FDA MEDICAL DEVICE APPROVAL: IS THERE A BETTER WAY?

HEARING

BEFORE THE

SUBCOMMITTEE ON HEALTH CARE, DISTRICT OF COLUMBIA, CENSUS AND THE NATIONAL ARCHIVES

OF THE

COMMITTEE ON OVERSIGHT AND GOVERNMENT REFORM

HOUSE OF REPRESENTATIVES

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FDA MEDICAL DEVICE APPROVAL: IS THERE A BETTER WAY?

THURSDAY, JUNE 2, 2011

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON HEALTH CARE, DISTRICT OF COLUMBIA, CENSUS AND THE NATIONAL ARCHIVES,
COMMITTEE ON OVERSIGHT AND GOVERNMENT REFORM,
Washington, DC.

The subcommittee met, pursuant to notice, at 2:04 p.m., in room 2154, Rayburn House Office Building, Hon. Trey Gowdy (chairman of the subcommittee) presiding.

Present: Representatives Gowdy, Gosar, McHenry, DesJarlais, Walsh and Davis.

Staff present: Ali Ahmad, deputy press secretary; Brian Blase, professional staff member; Molly Boyl, parliamentarian; Drew Colliatie, staff assistant; Linda Good, chief clerk; Christopher Hixon, deputy chief counsel, oversight; Sery E. Kim, counsel; Ronald Allen, minority staff assistant; Yvette Cravins, minority counsel; and Christopher Staszak, minority senior investigative counsel.

Mr. GOWDY. Good afternoon, and thank everyone for their accommodating our voting schedules. We apologize for any inconvenience. This is a hearing on FDA Medical Device Approval: Is There a Better Way?

First I will read the mission statement for the Oversight Committee. We exist to secure two fundamental principles: First, Americans have the right to know that the money Washington takes from them is well spent. And second, Americans deserve an efficient, effective government that works for them. Our duty on the Oversight and Government Reform Committee is to protect these rights. Our solemn responsibility is to hold government accountable to taxpayers because taxpayers have a right to know what they get from their government. We will work tirelessly in partnership with citizen watchdogs to deliver the facts to the American people to bring genuine reform to the Federal bureaucracy. This is the mission of the Oversight and Government Reform Committee.

At this point I will give an opening statement, and then I will recognize my distinguished colleague for his.

I want to start by acknowledging what everyone knows, which is the FDA performs a necessary, vital function in or country. Doctors, patients, nurses, health care professionals and businesses rely on their work every day, whether it's a doctor utilizing a medical device to save the life of a patient, or a business introducing the latest innovation to the market. From bandages and pacemakers, the American people deserve and the Federal Government de-

mands safe and effective medical products across the health care industry.

There is a balance, an important balance, to be struck. Of paramount concern is always the well-being of American citizens in need of medical care. In an industry with such wide-ranging economic implications, however, efficiency and safety need not be mutually exclusive.

The FDA's goals as an agency are to make safe and effective devices available to consumers, and to promote innovation in the medical device industry. Distilled down to a simple mission statement, this philosophy represents a proper and attainable goal. However, the FDA is perhaps failing to meet these standards for myriad reasons: inconsistent review procedures, unpredictability of decisionmaking, and an amorphous process that fosters uncertainty and inefficiency.

And perhaps most troubling, instead of identifying the issues and implementing reforms designed to ameliorate the substantive shortcomings of the approval process, the conveyer belt of medical device approvals has come, in some instances, to a grinding halt. In the premedical application and 510(k) approval processes, device approval times have increased 50 to 100 percent. Decision times, preliminary procedure durations, and the number of FDA requested question cycles are all on the rise at the cost of patients and businesses who suffer from these delays. As a result, medical device businesses are exporting products to international consumers long before American buyers, or they are leaving the United States altogether, harming both the U.S. economy and patients who rely on lifesaving new technologies.

This lack of predictability hurts American businesses, consumers and patients. We are here today to determine what can be done on their behalf and ask simply whether or not there is a better way.

And with that, I would recognize the distinguished gentleman from the State of Illinois, the ranking member of this subcommittee, Mr. Davis.

Mr. DAVIS. Thank you very much, Mr. Chairman. Let me, first of all, thank you for calling this very important hearing. And I also want to thank you for yielding.

I call it important because the Food and Drug Administration is an agency that I have watched closely for a number of years. As a matter of fact, one of my constituents, Dr. Alexander Max Smith, was the director of this agency, and he also was the dean of the medical school at the University of Illinois. And so we've looked at it for a long time.

The Food and Drug Administration is responsible for ensuring the safety and effectiveness of medical devices that millions of Americans use to help them walk, to help their hearts beat, and to help their children regain their health and live a normal and productive life. The regulations that govern the approval of medical devices are, therefore, critical and simple reason. They save American lives and prevent injury by medical devices that are unsafe or ineffective.

We all understand the importance of protecting jobs and fostering innovation. Illinois is home to hundreds of large and small medical device manufacturers, employing thousands of my constitu-

ents in many of these facilities I have visited. I applaud the technological advances being made each day, some of which have allowed close friends and family to lead productive lives. Nevertheless, I fully understand the importance of striking the right balance between innovation and safety.

There are those who believe that the Food and Drug Administration takes too long to review medical devices. For its part, the FDA has offered statistics that the agency says shows that it is performing well in this regard.

We will hear today from both the FDA and those involved in the medical device industry. As we listen to the testimony today and consider the views of the witnesses, we cannot lose sight of what is ultimately at stake: the lives of average Americans who rely on the FDA to protect them from faulty medical devices that may cause harm. It is the FDA who bears the awesome responsibility of protecting lives by ensuring that medical devices do what the manufacturers claim they do.

There are those who have suggested that the FDA's approval process of medical devices should be more like the approval process in the European Union. That is troubling to me because in the European Union medical device manufacturers do not have to show that their product is actually effective in treating the particular ailment it is supposed to treat. I am sure there isn't anyone in this room who would want a hip implant, a heart stent, or any other device in their body that was not effective.

In the past 5 months, at least 15 recalls of medical devices were announced. These recalls involve such products such as glucose test strips, catheters, an insulin delivery system, and an implantable infusion pump. Last year there were over 2,500 recalls of medical devices. One of the most widely covered device recalled the last year involved hip implants that had already been used in 93,000 patients before they were recalled by the company.

There's no greater responsibility that our government has than to protect the health and lives of its citizens. That is a responsibility that Congress has bestowed on the FDA, and so I thank our witness for being here today and look forward to their testimony.

And again, thank you, Mr. Chairman, for calling this hearing, and I yield back.

Mr. GOWDY. Thank you, Mr. Davis.

Members may have 7 days to submit opening statements and extraneous material for the record.

It is all of our pleasure, all members of subcommittee, to welcome our colleague from the great State of Minnesota, Congressman Erik Paulsen, who represents the Third District. In addition to serving on Ways and Means, Mr. Paulsen chairs the Congressional Medical Device Caucus.

Congressman Paulsen, the committee welcomes you and recognizes you for 5 minutes.

STATEMENT OF HON. ERIK PAULSEN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF MINNESOTA

Mr. PAULSEN. Well, thank you, Mr. Chairman and members of the committee, for the opportunity to appear before the committee. My name is Erik Paulsen. As you mentioned, I represent Min-

nesota's Third Congressional District, and I do serve as cochair of the Medical Technology Caucus.

And I would like to share with you why I believe the medical technology industry, an American success story, one that routinely revolutionizes patient care and creates thousands of high-tech jobs, is at risk of drying up and moving overseas.

Now, I can tell that you promoting made-in-America medical devices and encouraging innovation is near and dear to my heart. Across this country there are 8,000 medical device firms employing 400,000 dedicated, hard-working and innovative people. Currently the United States is a world leader in this industry. Its supremacy is threatened not by cheap overseas labors or countries with more competitive tax structures, but by the bureaucracy within our own borders.

Whether I'm meeting with medical innovators back home in Minnesota or across the country, I hear the same story: It's getting harder and harder to bring lifesaving devices to the marketplace in the United States because of a lack of consistency, predictability and transparency in the Food and Drug Administration's premarket review processes.

Device companies that deal regularly with the FDA cite many reasons for this inconsistency. One problem is that the FDA seems to be routinely proposing new end points midway through the review process. Now, of course, if the scientific information calls a device into question, the FDA should request more information. But many of my constituency companies are reporting that the FDA reviewers make new arbitrary demands late in the product review process, and these inconsistencies are frustrating and costly for all innovators, but small companies in particular cannot keep up when the FDA continually moves the goalpost, which is causing some firms to go out of business.

One company in Minnesota, Acorn Cardiovascular, recently had to close its doors due to such inconsistencies. The company had conversation after conversation with the FDA staff about how to test its device. Acorn performed a randomized trial, met its targets, and in the end thought it would be approved, but reviewers at the FDA moved the goalpost and required a new trial. Because of this, investors shied away, and Acorn couldn't raise the capital to perform another multimillion-dollar trial and had to close its doors. Ultimately 50 jobs were lost, and a lifesaving technology for patients is now not available in the United States.

Additionally, companies have been frustrated with what appear to be FDA's stalling techniques. Many entrepreneurs I have met with have had agency reviewers pursue one line of questioning early in the review process and then switch to a new, previously unaddressed topic after the third or fourth submission.

In 2008, Xtent, a Menlo Park, California, company, coronary stent company, tried to gain approval to start a U.S. clinical trial. Over the next 2 years, the FDA asked round after round of questions and required long preclinical animal trials. Now, at the time Xtent had clinical experience and hundreds of European patients, some with over 3 years of followup in world-class hospitals. But the FDA refused to consider the data, and as a result of the delays, the company closed, 150 employees were laid off, and the assets were

sold to foreign interests for pennies on the dollar. Members, today the technology is now being developed in China and in Europe, with no plans to return to the United States.

Now, this is just one of many examples, and if it pleases the committee, I would like to submit several more for the record.

And thanks in part to the inconsistencies like these, we are starting to see our competitive edge disappear. Currently devices are approved 2 years earlier in Europe than they are in the United States, which deny our patients access to lifesaving technology. If this trend continues, more companies will look for greener pastures and take their innovations and their 400,000 high-paying jobs with them.

The FDA has a statutory mandate to consider the least burdensome means of demonstrating devices that they meet safety and efficacy standards, and unfortunately in recent years the agency has abandoned this principle. The least burdensome provisions should force the agency to find appropriate balance between patient protection and the development of new lifesaving products.

I'm working on legislation to restore this balance at the agency and other efforts to modernize and streamline the FDA. It is my hope as well, Mr. Chairman, that today's hearing will help us find that balance and a pathway to a more consistent, predictable and transparent FDA premarket review process to help the medical technology industry continue to be a bright spot of our economy and ensure patient access to lifesaving technologies.

Thank you again for the opportunity to appear before the committee today, Mr. Chairman.

[The prepared statement of Mr. Paulsen follows:]

TESTIMONY

OF

ERIK PAULSEN

MEMBER OF CONGRESS

HOUSE COMMITTEE ON WAYS AND MEANS

CO-CHAIR, HOUSE MEDICAL TECHNOLOGY CAUCUS

Before the House Committee on Oversight and Government Reform

"Pathway to FDA Medical Device Approval: Is there a Better Way?"

June 2, 2011

Thank you Mr. Chairman, and members of the Committee, for the opportunity to appear before this Committee.

My name is Erik Paulsen; I represent Minnesota's Third Congressional District and serve as co-chair of the House Medical Technology Caucus. I'd like to share with you why I believe the medical technology industry – an American success story, one that routinely revolutionizes patient care and creates thousands of high-tech jobs – is at risk of drying up and moving overseas.

Promoting made-in America medical devices and encouraging innovation is near and dear to my heart. Across the country, there are 8,000 medical device firms employing 400,000 dedicated, hard working and innovative people.

Currently, the United States is a world leader in this industry. Its supremacy is threatened not by cheap overseas labor or countries with more competitive tax structures, but by the bureaucracy within our own borders.

Whether I'm meeting with medical innovators back home in Minnesota or across the country, I hear the same story: it's getting harder and harder to bring life-saving devices to the marketplace in the U.S. because of a lack of consistency, predictability, and transparency in the Food and Drug Administration's pre-market review processes.

Device companies that deal regularly with the FDA cite many reasons for this inconsistency. One problem is that the FDA seems to be routinely proposing new endpoints midway through the review process. Of course, if new scientific information calls a device into question, the FDA should be allowed to request more information. But many of my constituent companies report that FDA reviewers make new, arbitrary demands late in the product review process.

These inconsistencies are frustrating and costly for all innovators, but small companies in particular cannot keep up when the FDA continually moves the goal posts, which is causing some firms to go out of business.

One Minnesota company, Acorn Cardiovascular, recently had to close its doors due to such inconsistencies. The company had conversation after conversation with FDA staff about how to test its device. Acorn performed a randomized trial, met its targets, and, in the end, thought it would be approved. But reviewers at the FDA moved the goalposts and required a new trial. Because of this, investors shied away, Acorn couldn't raise the capital to perform another multi-million dollar trial and had to close its doors. Ultimately, fifty jobs were lost and a life-saving technology for patients is now not available in the U.S.

Additionally, companies have been frustrated with what appear to be FDA stalling techniques. Many entrepreneurs I've met with have had agency reviewers pursue one line of questioning early in the review process and then switch to a new, previously un-addressed topic, after the third or fourth submission.

In 2008, Xtent, a Menlo Park, CA, coronary stent company, tried to gain approval to start a U.S. clinical trial. Over the next two years, the FDA asked round after round of questions and required long pre-clinical animal trials. At the time, Xtent had clinical experience in hundreds of European patients, some with over three years of follow-up in world-class hospitals. But the FDA refused to consider the data and as a result of the delays, the company closed, 150 employees were laid off, and the assets were sold to foreign interests for pennies on the dollar. Today, the technology is being developed in China and Europe, with no plans to return to the U.S.

This is just one of many examples. If it pleases the Committee, I would like to submit several more for the record.

Thanks in part to inconsistencies like these, we're starting to see our competitive edge disappear. Currently, devices are approved two years earlier in Europe than in the U.S., denying our patients access to life-saving technology. If this trend continues, more companies will look for greener pastures, and take their innovations and their 400,000 high paying jobs with them.

The FDA has a statutory mandate to consider the "least burdensome" means of demonstrating devices meet safety and efficacy standards. Unfortunately, in recent years the agency has abandoned this principle. The least burdensome provisions should force the agency to find an appropriate balance between patient protection and the development of new, life-saving products. I'm working on legislation to restore this balance at the agency and other efforts to modernize and streamline.

