proportional share of support activities associated with the review process.

The preceding tables show an increase in the number of FTEs applied to the review of 510(k) and PMA submissions during the user fee program. This was an intended result of the program. When the Medical Device User Fee and Modernization Act (MDUFMA) was first enacted in October 2002, it was widely recognized that the process for the review of device applications was significantly under-funded, and that the costs of the review process (and unit costs) would increase each year over the five years of MDUFMA as more adequate levels of resources were provided for the conduct of device application reviews. As

²⁶ See FDA, FY 2009 MDUFMA Financial Report to Congress (July 2010), at p. E-3, available at <http://www.fda.gov/downloads/ForIndustry/UserFees/MedicalDeviceUserFeeandModernizationAct/UCM221553.pdf>.

additional resources were applied. FDA achieved significant improvements in the timeliness of its reviews, first with 510(k) submissions—which became subject to the 90-day MDUFMA decision goal for submissions received in FY 2005 --and subsequently with PMA applications, which became subject to the 180-day MDUFMA decision goal for submissions filed in FY 2007 (see charts).



*Performance data are for CDRH only. For consistency, PMA performance calculations are based on MDUFA II criteria for all cohorts.

**These cohorts are still open as of February 28, 2012. The range in percentages shows worst-best case possibilities.

During MDUFA II, the performance goals became more challenging with the addition of a second tier of decision goals and other heightened commitments. In addition, the numbers of incoming 510(k) and PMA submissions have increased since the last year of MDUFMA (see table). These factors have contributed to the need to apply increased numbers of FTEs to the review of 510(k) and PMA submissions, as has the continuing increase in the complexity of medical device technology, and other challenges.

Comparison of Submissions Received or Filed in FY 2007 and FY 2011: CDRH			
Submission Type	FY 2007	FY 2011	% Change
510(k)s	3,656	3,833	+ 5 %
PMAs and Panel-Track Supplements (non-expedited)	37	44	+ 19 %
PMAs and Panel-Track Supplements (expedited)	2	7	+ 250 %
180-Day PMA Supplements	140	145	+ 4 %
Real Time PMA Supplements	265	245	- 8 %
30-Day Notices and 135-Day PMA Supplements	574	1,569	+ 173 %
All Other PMA Supplements	184	305	+ 66 %

The Honorable Marsha Blackburn

1. On November 10, 2011, CMS issued a final rule that revised the definition of durable medical equipment (“DME”) to add a three-year minimum lifetime requirement (“MLR”) which products must satisfy in order to be eligible for reimbursement under the Medicare DME benefit category. See 76 Fed. Reg. 70228 (Nov. 10, 2011). On October 14, 2011, 10 House colleagues and I sent a letter to Secretary Sebelius expressing our serious concerns that the proposed rule would stifle innovation and hinder patient access to critical treatments. I have yet to receive a response to our letter. On December 9, 2011, I joined three House colleagues in sending a follow-up letter to Secretary Sebelius to reiterate our concerns regarding the final rule and announce the possibility of introducing legislation to directly address these concerns. To date, we have yet to receive a response from the Administration. When can we expect to receive a response to our letters?

FDA does not have jurisdiction or control over correspondence pertaining to rulemaking by the Centers for Medicare and Medicaid Services (CMS).

2. On November 10, 2011, CMS issued a final rule that revised the definition of durable medical equipment (“DME”) to add a three-year minimum lifetime requirement (“MLR”) which products must satisfy in order to be eligible for reimbursement under THE Medicare DME category. See 76 Fed. Reg. 70228 (Nov. 10, 2011). The final rule stated that the MLR would only be applied prospectively to newly-approved DME products after January 1, 2012. The final rule also stated that, “To the extent that a modified product is not a new product (including an item that has been upgraded), the 3-year MLR rule will not be applicable.” The final rule did not, however, provide any detail regarding the extent of changes that could be made to an existing DME product before such a “modified” or “upgraded” product would no longer be considered “new.” CMS has indicated that it will be issuing additional guidance to provide further clarification on the grandfathering provision.
 - a. How does CMS intend to define the scope of this guidance (i.e., identify the extent of changes that may be made to existing DME items so that they are still reimbursed under the DME benefit even though they may not satisfy the MLR), so that CMS does not discourage innovation of existing DME items?
 - b. When does CMS plan to issue such guidance?

In keeping with FDA’s mission, CDRH is responsible for assuring the safety and effectiveness of a broad array of medical devices and is committed to fostering innovation in device development, assessment, and manufacturing, and to providing the public with accurate, science-based information about the products that the Agency oversees. However,

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FDA does not have jurisdiction over the content or timing of guidance issued, or planned to be issued, by CMS.