It is my hope that today's hearing will help us find that balance and a pathway to a more consistent, predictable, and transparnt FDA pre-market review process to help the medical technology industry continue to be a bright spot of our economy and ensure patient access to life-saving medical technologies.

Thank you again for the opportunity to appear before the committee today.

Mr. GOWDY. On behalf of all of us, Congressman Paulsen, thank you for your testimony, thank you for your insight, thank you for your work in this area. And I look forward to reviewing your legislation forthwith. Thank you.

We will take a quick, quick recess. In fact, I may not even leave so the second panel can approach and get situated. And when they are situated, we will start again. Until then we will be briefly recessed.

[Recess.]

Mr. GOWDY. We will now welcome our second panel of—I won't say witnesses—witness, singular, Dr. Jeffrey Shuren. Did I pronounce that correctly? Dr. Shuren is the Director of the Centers for Devices and Radiological Health at the U.S. Food and Drug Administration.

Pursuant to committee rules, all witnesses will be sworn in before they testify, so I would ask you to rise and lift your right hand and repeat after me.

[Witness sworn.]

Mr. GOWDY. Let the record reflect the witness answered in the affirmative. Thank you.

Dr. Shuren, we will recognize you at this point for your 5-minute opening statement. I'm sure you have done this before. If you have not, there are a series of lights that may help direct you, but if you have a point that you want to finish even with the red light, feel free to finish your point.

STATEMENT OF JEFFREY SHUREN, M.D., J.D., DIRECTOR, CENTERS FOR DEVICES AND RADIOLOGICAL HEALTH, U.S. FOOD AND DRUG ADMINISTRATION

Dr. SHUREN. Mr. Chairman and members of the subcommittee, I'm Dr. Jeff Shuren——

Mr. GOWDY. I may get to you turn that mic on?

Dr. SHUREN. Mr. Chairman and members of the subcommittee, I'm Dr. Jeff Shuren, Director of Center for Devices and Radiological Health at the Food and Drug Administration. Thank you for the opportunity to testify today.

Over the past decade most indicators of medical device industry success have gone steadily upwards, with solid job growth, venture capital investment and a positive trade balance. Although the medical device industry has weathered the recession better than most of our industries, including about 6 percent growth last year, the economic climate has had an adverse impact. And as recent reports note, the recession has also caused companies to change their business models to be more risk-averse and therefore more sensitive to FDA regulatory uncertainties.

We recognize that smart FDA regulation is critical to maintain U.S. competitiveness. We are the world's leader in medical device innovation, but we won't retain that position unless we address the challenges that face us today and assure that we have both a strong industry and a strong FDA.

According to a recent PWC report, formerly Pricewaterhouse Coopers, "U.S. success in medical technology during recent decades stems partially from the global leadership of the U.S. Food and Drug Administration. FDA's standards and guidelines to ensure

safety and efficacy have instilled confidence in the industry's products worldwide."

FDA has a responsibility to both facilitate device innovation and assure that devices are safe and effective. Our data reported to Congress in February shows that about 95 percent of the more than 4,000 medical device applications subject to user fees that we review each year are reviewed within the timeframes that were agreed to by industry under the Medical Device User Fee Act. In those few areas where we just missed some goals, our performance is generally improving.

The data also demonstrates a program under strain, with limited capacity to increase performance at the current funding levels. However, when I became the Director of the Medical Device Center in fall of 2009, I had already been hearing concerns expressed by our constituencies. Industry complained that inadequate predictability, consistency and transparency were stifling innovation. Consumer groups, third-party payers, and some health care professionals believed our largest premarket review process, called the 510(k) program, did not provide adequate patient protections or generate sufficient information for them to make well-informed treatment decisions. Even my own staff complained about regulatory programs that in their current form were not well suited for many newer, more complex technologies.

Much like a CEO of a big company with a large and diverse clientele, I and my team set about to identify problems and their root causes, starting with a comprehensive assessment of our premarket review programs. The two reports we released in August 2010 with our analyses and recommendations showed that we have not done as good a job managing our premarket review programs as we should, and that we needed to take several critical actions to improve the predictability, consistency and transparency of these programs.

For example, we have new reviewers who need better training. We needed to improve management oversight and standard operating procedures. We need to provide greater clarity for our staff and for industry through guidance about key parts of our premarket review in clinical trials programs and how we make benefit-risk determinations.

We need to provide greater clarity for industry through guidance and greater interactions about what we need from them to facilitate more efficient, predictable reviews. We need to make greater use of outside experts who understand cutting-edge technologies, and we need to find the means to handle the ever-increasing workload and reduce staff and manager turnover, which is almost double that of FDA's drug and biologic centers.

In addition, we need to assure that industry meets its responsibility to provide us with appropriate data. Poor quality submissions, such as those that do not follow current guidance documents or have problems with clinical data such as missing data, not doing the study we agreed to, or failing to meet endpoints, are significant contributors to delays in premarket reviews.

In January of this year, after extensive public input, we announced 25 specific actions we're taking this year to ensure that

our premarket review programs would foster innovation and assure the safety and efficacy of medical devices for American patients.

In February, we proposed the innovation initiative to accelerate the development and evaluation of important medical devices and improve and strengthen the Nation's research infrastructure, promote high-quality regulatory science for all medical devices. In March, we held a public meeting to discuss these proposals, and in the coming weeks we will announce what actions we plan to take.

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

Mr. GOWDY. Thank you, Dr. Shuren.

[The prepared statement of Dr. Shuren follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

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

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U.S. HOUSE OF REPRESENTATIVES

"PATHWAY TO FDA MEDICAL DEVICE APPROVAL: IS THERE A BETTER WAY?"

JUNE 2, 2011

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). Thank you for the opportunity to discuss FDA's regulatory pathways for the premarket review of medical devices. FDA recognizes the many important contributions that the medical device industry makes to the economy and to the public health. By increasing the predictability, consistency, and transparency of our premarket review programs, we can help provide better treatments and diagnostics to patients more quickly and stimulate investment in and development of promising new technologies to meet critical public health needs, which may result in increased global market position of U.S. medical devices. In just the last few months, FDA has approved marketing applications for a number of truly innovative medical devices, including the first implantable hearing system, a new device that provides neurosurgeons with another tool to treat brain aneurysms without performing open surgery, and a Humanitarian Device Exemption for the first transcatheter heart valve.

Background

I will begin with a brief overview of our regulatory authorities for medical devices. A medical device, as defined by federal law, encompasses several thousand health products, from simple articles such as tongue depressors and heating pads, to cutting-edge and complex devices such as implantable defibrillators and robotic equipment for minimally invasive surgery.

The Medical Device Amendments of 1976 to the Federal Food, Drug, and Cosmetic Act (FD&C Act or the Act) gave FDA specific authority to regulate the safety and effectiveness of medical devices. Medical devices are assigned to one of three regulatory classes based on risk.

Class I, General Controls, is the lowest risk category of devices and includes items such as adhesive bandages. These devices are subject to the general controls of the Act, which include establishment registration and device listing and compliance with current Good Manufacturing Practice (cGMP), labeling, record-keeping, and reporting requirements.

Class II, Special Controls, is a medium-risk category of devices and includes devices such as intravenous catheters and powered wheelchairs. They are subject to the general controls of the Act as well as Special Controls, which may include special labeling requirements, mandatory performance standards, and post-market surveillance, in order to ensure device safety and effectiveness.

Class III is the highest risk category of devices and includes devices such as heart valves and coronary stents. These devices are subject to the general controls of the Act, plus require approval of a premarket approval application (PMA) containing scientific evidence of the device's safety and effectiveness prior to marketing the device.

Most devices, however, are cleared via the premarket notification [510(k)] process. A 510(k) is a premarket submission to demonstrate that the device to be marketed is "substantially equivalent" to another legally marketed (predicate) device. If a device otherwise subject to premarket review is not substantially equivalent to another legally marketed device, it must go through either the PMA process or the *de novo* classification process (a review process for innovative, lower-risk products).

The Impact of Regulation on Innovation

FDA is charged with a significant task: to protect and promote the health of the American public. To succeed in that mission, we must ensure the safety and effectiveness of the medical products that Americans rely on every day, and also facilitate the scientific innovations that make these products safer and more effective.

These dual roles have a profound effect on the nation's economy. FDA's premarket review of medical devices gives manufacturers a worldwide base of consumer confidence. Our ability to work with innovators to translate discoveries into products that can be cleared or approved in a timely way is essential to the growth of the medical products industry and the jobs it creates. U.S.-based companies dominate the roughly $350 billion global medical device industry. The U.S. medical device industry is one of the few sectors, in these challenging economic times, with a positive trade balance.[1] In

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

2000, the U.S. medical device industry ranked 13th in venture capital investment—now, 10 years later, it's our country's fourth largest sector for venture capital investment.[2]

As noted in a January 2011 report on medical technology innovation by PwC (formerly PriceWaterhouseCoopers), the U.S. regulatory system and U.S. regulatory standard have served American industry and patients well. As that report states, "U.S. success in medical technology during recent decades stems partially from global leadership of the U.S. Food and Drug Administration. FDA's standards and guidelines to ensure safety and efficacy have instilled confidence in the industry's products worldwide. Other countries' regulators often wait to see FDA's position before acting on medical technology applications, and often model their own regulatory approach on FDA's."

FDA's FY 2010 Medical Device User Fee Act Performance Report to Congress indicates that FDA's device review performance has been consistently strong. Ninety-five percent of the more than 4,000 medical device applications subject to user fees that FDA reviews every year (FDA reviews over 9,000 submissions annually in total) are reviewed within the goals that were agreed to by the medical device industry under the Medical Device User Fee Amendments of 2007 (MDUFA). Under the 510(k) program—the pathway used by 90 percent of the devices we examine each year—90 percent of our reviews were completed in 90 days or less, and 98 percent of reviews were completed in 150 days or less, as we committed to do under MDUFA.

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

There are a limited number of areas in which we are not meeting the goals agreed to with the industry, although our performance in those areas is generally improving. This is the result of several factors, including increasing workload, turnover of key staff, growing device complexity, and poor-quality submissions by industry that require significant time and attention to address. The number of applications for premarket approval (for "breakthrough" devices) has increased by 56 percent over the past two years. In addition, medical devices are becoming more technologically complex, as reflected by the growing number and variety of technical experts with whom FDA must consult during the review process. Finally, a significant number of submissions received by the Agency are incomplete or fail to address basic elements such as the device's proposed indications for use. More than half of the 510(k) submissions received by FDA have quality problems. Although FDA is meeting its performance goals for 510(k)s, these submission quality problems delay the completion of the marketing clearance process and unnecessarily divert resources from more productive activities in the review process.

FDA recognizes that it can do a better job at managing its premarket review programs. We continue to look for ways to improve our ability to facilitate innovation and to speed safe and effective products to patients. We know that medical device development is expensive. And we agree that, in many areas, insufficient clarity, consistency, and predictability on our part contributes to those expenses. This is why we've undertaken a number of initiatives to improve our review processes, and I am happy to highlight a few.

510(k) Action Plan

In recent years, concerns have been raised, both within and outside of FDA, about whether the current 510(k) program optimally achieves its goals of fostering innovation while making safe and effective medical devices available to patients. In light of these concerns, and in keeping with the good government practice of periodically assessing the effectiveness of existing programs, FDA set about to identify problems and their root causes in a methodical manner. In September 2009, we launched a two-pronged, comprehensive assessment of the 510(k) process to determine whether changes should be made to the program so that it can better achieve its goals.

Under the first part of this assessment, FDA created two staff working groups: one to review the 510(k) program and make recommendations to strengthen it; the other, to review how the Agency incorporates new science into its decision-making process, including our PMA program, and recommend how it can do so more predictably. The other part of this assessment is an independent evaluation by the Institute of Medicine (IOM), which is still underway. The IOM is expected to publish its final report in summer 2011.

In keeping with our commitment to transparency, FDA sought public input during the development and review of the two internal reports. We engaged in extensive public outreach, including two public meetings, three town hall meetings, three public dockets, and many smaller meetings with a variety of stakeholder groups. In August 2010, FDA

issued final reports containing 55 recommendations and again sought public comment on the reports and recommendations before taking action.

In January 2011, after reviewing the public comment, the Agency announced the proposed actions it would take to improve the 510(k) process and its use of science in decision-making generally. In particular, these actions are intended to improve the predictability, consistency, and transparency of the 510(k) program and aspects of our PMA program, such as decisions regarding clinical trial protocols, to facilitate innovation while assuring that devices available to patients are safe and effective. A few examples include:

- Streamlining the review process for innovative, lower-risk products, called the *de novo* classification process;
- Publishing guidance for industry to clarify when clinical data should be submitted, in order to increase predictability and transparency;
- Developing a network of external experts who can use their knowledge and experience to help the Agency address important scientific issues regarding new medical device technologies; and
- Establishing a new Center Science Council of senior FDA experts within the Agency's medical device center to ensure more timely and consistent science-based decision-making.

More information about FDA's plans to improve the 510(k) process and the Agency's use of science in decision-making is available on the Agency's web site at *http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDRH/CDRHReports/UCM239450.pdf*.

Innovation Initiative

In addition to our review of the 510(k) program, we recently announced a proposed Innovation Initiative. This Initiative seeks to accelerate the development and regulatory evaluation of innovative medical devices, strengthen the nation's research infrastructure for developing breakthrough technologies, and advance quality regulatory science. As part of this initiative, CDRH is proposing additional actions to encourage innovation, streamline regulatory and scientific device evaluation, and expedite the delivery of novel, important, safe and effective innovative medical devices to patients, including:

- Establishing a priority review program for pioneering technologies;
- Establishing a voluntary, third-party certification program for U.S. medical device test centers, designed to promote early and faster clinical testing during a product's development and assessment stages;
- Issuing guidance on leveraging clinical studies conducted outside the United States;
- Advancing regulatory science through public-private partnerships;

- Creating a publicly available core curriculum for medical device development and testing to train the next generation of innovators; and
- Engaging in formal horizon scanning—the systematic monitoring of medical literature and scientific funding to predict where technology is heading, in order to prepare for and respond to transformative, innovative technologies and scientific breakthroughs.

Facilitating medical device innovation is a top priority for FDA. As part of its 2011 Strategic Plan, FDA's medical device center has set goals to proactively facilitate innovation to address unmet public health needs. A public docket has been set up to solicit public comment on the Innovation Initiative proposals, and a public meeting on the topic took place on March 15, 2011.

MDUFA Reauthorization

In 2002, Congress enacted the Medical Device User Fee and Modernization Act (MDUFMA I), authorizing FDA to collect fees from companies who submit certain applications for marketing of medical devices. In return, MDUFMA I required FDA to pursue a comprehensive set of device review performance goals that were intended to significantly improve the timeliness and predictability of FDA's review of new devices. Five years later, in 2007, MDUFA II was enacted, which reauthorized medical device user fees and identified rigorous new premarket review performance goals for fiscal years 2008 through 2012. These performance goals, which are intended to achieve progressive,

year-by-year improvements in the review processes for medical devices, were developed with input from industry and were a key part of the negotiated package of user fees and other changes made by MDUFA II.

Medical device user fees have constituted an increasing proportion of FDA's program level device review budget since MDUFMA I was originally enacted. In 2003, user fees comprised less than 7 percent of FDA's device-related budget—in 2010, they accounted for almost 20 percent of medical device review costs. The remainder of the cost of administering the medical device review program is funded through Congressional appropriations.

As you know, the statutory authority for MDUFA expires on September 30, 2012. At that time, new legislation will be required for FDA to continue collecting user fees for the medical device program. FDA is currently engaged in negotiations with the regulated industry to prepare recommendations for the reauthorization of MDUFA. In addition, the Agency is holding regular monthly discussions with representatives of patient and consumer advocacy groups, while the negotiations with industry are taking place, as required by the statute. Minutes of both the industry negotiations and the monthly stakeholder meetings are being made publicly available on the FDA website to ensure transparency of the reauthorization process and to facilitate stakeholder involvement in that process. Finally, FDA will hold a public meeting on MDUFA reauthorization later this year.

Issues of concern to industry will appropriately be addressed in these negotiations, and during this process, all other stakeholders, including the scientific and medical community, and patient and consumer groups, will be afforded the opportunity to make their views heard with respect to the reauthorization of MDUFA.

CONCLUSION

Mr. Chairman, I commend the Subcommittee's efforts to understand the impact of FDA's regulatory policies on medical device innovation. FDA is a unique and essential agency—a science-based regulatory agency with a public health mission to promote and protect the health of the American people. This includes ensuring the safety and effectiveness of products that the American people rely on in fundamental, sometimes lifesaving, ways—drugs, vaccines, blood and blood products, medical devices, our nation's food supply, and more. But it also includes working proactively to foster the scientific innovation that will lead to tomorrow's new breakthrough products. We are committed to doing both. FDA strives toward a reasonable and fair approach to regulation that will foster innovation in the medical technology industry while assuring that the medical devices marketed in the United States are safe and effective.

Mr. Chairman, this concludes my formal remarks. I will be pleased to answer any questions the Subcommittee may have.

Mr. GOWDY. At this point I would recognize the ranking member of the subcommittee, the gentleman from Illinois Mr. Davis, for his 5 minutes of questions.

Mr. DAVIS. Thank you very much, Mr. Chairman.

Thank you, Dr. Shuren.

Congressman Paulsen just testified, and you were here during that period, and indicated that we might want to look at the way the European Union handles its process. And yet I was thinking that the Pricewaterhouse study determined that the U.S. medical device industry is the best in the world. How do you respond to those two assertions?

Dr. SHUREN. I do have concerns about importing the European model here to the United States, and I'm actually astonished that some in the device industry are calling for us to lower our standards to that of Europe. I don't think it's in the best interests of American patients, our health care system or the U.S. companies.

In Europe you do not need to show that your device is effective, in fact provides benefits to patients. For example, you will put, let's say, a drug-eluting stent on the market. That device may not work. And so patients can get a device that's ineffective when they had alternative effective treatments. As a result, they put their health at risk, and the health care system winds up paying for it.

In addition, in Europe you have your pick and pay for your private-party reviewer. Reviews are conducted by third parties called notified bodies. But concerns have been raised about them. In fact, the clinical director of the U.K. Regulatory agency said just last year, I am appalled at how many devices are brought to market with a lack of appropriate clinical data. Nor are notified bodies doing enough to pick up manufacturer shortcomings. She pointed out that many do not know how to adequately assess or challenge clinical data, or tell these companies relying on equivalence that they actually need to do clinical investigations. In fact, these are commercial organizations, "many of whom are reluctant to challenge because they fear losing their clients and for their survival." And many of these concerns were pointed out recently in articles that came out in the British Medical Journal and by European Society of Cardiology.

Mr. DAVIS. Do you think that there is any evidence that the longer and more intense process has any negative impact on the development of jobs and work opportunities?

Dr. SHUREN. Well, I do think that there is—we can do a far better job than what we are already doing, and there are steps that we have announced and are already taking that we think can actually make the process more efficient and try to get innovative technologies out to the market in a more timely manner, but not compromise our standard of safety and effectiveness.

We do have a great standard that we need to stand behind, and if we had to take a play out of the playbook of the European Union, the European Commission is now getting behind their approval process they call the CE Marking. Here in the United States we beat ourselves up, and the Europeans are taking advantage of it. But we need to get behind a system that, quite frankly, has good standards. We need to make it more robust and efficient. And if we can promote our system as the gold standard, we can actually pro-

mote greater competitiveness for the United States and for U.S. companies.

Mr. DAVIS. I know that diabetes is a major health problem and issue in the country, and research is being done. There's research relative to the creation of pancreas activity and how to better regulate that. Where do we stand now with this?

Dr. SHUREN. Sir, trying to promote the development of an artificial pancreas is a high priority for the agency. I'm a physician. If we can really crack the nut and have truly a replacement, if you will, for the pancreas for type 1 diabetes patients, it will be a huge advance in health care.

We have already set up a special team, by the way, who is headed by someone who has Type I diabetes, very invested in the technology.

We've approved already 16 clinical trials. We've worked to help to develop a sort of computer model that will allow the developers of these technologies to test drive their software algorithms without having to do animal studies and so speed development, and in just a few weeks, we will be releasing a guidance document that lays out expectations for bringing the early generation of an artificial pancreas.

Mr. DAVIS. Thank you very much. I'm a big fan of research, and I think that we have made enormous gains, and so I wish you well with this one, and I yield back.

Mr. GOWDY. Thank you, Mr. Davis. The chair would now recognize the gentleman from Illinois, Mr. Walsh.

Mr. WALSH. Thank you, Mr. Chairman and Ranking Member Davis from Illinois.

Dr. Shuren, thank you for appearing before us today. A couple quick questions, and Congressman Paulsen alluded to this in his testimony, and it's probably fairly common with what most of us hear back home. The refrain is fairly similar. It's getting tougher and tougher, many of these constituents and companies say, to deal with the FDA. Delays, issues of transparency, issues of confusion have become real passionate concerns that have been voiced to many Members of Congress. First quick, broad question, do you share—do you hear similar concerns with some of the members in the industry?

Dr. SHUREN. We do hear some of the concerns.

Mr. WALSH. The second refrain that seems to be fairly common when I talk to my colleagues, because I hear this over and over back home, that it has become noticeably more difficult to work with and deal with FDA in the last 2 to 3 years. Have you heard any sort of similar timeline concern as well?

Dr. SHUREN. I've heard concerns regarding interactions from some in industry. You know, interestingly enough, PWC did a survey and they had reported—their respondents reported that 39 percent felt that interactions had actually gotten better between industry and the agency, and the rest of the people who responded were somewhat neutral.

Mr. WALSH. Can you sort of broadly generalize, though, what—the feedback you've gotten in the last 2 to 3 years?

Dr. SHUREN. And I can't say in the last 2 to 3 years since I've only been at the Agency—the Agency—the Center for a little over

a year and a half. So I kind of came in in the middle of all of this. But the concerns in terms of interactions go along the following lines. First of all, they would like more interactions with us and we agree. One of the challenges we have is that our request for meetings before doing a clinical trial or submitting an application, called presubmission meetings, has almost doubled in the past 5 years, but without the staff to actually make good on those commitments to have the meetings.

We've heard, too, that there's a greater desire that when they get advice at the meeting, will the agency stand behind it, and in addition, that they have opportunities for more engagement with the center during the time of the review of an application.

Mr. WALSH. One of the big points we've heard is that—from folks in the FDA is that one of the reasons for the delays in product approval of the last 2 to 3 years is the poor quality submissions that device manufacturers are sending to the FDA, poor quality, incomplete submissions. Are those contributing issues to the delay in product approval?

Dr. SHUREN. They are a contributing factor. We did an analysis of the letters we send to companies for 510(k) submissions. We call them additional information letters, and we looked at about a hundred of them for 2010. And what we found is that from a little over 50 percent of the 510(k)'s we were receiving we did have issues with poor quality. This would be that we put out a guidance document, current guidance document, explained what our expectations were, and the company didn't follow it, and also didn't justify why they didn't comply with the guidance because they have flexibility, but they would have to then provide an alternative method, or there was testing that they would conduct that was the same kind of testing you do for that kind of device.

In some cases, a company even made that kind of device before, did that kind of testing, and now didn't do it, didn't submit it to us, no testing whatsoever. That's the kind of poor quality that we have seen, and it is a contributing factor but it's not the only factor.

Mr. WALSH. OK. Again, according to the FDA's own data, A1 requests rose from, I think, 38 percent in 2001 to 77 percent in 2010. Total review times have risen 45 percent since 2007, and maybe you're saying this. It just doesn't seem plausible that those declines in FDA performance can all be put at the laps of the manufacturers. How much of the problem is with the FDA itself in this sort of declining performance? Maybe in not being clear what it requires in the submission or that requirements are constantly changing. How much of a factor are those issues?

Dr. SHUREN. So, first, just to clarify, our performance against the goals that we committed to meet with industry had actually overall improved over time, and we are meeting the goals for 510(k). We're meeting one or close to meeting another goal for PMA, and that even over this time of MDUFA, we've seen improvement in our performance. However, there have been longer times overall from between our time and industry time, what we call total time.

So the contributors, one, is where we get submissions that they don't have the information they really should have and they know they should have. Now, in some cases, though, we do ask for things

that we hadn't asked for before that are appropriate, and there are cases where we can do a better job communicating that beforehand. So one of the actions we're taking is to put out what we call a notice to industry letter where we can quickly communicate if there's a change in expectations and the basis.

I will tell you as well, to be frank—and that occurs about less than 10 percent of the time where we ask for additional but we think appropriate. There are times, though, when we went back on the analysis, where we found that we asked for additional information or we asked a question we shouldn't have asked. It's about less than 10 percent of the 510(k)'s, but that is concerning to us, and so we have already been starting to put in place changes into the program to address that because we'd like—we don't want to see that happen.

Mr. WALSH. Last quick question, Mr. Chairman, and I know I'm running out of time. This is a pendulum. We want to make sure we've got quality products and we want to promote innovation. Do you see at all that the pendulum in the last few years has swung too far in one direction and it's stifling innovation?

Dr. SHUREN. I wouldn't exactly say the pendulum is swinging far one way versus the other. I think we've got multifactorial issues.

Mr. WALSH. Are you concerned about innovation right now?

Dr. SHUREN. I do. I am concerned about innovation. I'm also concerned that we assure that the devices that come on the market are safe and effective. What we ultimately want is, call it a pendulum or anything, that the goalposts, if you will, aren't moving all that much. I think have a far more predictable——

Mr. WALSH. Thank you, Mr. Chairman.

Mr. GOWDY. I thank the gentleman from Illinois. The chair would now recognize the gentleman from Tennessee, Dr. DesJarlais.

Mr. DESJARLAIS. Thank you, Mr. Chairman. Thank you, Dr. Shuren. You're a physician. When did you last practice medicine?

Dr. SHUREN. In the 1990's.

Mr. DESJARLAIS. In the 1990's, OK. Certainly then you've experienced the rise in health care costs that continue to increase yearly to a point where we're almost unsustainable. We see Medicare and Medicaid, private insurance going through the roof to where people just simply can't continue to go on. Do you recall when that change really started taking place in terms of rising costs? What would be your opinion on that?

Dr. SHUREN. That's outside my purview at the FDA, so I don't have an official opinion on that.

Mr. DESJARLAIS. OK. Well, I practiced for about 18 years, and through the 1990's, the costs certainly increased and there was an increase in regulation in the practice of medicine. There certainly has been an increase in pharmaceuticals, increase in devices, and you know, the FDA oversees this, and most people, whether it's in the medical industry or any other number of businesses feel that burdensome Federal regulations are causing increasing costs. So we were talking earlier about Europe, and on average, medical devices are approved 2 full years later in the United States, and why did you say it takes so much longer for the FDA to approve these devices than the European firms?

Dr. SHUREN. Well, actually if you look at the report from the California Healthcare Institute for 510(k) devices that don't have clinical data—and that's about 80 percent of the devices that we review—they come on the market in the United States first, as compared to Europe, at least half the time or more frequently, and in fact, the performance there looks like it's getting better in 2009 and 2010.

Now, when we deal with the high-risk devices, the PMA devices, these are a lot of the implantable lifesaving technologies, those devices have tended to come on the market in Europe before the United States for a very long period of time, and as mentioned beforehand, the standards there are very different, and with the global recession, companies now are looking to go to the market where it's easiest to get onto. Companies that are looking to sell, where before you could sell before you got approved, now are being expected, get approved somewhere, and then you can get brought up. So the enticement to go to any country that has a lower standard is going to be greater.

The solution here isn't for us to lower our standards. It's to get our program more predictable and efficient so that we can get innovative technologies to market more quickly, but we can assure that they're safe and effective because if not, and as a physician, we put patients at risk. If we give to them a device—I don't know anyone here who wants a device that they don't——

Mr. DESJARLAIS. Are you familiar with Mackauer survey?

Dr. SHUREN. Yes.

Mr. DESJARLAIS. It would contradict significantly what you're saying right now in terms of devices. Is that a credible study?

Dr. SHUREN. No. I have concerns with the Mackauer study. It's actually less than 10 percent of the industry actually responded to it. Even of the population, they were looking at is less than 20. Many of the questions had less than 10 percent. If you compare the United States to the E.U., at most, less than 8 percent of the people they sent the survey to actually could have had the same product come on the market in the E.U. And in Europe, for some of the things where they try to——

Mr. DESJARLAIS. You're saying the United States is actually quicker to get devices through than European companies? It sounds as though you're spinning it.

Dr. SHUREN. So according to some of the reports from industry, some of these devices are actually coming on the market first in the United States as opposed to the E.U., but for the high-risk devices, as a general matter, for many years they come on the market first in Europe, then in the United States.

Mr. DESJARLAIS. Now, these delays costs these companies $20 to $40 million. Do you know the corresponding cost—what the corresponding cost is to patients of having delayed access to medical devices?

Dr. SHUREN. The cost of the delayed access for an ineffective medical device I would say would be huge, but not in favor of the patient. Look, as a doctor, if we have good technologies that are safe and effective, we want to get them out to patients. We also want to make sure they're safe and effective because we don't do ourselves, we don't do patients, we don't do our health care system

justice if we're getting out devices that are not effective. And in Europe, there have been a number of cases since the late 1990's where they approved the device and then later they actually did the studies and they found it was ineffective or unsafe.

Mr. DESJARLAIS. I have to interrupt just for a second. I understand that you're defending the agency you work for, but being a practicing physician at one time and myself being a practicing physician, I know that there's a line there that's being crossed on the Federal level and that we're driving up patient costs, sometimes unnecessarily, and I know that a lot of patients feel the same way, again, whether it's pharmaceutical or devices, and the United States is one of the most expensive places right now on health care, and we're going to have to do something about that.

So, you know, the testimony that you're giving today sounds good from an FDA standpoint, but doesn't pass the practical test for me as a physician and many of my colleagues, but I appreciate your statement.

Mr. GOWDY. I thank the gentleman from Tennessee. The chair would now recognize the gentleman from the great State of North Carolina, Mr. McHenry.

Mr. MCHENRY. Almost as great as the State of South Carolina, right, Mr. Chairman?

Mr. GOWDY. Almost.

Mr. MCHENRY. Almost. Doctor, thank you for your testimony. We understand you've been on the job now for how long, how many months?

Dr. SHUREN. About 19.

Mr. MCHENRY. Nineteen, that's OK. And you know, we know that you're taking on an active agency and so change often comes slow in government, and so, you know, we appreciate the position you're in. You know, you talked about the E.U. Standards versus our standards, and getting a product to market in the E.U. Versus here. It's just a different process, right?

Dr. SHUREN. That's correct.

Mr. MCHENRY. What is the safety record? Is there a difference in the safety record?

Dr. SHUREN. Sir, one of the challenges with the E.U. Is they do not have publicly available centralized data base for that kind of information, as you have here in the United States, but we are aware of a number of cases of devices that got approved in Europe, that subsequently were found to be ineffective or unsafe, a number of them were withdrawn from the market——

Mr. MCHENRY. Do you have any studies you could point to?

Dr. SHUREN. Studies, no, but we have the cases. I will——

Mr. MCHENRY. Then my colleague here. You had a problem with the statistical relevance of a Mackauer study. You're saying it was only 10 percent, and you know, so you're saying that study is not statistically sound.

Dr. SHUREN. In terms of the numbers that you look at——

Mr. MCHENRY. OK. Then I would question your saying that the E.U. Has a lower safety standard or a worst safety standard than United States if there's not relevant data.

Dr. SHUREN. They have a lower standard to market because they do not require that a device be shown effective.

Mr. MCHENRY. OK. So in terms of the effectiveness of our regulation, because we're not arguing that we have a government agency allow unsafe products that are not going to be helpful onto the market. Likewise, I want to ensure that my constituents have access to the lifesaving, whether it's devices or health care, medicine, or procedures possible. So there is a balance, and I think, you know, I think we all care about and maintaining that.

The difference in the Mackauer report from Stanford, it took 31 months from first communication to be cleared to market here in the United States like for low and moderate risk devices it took 7 months in Europe. Can we reduce that gulf? What are you doing to reduce that 31-month timeline?

Dr. SHUREN. The comparison is apples to oranges. When they went in the E.U.—first of all, it looks like it's 15 companies they got a response from.

Mr. MCHENRY. OK. Actually, let me ask you a question then—let me ask a question because you don't really want to respond to the Stanford research.

Dr. SHUREN. No, I do want to respond——

Mr. MCHENRY. Well, you just want to dismiss it. So let me ask you this question. What is the average time from first communication to clearing to market for a device?

Dr. SHUREN. For first—depends what you mean on first communication. If it's from the application coming in the door, which is actually the comparison for Europe so often times for those devices not go to the notified body beforehand, and that's why it's apples and oranges. You come to us because you're going to do a clinical study——

Mr. MCHENRY. So first application to clearing to the market.

Dr. SHUREN. So, if you're talking about for a 510(k), the average now is—and I will double-check on the exact numbers—it's around 140 days, thereabout.

Mr. MCHENRY. 140 days?

Dr. SHUREN. Uh-huh.

Mr. MCHENRY. OK. And what is that in Europe?

Dr. SHUREN. In Europe we don't know. There's no publicly available data regarding the reviews that occur in Europe, both timeframes and the basis for the decisions. We have no idea what they even rely on when they make a decision in Europe.

Mr. MCHENRY. So you're saying the Europeans are just in a different world when it comes to safety and soundness of medical devices, and there's no way for us to know a reasonable comparison?

Dr. SHUREN. They don't make the data available. In fact, the lack of transparency was recently criticized.

Mr. MCHENRY. OK. So let me ask you, are you happy with the length of time it takes from first communication to getting a device on the market? Are you pleased with the track record so far.

Dr. SHUREN. I'm not pleased with the time, and that's why we're taking actions to try to make this program more predictable, consistent, and transparent. It will require several things to get there. There are changes FDA has to make. There are things we need from industry. We need to get the quality submissions to us, and we want to work with industry on that. We need to have adequate and stable resources to do it.

I will tell you as comparison to the drug program—and I'm not suggesting the same by way of funding—but the user fees collected in drugs are 10 times the amount as for the device program, 10 times the amount.

Mr. MCHENRY. OK. And also the revenue gained from that in the marketplace is significantly greater than that. But let me ask you another question. Is the length of time from submission—well, from first communication to getting a device on the market, is that longer or shorter than it was 5 years ago?

Dr. SHUREN. The length of time for the total—our review times have gotten generally shorter.

Mr. MCHENRY. They have?

Dr. SHUREN. They have overall for the different goals. The total time, our time, industry time has lengthened for 510(k)'s. It's over the past few years remained roughly the same on PMAs.

Mr. MCHENRY. Interesting. OK. Is it getting less costly or more costly?

Dr. SHUREN. I don't know.

Mr. MCHENRY. Why don't you know?

Dr. SHUREN. Because we don't do cost analyses for what the manufacturers are doing.

Mr. MCHENRY. OK. So there is no cost estimate? The government would have no cost estimate of the regulatory hurdles that they're putting in place for industry?

Dr. SHUREN. No, I would not know of the total cost to a particular company, no.

Mr. MCHENRY. OK. That in itself, Mr. Chairman, I think is a problem when a government agency doesn't realize the impact they're having, because it's my constituents that are going to be paying this, you know, this cost that's passed along to consumers once we get the devices on the market. I empathize with you, I do, but my concern is with the data that we've seen is that it takes longer now than it did than just a few years ago to get a device on the market and that is a big concern, and that's a big regulatory concern that—I appreciate the fact that you're looking at that and trying to reduce that time, but I would encourage you to look at the cost as well with—industry's going to have to bear in order to comply with these regulations. Thank you.

Mr. GOWDY. I thank the gentleman from North Carolina. The chair would now recognize the gentleman from Arizona, Dr. Gosar.

Mr. GOSAR. Dr. Shuren, I'm a dentist, and I'm very principled about process. So I'm sure you're aware of the FDA's regulatory procedures manual that just came out in March 2010?

Dr. SHUREN. I know of the manual, yes.

Mr. GOSAR. OK. So I mean, I'm coming back down to basics. Is there any other regulatory procedures manual that a case study on how medical devices should be approved whether they're a class one, class two, class three?

Dr. SHUREN. To my knowledge, I'm not aware of that.

Mr. GOSAR. See, once again, these are fundamental problems because what we have to do is we have to have everybody on the same line of expertise, what it takes for a one, two, and three. So I take it that the staff is not trained in those procedural aspects?

Dr. SHUREN. No. In terms of how to treat the different devices, they are, but if you want to put out what you need to do for a particular device, there will be some differences depending upon the type of device, and this is why industry says to us can you please put out more guidance on the specific types of devices to clarify what the expectations are, and we agree, there should be more guidance that's put out.

Mr. GOSAR. So have you a framework for these 510(k) reviewers?

Dr. SHUREN. We do have a framework for the 510(k) reviewers, and we're also right now doing a guidance in terms of clarifying that standard because there has been confusion on some of our reviewers. We found that on our own analysis, and we've had confusion on the part of industry, and the best way to deal with that is to clarify that through guidance and then to have training on it.

Mr. GOSAR. What kind of impact would that have on the end point that seem to randomly move with the reviewers?

Dr. SHUREN. Well, I think in terms of clarifying what the standards are and what needs to be done, you will have far more consistency in both what we do, and I think also what industry does.

Mr. GOSAR. Is there a way or do you provide interaction, you know, like how-to seminars where you actually have reviewers and manufacturers coming together and looking at this process? See, one of the things I'm seeing over and over again, I sit on Natural Resources as well as this Government Oversight, is this huge proliferation of agencies pending different checkpoints and time delays because time is money, OK, and I heard you say something earlier about the pharmaceutical aspect. You don't want to get me started there because out in rural Arizona we've got problems. We can't even get medications properly for surgeries. We're actually rescheduling surgeries. So, once again, we're not doing something good on the drug manufacturing as well.

But when you were taking these delays—and there's—you know, venture capital is at a minimum here and we have to have a return on investment. That's what the business model is talking about, and that's what my good friend over here was talking about and alluding to—is that we're forcing people to go to Europe because we're becoming so antiquated. We're not trying to work with people. We're trying to stymie the process because what I see here is, if you take statistics, you can juggle them any way you want to. It seems to me, when the science is easy, you bring them here. When the science is hard you go to Europe.

So something is wrong there, and I agree, we're not comparing apples to apples, Europe to United States. But we're forcing people to go to Europe because of the finances, because of the process. It's all of this. Does that make sense to you?

Dr. SHUREN. I understand the concern. I think to the extent that FDA, any unpredictability or inconsistency in our process that may contribute to companies making business decisions, is something that we are trying to address.

There's also the impact of the global recession. I will take responsibility for changes in weather patterns but maybe not for the global recession, and that has also impacted the dollars that are available for investment and the decisions that are made, and that aspect of it is not in my control. But to the extent we can make the

program more predictable and consistent, that's what we are trying to do with the actions that I laid out previously.

Mr. GOSAR. So wouldn't it be—I mean, no one wants a recall. So wouldn't it behoove us to work with industry, to sit down jointly in a venture to say, listen, there's limited capital, we definitely want to have the innovative spirit, we want to definitely keep that here, how do we streamline this, how do we work this, and it starts with basic building blocks, and it comes back to the basic building blocks of what business is about, and that's one thing I'm seeing constantly over and over again in government is a lack of business skills in understanding what it takes to actually get something to the market.

Dr. SHUREN. Actually, we've been going out to industry for a long time. This assessment that we talked about where we said identify the root causes, let's not do superficial surveys, let's do the deep dive, we went out, we had significant engagement with the public. We had public meetings, two of them; three town hall meetings. I traveled around to different parts of the country, both in open meetings and in closed-door meetings with different groups. We had three public dockets available for comments, and we got comments on the assessment. We made recommendations. We got comments on those, and based upon all of that input over a period of time and analyses is when we then put out the different actions we will take, and that is more guidance. That's more training for our folks. That's different—changes in the procedures, in the processes within the center.

Mr. GOSAR. Well, then, it seems like you're gathering information but then it's implementation. So let me give you an example. In July 2010, the Advancing Patient Safety Coalition which is made up of patients facing groups such as the American Hospital Association, the American Nurses Association wrote a letter to the FDA Commissioner Hamburg asking for a firm timetable for the FDA to establish a unique device identifier system. It is widely understood that a system of UDIs for medical devices would improve patient safety, improve clarification for medical device users, and make the recall process more efficient. Yet, over 9 months after this letter and 4 years after the passage of the FDA Amendment Act, we have no UDI uniform rule. When will you be putting the regulations for this unique device out and why is it taking so long?

Dr. SHUREN. This year. The rule is in administration clearance. It will be out this year.

Mr. GOSAR. Well, can you be a little bit more specific because, I mean, there's not—these timetables, there is no fixation about timetables. They just continue to be pushed and pushed and pushed.

Dr. SHUREN. For right now, it's in the process that's outside of my control. So I can't give you the exact date when it will come out, but it's been a high priority for us.

Mr. GOSAR. Thank you.

[The prepared statement of Hon. Paul A. Gosar follows:]

Opening Statement
Congressman Paul Gosar
Oversight and Government Reform Subcommittee on Health Care, District of Columbia, Census and National Archives
"FDA Medical Device Approval: Is there a better way?"
June 2, 2011

Chairman Gowdy and Ranking Member Davis: I thank you for holding this important hearing on the Food and Drug Administration's device approval process. We have three outstanding panels of witnesses from which we will hear today, to explore the important question of how we can ensure that our medical device industry can continue to innovate safe, dynamic, life saving products while creating jobs, contributing to our economy, and sustaining our health care system.

It is clear that the 510(k) process, by which the Food and Drug Administration approves medical devices, is causing confusion and uncertainty for medical innovators. A recently published Northwestern University study shows that companies developing some of the most innovative medical devices are going to the European Union for market approval before the U.S., because the European Union has developed a more predictable, consistent, and common sense approach to approving medical devices. In a country with an entrepreneurial spirit as strong as that of the United States, it is especially troubling to learn from this study that small companies are expressing the most severe frustrations with the device reviewers at FDA. Specifically, smaller firms do not have the staff or financial capability to engage in the morass that has become the FDA 510(k) process.

Over three fourths of companies surveyed in this study say that the Food and Drug Administration is unclear about what is requires from application to application, and that FDA reviewers often require more information than companies are required to provide in their initial application, leading me to believe that FDA is conducting these approvals on a case by case basis. Not only has this ad hoc approach to science contributed to a large backlog in device approvals that is sending medical device business overseas in droves, but it is not good governance. The ad hoc approach is also contributing to a risk averse culture at FDA that is killing innovation at the expense of jobs, revenue, and most importantly medical patients. PriceWaterhouseCooper, Institute of Medicine, California Healthcare Institute have all conducted nonpartisan studies that confirm this.

I wish these issues were new...but unfortunately, the need for reform has been recognized for decades. And yet, FDA has undergone staffing changes, regulatory changes, and a staggering 136% increase in funding over the past twenty years without successfully addressing this uncertainty. The time is now, and no later, to work with FDA toward a solution. While we wait, the medical device industry has lost $1 billion per year in venture capital since 2008. Until recently, life science innovation was a dynamic part of venture capital; now social networking is seen as a more reliable investment, and venture capitalists are pulling their money out.

Let me be clear: these issues are not simply health care policy issues; they are meaningful economic issues as well. The medical device industry accounts for 7,100 jobs in the state of Arizona alone; the companies that employ these folks are worth $1.7 billion – again, in Arizona alone. Those jobs, and that access to life saving technological advances, is being threatened as other countries provide more favorable regulatory environments, and studies show that other countries' favorable environments do not even result in a less safe marketplace.

I look forward to hearing testimony from the witnesses today about how we can best move forward on this critical issue. Thank you.

Mr. GOWDY. I thank the gentleman from Arizona.

Dr. Shuren, I want to start by commending you for doing something that I haven't seen in the brief time I've been here, which is acknowledge that there may be problems with the agency that you sit there representing. It may not be unique, but it's certainly unusual to have someone do that. So, with respect to that, I think—and I hope I'm using your words—unpredictable, inconsistent, and opaque. The opaque may not be your word. It may. I certainly heard you use the word "unpredictable" and "inconsistent." I think in your written testimony you just simply acknowledge the FDA recognizes it can do a better job.

My question—well, let me first ask you this first. You solicited input from industry on how FDA can improve itself, correct?

Dr. SHUREN. That's correct.

Mr. GOWDY. And how many recommendations would you say that you got back that had merit?

Dr. SHUREN. I would have to go back and check. I will say we got a limited number of recommendations from different groups. Most of it was feedback to the recommendations that we put out.

Mr. GOWDY. All right. Again, I stand to be corrected. It strikes me that of the recommendations you received or the recommendations that you seek to implement, you're going to use a "case-by-case analysis." Now, I want to ask you to put on your other hat, your JD hat. There's nothing in the world less predictable in the world than a case-by-case analysis. It frustrates law enforcement. I suspect it frustrates industry. What bright line reformative measures came out of that survey—in other words, if we're pleased to host you a year from now, what statistically measurable progress can we expect as a result of your asking for input in your own reforms?

Dr. SHUREN. First off, we're not using a case-by-case analysis as we go through for doing pre-market reviews. In those cases, we're actually looking to have more guidance on the expectations across a particular kind of device. We have many of them out now. We think there should be more of them. We'll be able to get a few more out with some changes in efficiencies that we're putting in place like a core staff to oversee the process and the tracking system and standard operating procedures. But a big increase in guidance documents isn't going to occur with the current resources because, right now, I have review staff who are getting pulled between trying to write a guidance document and reviewing applications. We need to have a core staff of technical writers, and we need to have enough of our own expert staff where we can spend the time to do the guidance and not have to pull people away from pre-market review to slow up any of those times.

Now, in terms of measurable progress from a year out, a year out most of the things we'll probably see will be on the qualitative side. I think, though, coming out from a year afterwards what we're hoping to see is some of the times in terms of overall times might start to come down. We will see actually if we go back and talk to people, you will hear less concerns about asking for data if data was inappropriate or asking for data with better clarification for why.

Qualitatively, I think greater success with our interactive review with manufacturers in terms of the engagements that we have.

Some of the things to make this work, we need to be able to get at the policies and procedures for everyone to get on the same page if we're going to get maximum value out of the system. So I think in the coming year we will see things start to turn around. We're going to see firmer implementation as we get a little bit beyond that and those policies are finalized.

So you asked about challenges in doing things. When we put out guidance, we open that up for public comment. That's a good thing. We should get public comment. It also takes time. I got asked about the unique identification rule coming out. That's rulemaking. I have to do an economic analysis. It's required by law. It lays in time. People like that. But it adds time to it. So there are things we're doing it, some of it because of the process imposed on us by law will take a little bit longer. The internal changes will take less time.

I will give you one last example. We have set up what we call a Center Science Council. It is almost senior leadership and experienced staff to oversee our science programs. This includes pre-market review. One of the issues that now comes to the Center Science Council is if the review team feels that they want to change what is going to be asked for across a type of device that is being brought up to senior management for input before a decision is made on it.

So we get the weigh in from senior leadership and more experienced staff. We've already had a case come up as a result and that wound up changing the dialog about what we're doing. Those kinds of changes are already going into place, and we're starting to see a difference. I think that will have ripple effects over the coming months.

Mr. GOWDY. Dr. Shuren, I'm sure that you can appreciate the concern that you've heard today from my colleagues, and your challenge is a large one, balancing innovation and safety. I don't minimize that. That is a challenge. My colleagues' challenge is to create an economic environment that is conducive with entrepreneurship and to create a regulatory and, in some instances, litigation scheme that doesn't bleed jobs to other countries. So I look forward to having you back and hearing about the progress that you've made, and I would yield a couple of seconds to my colleague from Tennessee because I promised I would, and I will—whatever time he consumes, I will give to my colleague from Illinois to balance it out. Dr. DesJarlais.

Mr. DESJARLAIS. Dr. Shuren, I was just listening to the testimony as a whole, and I think that it would be fair to say that you believe that the FDA's oversight is superior to that of the Europeans?

Dr. SHUREN. I believe that the U.S. standard for approval is the robust standard that we should stand behind, and I think that the FDA needs to do a better job in terms of how we run the programs for that standard to make the system work. We also need industry to provide us with the proper and high quality submissions and with clinical trials of high quality. That will go along the way, and ultimately, though, we need adequate and stable resources to run this program if we're doing it right.

You heard from industry that one of the big issues for them is the high turnover rate of our reviewers. We're not going to solve that without the resources to do it. If we're going to put out guidance documents, more of them, that will require additional resources. If we're going to have the capacity, we need to handle the growing workload, there will be a resource issue. In fact, from 2007, my workload went up 26 percent, but under the user fee program, the FDA assumes 100 percent of the risk of the increase in workload. None of that is built into the user fee program. None of it was considered or thought going to happen when we renegotiated MDUFA two, and that's had an impact.

Mr. DESJARLAIS. As a physician moving forward looking at our patients which we both have great concern for, does it bother you at all that the Affordable Health Care Act is based on the European model?

Dr. SHUREN. The Affordable Health Care Act, for better, for worse, and I'm beginning to think maybe for better, left the medical device center out of it. So it hasn't—isn't an issue for me to talk about.

Mr. DESJARLAIS. Thank you. I yield back.

Mr. GOWDY. I thank the gentleman from Tennessee. I would recognize the gentleman from Illinois.

Mr. DAVIS. Thank you very much, Mr. Chairman.

You know, as we went through the discussion, I couldn't help but be reminded of my mother who used to tell us that haste sometimes will make waste and that it makes more sense to take the time that you need to thoroughly review whatever it is that you're doing with the idea that the quality of it is just then perhaps even more important than how quickly you're able to process it or get it done. I am convinced, quite frankly, that the process used by our Food and Drug Administration is, in fact, superior to what we find taking place in other places.

I've had the personal experience of having to wait until something was perfected in order to have the level of comfort that my physician wanted to have before we did the treatment. I would urge you not to lower any standard or not even to think of lowering any standards but to continue with the intensive effort to make sure that the quality of the instruments, quality of the devices, that are going to be used on the American public is of the highest standard.

And so I commend you for doing that. I commend the agency for doing it, and if you would care to respond, please do so.

Dr. SHUREN. I couldn't agree more that the standard we have in place is the right standard and the one we should rely on. I'm not saying that as a defender of the FDA. I'm saying that as a physician who has taken care of patients. I'm saying that as a person who has been a patient myself and the same for my family members and friends. I never want to give to them a device that isn't effective and that we don't know isn't effective, if we can have that data, because as a result, I put them at unnecessary risk and particularly when there are other alternatives out there for them. It's not good for our health care system, which does have its challenges. Why do we want to spend money on technologies that ultimately turn out not to work and the cost of care for people who

wind up having worsened conditions because they got an ineffective treatment when they could have gotten an effective treatment, and that is what has happened in Europe with devices that had been found subsequently to be ineffective and yet patients got them and not benign treatments.

We're talking about implantable devices. So at the end of the day, the U.S. system I think is the right system. We just need to get behind it, and we need to make sure that it's as predictable and efficient as it should be.

Mr. DAVIS. Thank you, Mr. Chairman. Thank you very much.

Mr. GOWDY. I thank the gentleman from Illinois. Dr. Shuren, we thank you. As you can tell, this issue transcends the typical partisanship that we see here. It's a very personal issue for all the Members on both sides who are, believe it or not, are real human beings and have children and parents and spouses, and I wish you luck as you balance innovation, safety, and time. It's a challenge, and I do look forward to checking back in with you in a reasonable period of time to see what progress you are making, and we wish you the best as you seek to lead the agency.

Dr. SHUREN. Thank you, and we're very happy to come by, talk to you, the other Members, or your staff at any time at your convenience.

Mr. GOWDY. Thank you. We will take a brief recess to set up for the next panel, and if you have a second, some of us might like to come down and thank you. We'll be briefly recessed.

[Recess.]

Mr. GOWDY. We will now welcome our third panel of witnesses, and we thank you for your patience.

With us this afternoon from my left to right, your right to left, Mr. Jack Lasersohn, is that close, general partner of the Vertical Group, a leading venture capital firm; Dr. David Gollaher, close? President and CEO of the California Healthcare Institute; and Dr. Rita Redberg is professor of Medicine at University of California, San Francisco, and the chief editor of the Archives of Internal Medicine.

Pursuant to committee rules, all witnesses will be sworn in before they testify. So I would ask you if you would rise and lift your right hands.

[Witnesses sworn.]

Mr. GOWDY. Let the record reflect all the witnesses answered in the affirmative. You may be seated.

I will recognize the witnesses for their opening statements in the order in which I introduced them. So we would start with Mr. Lasersohn and you are recognized for 5 minutes.

STATEMENTS OF JACK LASERSOHN, GENERAL PARTNER, THE VERTICAL GROUP; DAVID GOLLAHER, PH.D., PRESIDENT & CEO, CALIFORNIA HEALTHCARE INSTITUTE; AND DR. RITA REDBERG, PROFESSOR OF MEDICINE, DIRECTOR, WOMEN'S CARDIOVASCULAR SERVICES, DIVISION OF CARDIOLOGY, UNIVERSITY OF CALIFORNIA

STATEMENT OF JACK LASERSOHN

Mr. LASERSOHN. Thank you for the opportunity to be here today. My name is Jack Lasersohn. I'm testifying today on behalf of the National Venture Capital Association.

During my 30-year career as a health care venture investor, our government has partnered with entrepreneurs to safely speed innovative new devices to market. Over this time, the United States became the undisputed leader of global medical innovation. Americans have been first in line for the lifesaving devices that U.S. companies produce, and throughout this period, patient safety has always been paramount, and safety must continue to be paramount even as we strive for the next lifesaving innovation.

Although revolutionary research is ongoing, fewer groundbreaking medical devices are making it to the U.S. marketplace, and those that do make it are taking longer and costing significantly more. At the same time, other countries have emulated our successful model and have begun to draw innovators and capital away from the United States, and as a result, we are starting to see stagnation within the U.S. innovation ecosystem.

A growing body of research suggests that the performance of the FDA has played some role in this decline. For many entrepreneurs, the FDA process has grown unpredictable, if not inscrutable. Working on very short resources to fulfill a broad set of responsibilities, FDA personnel struggle to keep up with their workload.

This research shows that review and clearance times for medical devices has significantly increased since 2007. U.S. medical innovation is beginning to migrate overseas, and patients in foreign markets are benefiting before American patients, without a corresponding gain in overall U.S. health or safety.

The central problem is that the FDA's risk-benefit analysis for novel medical devices, as well as drugs, has grown out of balance relative to its past practices and to current practices in other countries. FDA now weighs risks too heavily and demands unrealistic levels of assurance of benefit, particularly for first generation therapies.

As you know, under current law, all medical devices and drugs must be both safe and effective, but in medicine safety does not mean the absence of risk. It means a reasonable assurance that the probable benefits of using a device exceed its probable risks. Effectiveness requires that the benefit be clinically significant, which means it must produce a clinically meaningful improvement in the health of a significant portion of the population.

We believe that the FDA should establish as a guiding principle a more flexible risk-benefit analysis. This means that while the general requirement for safety and efficacy will always continue to apply, the specific threshold for each element within the equation will change depending on the clinical context. Incidents and sever-

ity of disease, urgency of need in the marketplace, prior medical knowledge, and the relative safety of a device should all be considered to explicitly adjust the variables in the safety and efficacy equation. These adjustments might include, for example, reducing the level of evidence required to provide a reasonable assurance or what constitutes a, "clinically meaningful improvement in health," or what portion of a population is deemed to be significant.

The flexible safety efficacy paradigm that we are proposing is already implicit, and maybe even explicit, at the heart of current FDA law. We already have very different review standards for low versus high-risk devices, but research data suggests that this has not been applied correctly or uniformly. A legislative mandate would help FDA senior management implement this commonsense principle more broadly within the agency.

In addition, the FDA should continue to measure probable benefits against probable risks, instead of an emerging practice of requiring a higher absolute level of evidence of benefit to ensure against a hypothetical or possible risk to health. Medical breakthroughs begin with only a small advantage over the status quo and then dramatically improve over time. This has been true for the past 50 years. Angioplasty is a perfect example. Requiring that all novel products initially demonstrate a high absolute threshold of benefit versus risk will derail away on many promising new ideas.

For devices with low to moderate potential risks, the FDA should significantly expand the use of certified third party entities for review, as the research suggests this practice is widely used in Europe without sacrificing safety, and we continue to believe in the safety and efficacy standard.

We are also advocating for a number of broader reforms, and mending the statutory mission to include acceleration of novel therapies to the marketplace, ensuring that individuals with significant expertise can sit on advisory panels, and streamlining the regulation of cost-cutting innovation, including a pathway for personalized medicine are very, veryimportant. If we act now to implement reforms that bring the FDA risk-benefit equation back into balance, we can revive the U.S. medical innovation ecosystem and ensure that seriously ill patients continue to have access to breakthrough therapies and technologies in a safe and timely fashion.

Thank you for your attention.

Mr. GOWDY. Thank you, Mr. Lasersohn.

[The prepared statement of Mr. Lasersohn follows:]

U.S. House of Representatives, Subcommittee on Health Care, District of Columbia, Census and the National Archives of the Committee on Oversight and Government Reform

June 2, 2011

"Pathway to FDA Medical Device Approval: Is there a Better Way?"

Testimony of:

Jack W. Lasersohn

The Vertical Group

Summit, NJ

Chairman Issa, Chairman Gowdy, Ranking Member Davis, and members of the Committee, my name is Jack Lasersohn and I am a general partner at The Vertical Group, a venture capital firm with offices in Summit, New Jersey and Palo Alto, California. My firm invests in innovative startup companies in the fields of medical technology and biotechnology. For more than 30 years, the principals of my firm have been founders, early stage investors, major shareholders and executives of many of the medical technology industry's most successful companies. These include the startups that developed ultrasound and MRI imaging, coronary angioplasty, minimally invasive spine surgery, artificial spinal discs, AAA stent grafts and beating heart CABG surgery. As a general partner of the firm, I serve on the boards of many companies with products either engaged in or preparing for FDA review.

In addition to representing my firm and its portfolio companies here today, I am also testifying on behalf of the National Venture Capital Association (NVCA) based in Arlington, Virginia. The NVCA represents the interests of more than 400 venture capital firms in the United States. These firms comprise more than 90 percent of the venture industry's capital under management. I currently serve on the Executive Committee of the NVCA Board of Directors and was a founding member of the Medical Innovation and Competitiveness Coalition (MedIC), which is a new organization under NVCA that brings venture capitalists, early-stage companies and entrepreneurs together to advance policies that will promote medical innovation and job creation in the U.S.

It is my privilege to be here today to share with you, on behalf of the venture industry and entrepreneurs, our perspective on the impact that FDA performance has on innovation in the U.S. medical devices industry. During most of my 30 years as a healthcare venture investor, our government has partnered with entrepreneurs and investors to safely speed innovative new devices to market, where U.S. patients can benefit from their use. Over this time, the U.S. grew into the undisputed center of global medical innovation and Americans were first in line for the life-saving and life-changing devices that U.S. companies produced.

For decades, venture capital has provided the fuel for U.S. medical innovation. Virtually every major new medical device and biotechnology drug from the last 30 years was developed by a U.S. start-up company and funded by venture capital. Venture-backed innovation has an impressive track record of spawning entirely new industries, as it did with biotechnology and personalized medicine, and thus provides a major source of job creation. In addition, small, venture-backed companies have served as the de facto research and development pipeline for larger medical device manufacturers, who buy startups, their products and the research that went into developing them only after venture backing has shepherded these companies through their riskiest stages.

Unfortunately, the environment that allowed these innovations to flourish has changed significantly over the last decade. Today, America's medical innovation ecosystem has come under intense strain. Although revolutionary research is ongoing, fewer groundbreaking medical devices are making it to the marketplace, and those that do make it are taking longer and costing significantly more to get there. As a result, investment in medical devices is beginning to dwindle. In fact, since 2008, total annual venture investment in the medical devices sector has declined by $1 billion. The economic downturn has certainly impacted investment in the life sciences space; however, changes in the U.S. regulatory environment over the last several years have also played a role.

In addition, there is a small but vocal minority in the community, the press and in Congress who are beginning to question the value of medical technology innovation in general. For example, coronary stenting is criticized for not providing a mortality benefit in "stable" cardiac

patients when compared to aggressive drug therapy. However, this narrow perception completely ignores the substantial benefit of stenting in reducing angina and improving quality of life for such patients.

Moreover, the 'aggressive drug therapy', that now clearly does improve mortality in stable patients, is itself the result of decades of astonishing innovation in pharmaceuticals, such as statins and ACE inhibitors, another vital part of America's medical innovation ecosystem.

Similarly, in the large portion of the population with 'unstable' cardiac disease and heart attacks, primary treatment by DES stenting, and vastly improved CABG surgery, provide clear and dramatic mortality benefits. In fact, the enormous improvement in mortality and morbidity due to coronary disease over the past thirty years, which every American is well aware of, has been due in great part to technological innovation, as well as the public health initiative to reduce smoking. This attack on innovation predicated on a narrow view of benefit is highly misguided and fosters an atmosphere that is increasingly hostile to entrepreneurial risk taking and may contribute to increased FDA risk aversion.

These environmental changes are beginning to stifle the economic growth and job creation that this industry has fueled in the U.S. for so many years and made our nation a world leader in medical device innovation, to the enormous benefit of the American public and patients.

At the same time, other countries have emulated our model – from financing methods to clinical research infrastructure – and have begun to draw innovators and capital away from the U.S. As a result, we are starting to see stagnation within the U.S. innovation ecosystem. Increasingly, seriously ill patients must wait in line behind patients in other countries for the groundbreaking devices they so urgently need – even when those devices were originally developed by U.S. companies. Percuataneous heart valves are the latest example of this unwelcome trend. Worse, a growing body of research suggests that the performance of the FDA has played a direct role in this decline. For most entrepreneurs and investors, the process has grown unpredictable – if not inscrutable. Working on short resources to fulfill a broad set of responsibilities, FDA personnel struggle to keep up with their workload. The effect can be frustrating and demoralizing for all parties.

Research provides the context for change

Many of my colleagues in the medical innovation ecosystem and the larger innovation economy have shared recent data and insights with Congress that provide evidence of this concerning trend. I believe it will be beneficial, for purposes of context, to briefly review the findings of some recent and important research on our topic today and I have summarized them below. I believe this research not only identified challenges, but also points to solutions.

"FDA Impact on U.S. Medical Technology Innovation, A survey of over 200 medical technology companies." (November 2010) In surveying more than 200 medical device startups on their experiences with FDA reviews, Stanford University's Dr. Josh Makower found that it took companies up to two years longer to navigate the FDA approval process for low- and moderate-risk devices, as compared with the same process in Europe. For high-risk devices, the FDA process took five times longer than the corresponding approval process in Europe. A significant majority of companies also characterized the European regulatory process as more predictable and transparent than the FDA's. Finally, nearly half of respondents indicated that key personnel assigned to their review by FDA changed during the review process, while one-third indicated that appropriate FDA staff did not attend meetings set up between the company and FDA to discuss review issues.
http://www.medicaldevices.org/node/846

"EU Medical Device Approval Safety Assessment: A comparative analysis of medical device recalls 2005-2009." (January 2011) Conducted by the Boston Consulting Group, this study compared public data regarding severe recalls of medical devices in Europe vs. in the U.S. over a four year period. It found that the number of such recalls was identical to that in the U.S. The conclusion was that the standards in place in Europe have not led to greater numbers of safety issues or recall rates versus the U.S., and that increasingly U.S. consumers have been sacrificing timely access to the most innovative devices without a corresponding gain in overall health or safety.
http://www.advamed.org/NR/rdonlyres/061A4AC8-D6A3-4960-826B672214A0A623/0/REPORTBCGEuropeanUSSafetyFINAL.pdf)

"Competitiveness and Regulation: The FDA and the Future of America's Biomedical Industry." (February 2011) This study, conducted by the California Healthcare Institute and Boston Consulting Group, examines the impact of FDA performance on U.S. competitiveness in the global medical innovation ecosystem since 2007. It found that review and clearance times for medical devices have increased significantly during this time – driven in part by the addition of new responsibilities assigned to the agency by Congress. Concurrently, a number of "high-profile safety problems" prompted the agency to give disproportionate weight in its risk-benefit analyses to mitigating potential risks rather than to the benefits of getting new technologies to market in a timely fashion. The result has been a U.S. regulatory process that discourages medical innovation and investment. Meanwhile, competing countries have streamlined their regulatory processes to draw U.S. companies abroad.
http://www.chi.org/uploadedFiles/2011%20CA%20Biomed%20Industry%20Report_FINAL.pdf

"Medical Technology Innovation Scorecard: The race for leadership." (January 2011) Conducted by PricewaterhouseCoopers (PwC), this study revealed three trends that bode poorly for future U.S. global leadership in medical device innovation. First, innovation is beginning to migrate overseas as more technologists and entrepreneurs build their companies, conduct their clinical trials, register their products and enter the marketplace in countries other than the U.S. Second, patients in foreign markets are beginning to benefit from advances in medical technology before their American counterparts with increasing frequency. Third, emerging-market countries are practicing a fundamentally different form of innovation that emphasizes "smaller, faster and more affordable devices" that reduce healthcare costs system-wide.
http://www.pwc.com/us/en/health-industries/health-research-institute/innovation-scorecard/index.jhtml

The overarching message delivered by all of these reports is unmistakable: The U.S. is losing its competitive lead in medical innovation, and will continue to do so unless lawmakers, regulators, and the private sector work together to bring the FDA's risk-benefit analysis back into balance.

Today, I would like to use this opportunity to provide recommendations on how innovators, investors and policymakers can work together to recalibrate the FDA's approach and regain

America's competitive edge in the field of medical devices, and more importantly, ensure that providers and patients have timely access to innovative therapies. Although my comments are focused on medical devices, it is important to clarify that NVCA and MedIC believe that any FDA reform efforts should focus on both the medical device and the drug/therapeutics regulatory process. NVCA would be happy to provide our recommendations for improving the regulatory process for drug/therapeutics at the appropriate opportunity.

NVCA's Recommendations for Change

Overview

Historically, the FDA has played two parallel roles in the U.S. medical innovation ecosystem. The first has been to assure the safety, quality and efficacy of medical devices for public use. This role is explicitly mandated by law. The second, which is not mandated in FDA law but has grown out of the agency's execution of the first role, has been to ensure that American patients have access to the most innovative treatments and technologies by providing a timely and predictable path to market. In balancing these roles, the agency has promoted the general health of the American people for decades.

The venture capital community supports the FDA in both of these roles and views the agency as a partner in bringing innovative treatments and devices to the American public. My colleagues and I are encouraged by the FDA's willingness to address many of the challenges revealed or confirmed, as the case may be, by the research I describe above. The challenges identified in the research present opportunities for action, and we want to be partners in developing positive changes to the FDA review process – changes that will put innovative medical devices in the hands of doctors and patients more quickly and safely than it does today.

The FDA took a first step in this regard in January, when it announced its Medical Device Innovation Initiative (MDII). NVCA applauds the FDA for recognizing the importance of establishing a collaborative, efficient and predictable regulatory review process for novel, life-saving technologies. Now, implementing this initiative in a rational and effective manner so that it can meet its stated objectives will be critical. We believe that maintaining America's competitive edge in medical innovation depends on it.

Venture capitalists also understand the enormous difficulty of the FDA's task. Medical devices are more complex than ever before, and the rate at which this complexity grows continues to accelerate. We also believe that the FDA needs more resources in order keep up with the speed of innovation. Attracting and keeping the talent required to do so is difficult under the agency's current budget constraints – a reality that the Makower study illustrates. We understand that resources are a challenge, given the overall U.S. budgetary situation, and we acknowledge that every expenditure will be and should be scrutinized for its effectiveness. However, we cannot let these difficulties serve as excuses for inaction or acceptance of decline.

Rebalancing FDA's Risk-Benefit Analysis for Medical Devices

As I mentioned earlier, the research suggests that FDA's risk-benefit analysis for novel medical devices has grown out of balance relative to its past practices and relative to current practices in other countries – especially in Europe. There are two major steps that the FDA can take to bring its risk-benefit analysis back into balance. Each pertains to the type of device under review.

510(k) devices

For devices the FDA deems as posing a low to moderate potential risk to patients, the agency employs a premarket notification process, also called the 510(k) process. Such reviews often involve new or improved devices that have the same intended use as existing devices, and they allow companies to build on established scientific evidence of safety and effectiveness.

In the cases of Class I and Class II 510(k) devices, the FDA should significantly expand its use of certified third-party entities for reviews. As the research suggests, this practice is used widely in Europe without incurring a premium in lost safety performance. The members of these reviewing entities are certified and noted experts.

In the U.S., third-party boards could handle as much as 50 percent to 75 percent of 510(k) reviews. Such a shift would significantly reduce the resource burden on the FDA because the agency could redirect its efforts to reviews of pre-market approvals (PMAs) and higher-risk 510(k) devices. In all cases, the FDA would have the right to pull back any cases considered by an approved third-party for further review as it deems necessary.

Pre-Market Approvals (PMAs) and higher-risk 510(k) s

For truly novel devices or for devices that may pose a high potential risk to patients, the FDA employs a pre-market approval, or PMA, pathway. This review process is more extensive and usually requires that companies conduct clinical trials to demonstrate efficacy and safety.

Under current law and in medicine in general, safety is not defined as the absence of risk, but rather as a reasonable assurance that the probable benefit of using a device exceeds its probable risk. Effectiveness is defined to require that the benefit be clinically significant, which means it must produce a clinically meaningful improvement in the health of a significant proportion of the population in which it is used.

For PMAs and Class III 510(k) devices, the FDA should establish, as a general principle, that reviewers employ a much more flexible risk-benefit analysis than what is currently in use. This means that while the general requirement that benefit exceed risk will always apply, the specific threshold for each of the elements within that analysis will change depending on the clinical context for the specific device. The review should take into account the incidence and severity of the disease at issue, whether there is an urgent and unmet need in the marketplace, and any potential safety issues. The FDA should make clear to its reviewers that this calculus is explicitly adjustable.

These adjustments might include, for example: reducing the level of evidence required to provide "reasonable assurance" and assessing what is a "clinically meaningful" improvement in health or what proportion of a population is deemed "significant" in a more targeted manner.

In addition, the FDA should measure probable benefits against probable risks, as the law currently requires. This contrasts with the practice of requiring some "absolute" high level of benefit to insure against a "possible", hypothetical, risk to health in the broader population, which appears to be the FDA's emerging practice. This latter approach is a theoretical exercise that will lead to regulatory paralysis.

We should combine this flexible, common-sense approach with an expanded FDA mission to explicitly include the promotion of medical innovation. Medical breakthroughs follow a well-established learning curve. They usually begin with only a small advantage over the status quo, and then dramatically improve over time. This was certainly true for coronary angioplasty and all forms of medical imaging. In fact, it has been true for virtually all major medical innovations over the past 50 years. Requiring that all novel products meet some "absolute" threshold of risk/benefit, particularly when they are first introduced, can derail many promising new ideas.

The FDA will argue that it already employs a flexible risk-benefit approach. We agree that it does in some cases and, when it does, the system works very well. However, the research data I cited suggests that this is not its common practice, or that it is not being applied uniformly in all cases. We believe that endorsing this flexible approach in legislation, combined with a strong legislative directive to promote innovation, will enable the senior management of FDA to standardize this approach throughout the Agency.

This type of flexible risk-benefit analysis is not without precedent here in the U.S. In fact, it has generated some extraordinary results in the pharmaceutical space. For example, in the cases of HIV and cancer therapies, Congress explicitly recognized the need to adjust the risk-benefit analysis as health crises began to unfold around these two diseases. As a result, the accelerated approval process for drugs in those diseases has been extremely successful and should be expanded, as I discuss below.

Other Opportunities for Reform at FDA

In addition to the recommendations above, NVCA MedIC is advocating for a number of broader reforms at FDA. While these are not exclusive to medical devices, I believe they are relevant to our discussion today. They are:

Strengthen FDA Mission and Structure. As I mentioned before, Congress should amend the FDA's statutory mission to explicitly include promoting public health through acceleration of access to novel therapies and technologies. Congress should also require the agency to routinely assess the impact of its decisions, policies, and priorities on unmet medical needs and medical innovation using agreed upon metrics. This process should be collaborative and

transparent with the public. The agency's mission should be clarified to strengthen the role of healthcare providers in decision-making so that doctors, rather than the FDA, act as the arbiter of what products are cost-effective in the marketplace.

Ensure that Individuals with Significant Expertise can Participate as Advisory Committee Members. In its current Advisory Committee structure, the FDA is often unable to access the best expertise to evaluate breakthrough therapies and technologies because of the tightening of its conflict of interest rules. Let me assure you that NVCA understands and appreciates the important need for rules to guard against conflict. However, we are deeply concerned that the current rules have made it nearly impossible to recruit qualified scientific experts who have the knowledge and understanding of clinical trial design, analysis, and drug and medical device development expertise. Without this expertise, FDA Advisory Committee members face significant challenges in making decisions on innovative products. This situation is stifling the advancement of novel therapies and technologies, leading to delays in access for patients.

The statutory cap on conflict of interest restrictions should be amended to permit qualified experts to serve on Advisory Panels (but, perhaps, with more limited voting authority). Experts should be transparent and provide full disclosure of conflicts. The FDA should have the ability to recruit more widely from non-academic pools of candidates who have the expertise to evaluate medical products. Similar to the requirement of a patient representative, all Advisory Committees should include an "Innovation Advocate" drawn from the community of investors and/or entrepreneurs who finance medical innovation.

Streamline the Regulation of Cross-Cutting Innovation Including Regulatory Pathway for Personalized Medicine. The FDA's current classification for drugs, biologics and medical devices (which include diagnostics) is ill-equipped to keep pace with the direction of cross-cutting medical innovation. This is particularly evident in the area of personalized medicine, which is bringing cross-cutting therapies together in radically new ways to help develop more effective treatments for individual patients. There is currently no structure to evaluate these personalized medicine approaches, which often combine diagnostics with

therapies, or therapies with devices, despite the fact that this area of lifesciences represents some of the most promising medical innovations of the next century.

The FDA should promote the development of personalized medicine through a well-defined regulatory pathway for approval of new therapeutics and companion diagnostics or drug-device combinations. For example, in the area of cancer therapy, the FDA should be required to provide guidance on the targeted approval process, and a manual of policies and procedures for administrative coordination of interactions between the sponsor, the Center for Devices and Radiological Health (CDRH) and the Center for Drug Evaluation and Research (CDER).

Conclusion

I'd like to conclude my testimony by reiterating that the U.S. has led the world in developing and marketing innovative medical devices for decades. If we act now to implement policies and regulatory reforms that bring the risks and benefits of novel technologies back into balance, we can revive the U.S. medical innovation ecosystem and ensure that seriously ill patients continue to have access to breakthrough therapies and technologies in a timely fashion.

I want to personally thank you for the opportunity to discuss these important issues with you today, and to thank you for your service to our country in your capacity as Members of Congress.

Mr. GOWDY. Dr. Gollaher.

STATEMENT OF DAVID GOLLAHER

Mr. GOLLAHER. Thank you, Chairman Gowdy and Ranking Member Davis.

My name is David Gollaher. I'm the president and CEO of CHI, the California Healthcare Institute, and I appreciate the opportunity today to address several important issues concerning the review and approval of medical devices by the FDA.

My testimony is based on a recent report CHI produced with the Boston Consulting Group, BCG, called Competitiveness in Regulation, the FDA in the Future of America's Biomedical Industry. One major theme of this report is that the FDA has a de facto industrial policy, for better or worse, and its operations shape the future of the medical device industry.

Now, history shows that a strong, science-based FDA and well-articulated, predictable, and consistent regulatory processes are essential to medical device investment, innovation, and patient care. Unfortunately, in recent years, there has been a significant deterioration in the environment for medical device innovation.

Beginning in approximately 2007, evidence clearly confirms that regulation of medical devices has become increasingly slow and unpredictable for both 510(k), as well as more complex pre-market approval, PMA, products. As documented by the FDA's own data and our competitiveness and regulation report comparing 2010 with the period from 2002 to 2007—that's the period of the first medical device user fee law—we note two things: First, the 510(k) clearances have slowed by 43 percent during those two periods and that PMA approval times have increased by 75 percent.

Clearly, part of the problem for the slowdown lies beyond the direct control of the FDA and its leadership. In recent years, for example, Congress has enlarged the Agency's scope into new fields, like tobacco, and added to its responsibilities and authority. Yet Federal appropriations have largely failed to keep up with new mandates, forcing greater reliance on industry-funded user fees.

But perhaps the most important factor in the Agency's recent history has been a change in its culture. Faced with accusations from the press, from consumer groups, and some in Congress, that its reviews were too lax and failed to protect public safety, the FDA has shifted emphasis on product reviews from benefits of new devices to focus increasingly on their possible risks.

Meanwhile, outside the FDA, another form of risk has darkened the prospects for medical technology investment. Beginning in 2008, the Great Recession devastated investment portfolios, including the pension funds and institutional endowments that historically have been the main source of life sciences venture capital. Against this background, levels of regulatory uncertainty, delays, missed timelines, doubts about eventual approval, uncertainty that was uncomfortable in good economic times became intolerable after the economic downturn, especially because investors and executives came to realize that there were practical and more efficient routes to the market outside the United States.

Today, complex medical devices approved via the PMA process in the United States are approved in Europe on average nearly 4

years ahead of the United States, up from just a year earlier over a decade ago, and no evidence exists to suggest that these faster rule times in Europe lead to patient safety-related problems. In fact, a recent promising consulting group study comparing the period from 2003 to 2009 comprehensively in Europe and the United States found virtually no difference in product recalls and safety problems.

Today, Congress, the FDA, industry, patient groups, and other stakeholders can come together with the will and ideas to improve agency performance, to rejuvenate support, and sustain a strong science-based FDA and efficient, consistent, and predictable review process to approve safe and effective medical technologies.

Critical to this effort is the need to address through constructive congressional oversight more appropriate balance between benefit and risk. Today, the FDA, the press, Congress, consumer groups, and others overwhelmingly focus on direct risk, product side effects, adverse events, technical product failures, but just as important, perhaps even more important, to consider are indirect risks, the distortions in the regulatory process, for example. How should we calculate the public health loss to patients if investors and companies avoid entire diseases and conditions because the FDA's standards for data are so extensive and its standards for approval so uncertain?

Similarly, we need to understand the cost of regulation, again, both direct and indirect. As this committee and Congress look for ways to create jobs and create a more business friendly environment, the full cost of the regulatory system should be fully weighed. As the global economy grows ever more connected, American leadership in medical device faces intense competition for capital, for markets, for talent, and for jobs. As these competitive forces gather momentum, investors, managers, and policymakers ignore them at their peril. If FDA regulation is just one factor among several, it nonetheless can be pivotal.

Thank you, again, for this opportunity to testify. I would be happy to answer any questions you may have.

Mr. GOWDY. Thank you, Dr. Gollaher.

[The prepared statement of Mr. Gollaher follows:]

C·H·I
CALIFORNIA HEALTHCARE INSTITUTE

Prepared Statement

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U.S. House of Representatives
Committee on Oversight and Government Reform
Subcommittee on Health Care, District of Columbia, Census and the National Archives

Pathway To FDA Medical Device Approval: Is There A Better Way?

June 2, 2011

Good afternoon, my name is David Gollaher and I serve as the President and CEO of CHI, the California Healthcare Institute. I appreciate the opportunity to address with this committee several important issues concerning the review and approval of medical devices by the U.S. Food and Drug Administration (FDA). The FDA exerts critical influence on medical technology innovation and investment, which, in turn, affects job creation, U.S. competitiveness and, most important of all, the tests and treatments available to patients. My testimony is based on a recent report CHI produced with The Boston Consulting Group (BCG) entitled "Competitiveness and Regulation: The FDA and the Future of America's Biomedical Industry."

CHI is the statewide public policy organization representing California's innovative biomedical community, including the state's premier research universities and institutes, venture capital firms, and medical device, diagnostics and biotechnology companies. Our mission is to identify and advocate policies that encourage life sciences research, investment and innovation.

California's medical device industry is responsible for breakthrough treatments and technologies that are improving and extending the lives of millions in the United States and around the world. It is also a key component of our state and national economy. There are more than 8,000 medical device firms in the United States employing over 400,000 people. California is home to some 1,200 of these medical device firms, far more than any other state in the nation. In addition, the 107,000 medical device jobs in California represent roughly one-quarter of our country's total medical technology workforce.

Over the past generation, California has developed a remarkably rich and diverse biomedical ecosystem that has fostered the growth of medical technology companies. This ecosystem is shaped and influenced by many external factors that can bolster or weaken it. At the federal level, these factors include policies set by Congress and government agencies in areas such as science funding, tax policy, intellectual property law, as well as Medicare coverage and payment policy, and regulation by the FDA.

History shows that a strong, science-based FDA and well-articulated, predictable and consistent regulatory processes are essential to medical device investment, innovation and patient care. Until recently, FDA policies and organizational structure have served as models for regulators around the globe. Indeed, the technical strength of the Agency and the clarity of its regulatory processes helped the United States become the global leader in medical device and biotechnology innovation.

Unfortunately, in recent years there has been a significant deterioration in the environment for medical technology innovation. This is partly the result of the financial crisis and ensuing Great Recession, which sharply reduced investment capital. But the most important factor has been the declining performance of the FDA.

Beginning in approximately 2007, evidence clearly confirms that regulation of medical devices has become increasingly slow and unpredictable for both 510(k) as well as more complex premarket approval (PMA) products.

The evidence here is both anecdotal and quantitative. When asked to rate the influence of federal policies on their industry's ability to advance biomedical research, innovation and investment in California, over 80 percent of respondents to the CHI/PricewaterhouseCoopers/BayBio 2011 CEO survey described the FDA as "extremely important." They rated the FDA as more critical than coverage and reimbursement policy, intellectual property, and tax and finance issues.[1] And when asked whether the current FDA regulatory approval process has slowed the growth of their companies, 74 percent reported that it had. At the same time, 69 percent of the respondents *disagreed* with the proposition that the U.S. FDA regulatory approval process is the best in the world.[2]

These executives' views reflect the recent slowdown in product clearances and approvals that are documented by the FDA's own data in our "Competitiveness and Regulation" report. Comparing 2010 with the 2003-2007 period of the first medical device user fee law (the Medical Device User Fee and Modernization Act of 2002):

- 510(k) clearances have slowed by 43 percent
- PMA approval times have increased by 75 percent

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[1] California Healthcare Institute/PricewaterhouseCoopers/BayBio "California Biomedical Industry 2011 Report," page 17, http://www.chi.org/uploadedFiles/2011%20CA%20Biomed%20Industry%20Report_FINAL.pdf.
[2] Ibid, page 49.

No single factor explains this decline. But it is difficult to attribute the slowdowns to resource constraints at the Agency's Center for Devices and Radiological Health (CDRH). In fact, CDRH has seen funding associated with device review grow from $141 million in FY2003 to $271 million in FY2009. During the same period, the number of device full-time employees (FTEs) increased from 1,485 to 1,707.[3]

Clearly, part of the problem lies beyond the direct control of the FDA and its leadership. In recent years, for example, Congress has enlarged the Agency's scope into new fields (e.g., tobacco) and added to its responsibilities and authority. Yet federal appropriations have largely failed to keep up with new mandates, forcing greater reliance on industry-funded user fees. Similarly, expanded and tightened responsibilities under the FDA Amendments Act of 2007 (FDAAA), such as intensified conflict of interest rules on advisory committees, have constrained the Agency's capacity.

These increased responsibilities would be hard to manage even if science stood still. But, of course, it has not. The past decade has witnessed an explosion of knowledge that has transformed drug and device innovation. Today, for example, medical device makers are working on ways to integrate nanotechnology and wireless communications in leading-edge technologies. The accelerating rate of scientific and technological advances severely challenges the FDA's ability to keep pace — and poses significant limits on the Agency's future responsiveness and performance.

Perhaps the most important factor in the Agency's recent history, though, has been a change in its culture. Faced with accusations from the press, consumer groups, and some in Congress that its reviews were too lax and failed to protect the public from safety problems with devices and drugs, the FDA has shifted emphasis in product reviews from the benefits of new devices to an increasing weight on their possible risks. When broken down, industry anecdotes about Agency uncertainty, unpredictability, "moving goalposts" and the like all seemingly revolve around ever increasing demands that are not justified by science or by any increased risk profile of the devices to which those demands are associated. From the perspective of an FDA device reviewer, this is understandable. After all, an individual reviewer has nothing to gain by approving a product, but much to lose by approving a device that has a problem in the future.

In a larger sense, a serious problem for device and for drug innovation alike is that there is no shared understanding of the benefit-risk calculus. Most medical advances carry some risks. And a basic principle of medicine is that the risk of any intervention – a procedure, a drug, a device – should be commensurate with the seriousness of the patient's disorder. Accordingly, for example, patients with advanced coronary artery disease are typically willing to accept risks for new minimally-invasive procedures and technologies that have a chance to not only treat the condition but result in faster recovery times and shorter hospital stays. What has happened within the FDA, though, is that more and more attention has been

[3] FDA Annual Budget All Purpose Tables Program Level Total Device FTEs; FDA MDUFMA Annual Financial Reports; Total Cost of the Device Review Process; BCG analysis

focused on the potential risks of technologies without sufficient appreciation of potential benefits.

Concurrent with these trends within the Agency, another form of risk has darkened the prospects for medical device investment and innovation. Beginning in 2008, the Great Recession devastated investment portfolios, including the pension funds and institutional endowments that historically have been the main source of life sciences venture capital (VC). Meanwhile, VC firms themselves also sought to reduce risk, trending away from early-stage investments – ones that combine the greatest innovation with the greatest risk. To make matters worse, the initial public offering (IPO) market for medical device and biotechnology companies all but vanished. After the collapse of iconic firms such as Lehman Brothers, Wall Street had little interest in offerings from young companies with no operating revenues that would need continuing infusions of capital over many years.

Smaller companies especially were forced to adapt by redesigning the biomedical business model – receive regulatory approval, demonstrate adoption by physicians and patients, and present to potential acquirers as a lower-risk investment. From the perspective of company and investor alike, winning approval sooner in any market became far more valuable than gaining FDA approval later.

Levels of regulatory uncertainty – delays, missed timelines, doubts about eventual approval – that had been uncomfortable in good economic times became intolerable after the economic downturn. Especially, as investors and executives came to realize, there are practical, more efficient routes to market outside the U.S.

Overseas regulators, especially in Europe, have recognized that regulatory efficiency can bolster biomedical innovation, investment and job creation without undermining patient safety. Today, complex medical devices approved via the PMA process in the United States are approved in Europe on average nearly four years ahead of the United States, up from just over a year earlier this decade.[4] And even for 510(k) products there is a clear trend that the more complex a product is, the more likely it is to be approved in Europe before the United States.[5] Of course, in either case, the result is that European patients benefit from U.S. innovations before Americans do. And no evidence exists to suggest that these faster approval times in Europe have led to systemic patient safety-related problems.

The FDA and its regulatory policies profoundly influence the current state and future strength of the U.S. biomedical industry. It is, indeed, part and partner in the dynamic ecosystem of biomedical research and innovation. But its regulatory processes have become unpredictable and slow, which, when combined with the impact of the Great Recession, the capital markets crisis, and more efficient regulatory processes in Europe, have had enormous and far-reaching effects on the American medical technology industry.

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[4] Ibid, pg 14
[5] Ibid, pg 14

Today, Congress, the FDA, industry, patient groups and other stakeholders can come together with the will and ideas to restore Agency performance – to rejuvenate, support and sustain a strong, science-based FDA and efficient, consistent and predictable review processes to ensure safe and innovative technologies and devices for patients in need.

Six Recommendations on How to Improve the Overall Environment for Medical Device Innovation

First, focus on core principles: safety and efficacy. Instead of creating expansive new authorities and responsibilities requiring ever increasing user fee levels, Congress and the FDA should focus on re-centering the Agency to its primary mission and core competencies, addressing the serious inefficiencies and performance breakdowns of recent years. In preparation for 2012 reauthorization of the device user fee act, the time is also right to evaluate, and where appropriate, correct any measures within that law that may have detracted from the FDA's performance without any commensurate improvement to patient safety. One example, for both devices and drugs, is the stricter advisory committee conflict of interest rules instituted under the Food and Drug Agency Amendments Act of 2007 (FDAAA), which have made it increasingly difficult for the most experienced medical experts to serve on advisory committees.

Second, while increased funding might not always be the best solution, in this case, cutting the Agency's budget would be damaging. As mentioned earlier, Congress has underfunded the Agency for many years, and while recent budget increases have helped in terms of staff recruitment and retention, we are concerned with the recent House proposal that would cut $285 million from the FDA for FY2012, an 11.5 percent reduction from FY 2011. What is needed – to support medical technology innovation, job creation and patient and public health -- is a steady and sustained congressional commitment to FDA funding, even in today's difficult budget environment.

Third, more must be done to train Agency reviewers and managers. This is an area of widespread agreement across all stakeholders, and we applaud CDRH Director Dr. Jeffrey Shuren for making this a top Center priority, along with the publication of guidance documents important for both review staff and industry, for example, what is expected in a 510(k) submission and how it should be presented.

Fourth, while the European model of device review and approval differs significantly from that of the FDA, there still may be lessons in terms of process and managerial improvements to address the numerous consistency, predictability and efficiency concerns industry has experienced. To that end, CHI is undertaking a follow-up to our "Competitiveness and Regulation" report to explore and examine device approval processes in Europe. We plan to complete this project this summer and we hope it will provide this and other Committees, the FDA and others with the needed information to make the best decisions on possible Agency process improvements.

For example, the study may lead to ideas for improvements and enhancements to the Center's third-party review process.

Fifth, we believe that the Agency and industry stakeholders should be encouraged to collaborate, interact and work together more now than at any time in the past. For example, dialogue between a reviewer and a sponsor on a new submission can help identify important questions and provide clarity around Agency expectations early in the process – leading to fewer delays and improved certainty.

More generally, and as noted earlier, the rate of scientific and technological advancements is something the Agency is largely unable to keep up with. We applaud Dr. Shuren and the Center for its Innovation Initiative announced earlier this year. While the details of the various elements of the Initiative are still in the works, we hope that one important theme will include Agency, industry and other stakeholder partnerships and collaborations.

We believe this is an especially important element given the recent and disheartening decision by regulatory bodies, including the FDA, unilaterally to disband the Global Harmonization Task Force (GHTF), thus ending the co-equal partnership between international regulators and industry at the GHTF that, since its inception in 1992, has served "to achieve greater uniformity between national medical device regulatory systems" with two key aims in mind being "enhancing patient safety and increasing access to safe, effective and clinically beneficial medical technologies around the world."

Finally, and perhaps critical, is the need to address, including through constructive congressional oversight such as today, an improved, more appropriate balance between benefit and risk. Today, the FDA, the press, Congress, consumer groups and others overwhelmingly focus on "direct" risks: product side effects, adverse events and technical product failures. Just as important to consider are indirect risks – distortions in the regulatory process, for example. How do we calculate and consider the public health loss to patients if investors and companies avoid entire diseases and conditions because the FDA's demands for clinical data are so extensive and its standards for approving new products so uncertain?

Similarly, consideration must be given to the costs of regulation, both direct and indirect. As this Committee and the Congress seek paths to create new jobs and a more business friendly environment, the costs of the regulatory system should be carefully weighed. As the global economy grows ever more connected, American leadership in the medical device sector faces intense competition: for capital, for markets, for talent and for jobs. As these competitive forces gather momentum, investors, managers and policymakers ignore them at their peril. If FDA regulation is just one factor among several, it nonetheless can be pivotal.

That concludes my formal statement. That you again for the opportunity to testify on this important issue, and I would be pleased to answer any questions you may have.

Mr. GOWDY. Dr. Redberg.

STATEMENT OF RITA REDBERG, M.D.

Dr. REDBERG. Thank you, Chairman Gowdy, Ranking Member Davis, and other distinguished Members for inviting me to submit testimony on medical devices at this important hearing.

I am Rita Redberg, M.D., professor of medicine and full-time faculty and cardiologist at the University of California San Francisco Medical Center for the last 21 years. I'm also chief editor of the Archives of Internal Medicine, one of the most preeminent, peer-reviewed journals of scientific research and internal medicine. The journal frequently publishes articles related to use of medical devices.

As a practicing cardiologist, I appreciate the advantages that medical devices offer in care of my patients every day. I also know the problems and heart aches that can occur when an implanted device is found not to be effective or has been found to be defective and is recalled.

My first priority is high quality medical care of my patients. Thus, it is critical to me that any approved high-risk device first have been shown to be safe and effective. Unfortunately, this standard is too frequently not currently being met.

First of all, only 1 percent of all devices goes through the pre-market approval pathway. Congress envisioned that all class three devices, those with greatest risk, would be approved through the more rigorous pre-market approval process. However, the 2009 GAO report entitled, FDA Should Take Steps to Ensure that High-Risk Device Types Are Approved Through the Most Stringent Review Market Process found that this congressional directive was not being followed. The report found that the majority of high-risk devices do not go through the original PMA process and, instead, are commonly approved with no clinical study data.

Even the PMA process itself has been found to need improvement in its clinical data requirements. The gold standard for clinical data is randomized, controlled trials. Yet our recent study that was found in JAMA found that fully two-thirds of PMA cardiovascular devices were approved on the basis of only a single study. Moreover, only 27 percent of these studies were randomized, and only 14 percent were blinded. Only half had a comparison control group. Thus, the majority of high-risk implanted devices were approved without the support of high quality data on safety and effectiveness.

For example, as chronicled in the Chicago Tribute last week, the Myxo valve, an annuloplasty ring permanently implanted as a heart valve replacement, was approved through a 510(k) process. This valve clearly falls within the definition for a class three device and was originally classified as such by the FDA. However, according to the Tribune, the FDA "rubber stamped" the device industry's request to downgrade from class three to class two in 2001. The petition for reclassification cited studies finding that the rings were safe and effective. However, none of the studies were randomized clinical trials, and there were other problems.

Many of the study investigators were heart surgeons who invented the devices and had financial relationships and were receiv-

ing royalties from the manufacturer. These relationships were not revealed to the patients who received these annuloplasty rings. Moreover, Edwards had sold these devices for 2½ years without FDA 510(k) clearance as the company had determined from an FDA document that a new 510(k) was not needed. However, shortly after press reports on this missing FDA clearance, the company submitted a new 510(k) and FDA ultimately cleared the device in April 2009. There were no penalties to the company for this infraction.

In the most recent 5-year period, there have been more than 3,400 adverse events reported involving annuloplasty rings, and these rings have been linked to only 56 fewer deaths than heart replacement valves, yet the annuloplasty ring went through a 510(k) clearance without benefit of clinical trials. This number is especially disturbing as it's estimated that only 5 percent of all adverse events are ever reported. Adverse event reporting is voluntary for hospitals and doctors.

Manufacturers are required to report deaths and injuries. However, there are an unknown number of delays in adverse event reporting by the manufacturer. For example, last April, an FDA inspection of medical device maker Edwards Lifesciences identified six complaints of adverse events related to use of mitral annuloplasty rings and pericardial prosthetic heart valves that were not reported to the FDA within the required 30-day window.

The FDA is sorely underfunded for its enormous mission of protecting the public health by assuring food, drug, and device safety. FDA device review is partially supported by industry user fees, but currently, device user fees are lower than pharmaceutical user fees, even though drug trials are much more expensive to conduct than device trials. The PMA user fees provide less than one-fourth of the estimated $870,000 average cost of the review in terms of FDA staff and resources, thus, creating a disincentive for FDA to use the PMA process even when Congress had intended its use for high-risk devices.

Increasing the budget for the Center for Devices would help speed up device approvals by allowing more FDA staffers to review applications more expeditiously, but the process cannot and should not be speeded up by foregoing the requirement for data of safety and effectiveness.

Finally, the device approval process has been compared to the European process, but a recent review in the BMJ found that while European conditions may be more favorable for industry, they are not necessarily best for patients.

The decisionmaking process in Europe occurs behind closed doors. There is no publicly available reason for granting a CE mark, the European approval. The BMJ editors attempted to contact 192 manufacturers to get evidence of the clinical data used to approve their devices in Europe, and everyone denied access, stating that, "clinical data is proprietary information."

True innovations are welcome, but cannot be recognized as such without clinical trial evidence to show that new technologies are beneficial for patients. Only high-quality clinical trials can assure safety and benefit, especially for invasive devices from which patients incur risk of infection, bleeding and even death. It is well

worth the time up front to gather data of safety and effectiveness so that my fellow cardiologists and I can confidently tell our patients that implantation of a device is in their best interest.

Thank you for your attention. I would be happy to answer any questions.

Mr. GOWDY. Thank you.

[The prepared statement of Dr. Redberg follows:]

June 2, 2011
Congressional Hearing

Thank you Chairman Gowdy, Ranking Member Davis and other distinguished members of the House Oversight and Government Reform Subcommittee for inviting me to submit testimony on medical devices at this important hearing. I am Rita Redberg, MD, MSc, Professor of Medicine and full-time Faculty Member in the Division of Cardiology at the University of California, San Francisco Medical Center for 21 years. I am Director of our Women's Cardiovascular Service. I am also the chief editor of the *Archives of Internal Medicine*, one of the most preeminent peer-reviewed journals of scientific research in internal medicine. I am a member of the FDA Cardiovascular Device Expert Panel. Much of my own research has concerned the appropriate and optimal use of medical devices in patient care, and the journal frequently publishes articles related to use of medical devices.

As a practicing cardiologist, I appreciate the advantages that medical devices offer in care of my patients every day. I also know the problems and heartache that can occur when an implanted device is found not to be effective or has been found to be defective and is recalled. My first priority is high quality medical care of my patients. Thus, it is critical to me that any approved high-risk device has FIRST been shown to be safe and effective. Unfortunately, this standard too frequently is not currently met. First, *only 1%* of all devices go through the pre-market approval pathway. Congress envisioned that all Class III devices (those with greatest risk) would be approved through the more rigorous pre-market approval (PMA) process. However, the 2009 GAO report entitled FDA *Should Take Steps to Ensure That High-Risk Device Types Are Approved through the Most Stringent Premarket Review Process* found that this Congressional directive was not being followed. The report found that the majority of high-risk devices do not go through the original PMA process, and instead are commonly approved with no clinical study data. Class III devices are defined by the FDA as "usually those that support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury." Of over 10,000 submissions for Class II devices that FDA cleared via the 510(k) process, the GAO found that "over one -quarter were for devices that were implantable: were life sustaining; or presented significant risk to the health, safety or welfare of a patient" and thus should have gone through the PMA process. Even, the PMA process has been found to need improvement in its clinical data requirements. Our recent study published in JAMA found that fully two-thirds of PMA cardiovascular devices were approved on the basis of only a single study. Moreover, only 27% of those studies were randomized and only 14% were blinded, and only half had a comparison control group. Thus, the majority of these high-risk implanted devices were approved without the support of high quality data on safety and effectiveness.

For example, as chronicled in the *Chicago Tribune* last week, the Myxo valve, an annuloplasty ring permanently implanted as a heart valve replacement, was approved through a 510(k) process. This valve clearly falls within the FDA definition for a Class III device and was originally classified as such by FDA. However, according to the

Tribune, the FDA "rubber-stamped" the device industry's request to reclassify from Class III to Class II in 2001. The petition for reclassification cited studies finding that the rings were safe and effective, however, none of these studies were randomized clinical trials. Furthermore, many of the study investigators were heart surgeons who invented the devices and were receiving royalties from the manufacturer. These relationships were not revealed to the patients who received these annuloplasty rings. Moreover, Edwards had sold the device for two and a half years without 510(k) clearance, after the company determined from an FDA document that a new 510(k) wasn't needed. However, shortly after press reports on this lack of FDA clearance, the company submitted a new 510(k), and the FDA ultimately cleared the device in April 2009. There were no penalties to Edwards Lifesciences for this infraction. In the most recent 5-year period, there have been more than 3,400 adverse events reported involving annuloplasty rings and these rings have been linked to just 56 fewer deaths than heart replacement valves, yet the annuloplasty ring went through a 510(k) clearance without the benefit of clinical trials. This number is especially disturbing, as it is estimated that only 5% of all adverse events are even reported. Adverse event reporting is voluntary for hospitals and doctors. Manufacturers are required to report deaths and injuries. However, there are an unknown number of delays in adverse event reporting by the manufacturer. For example, last April, an **FDA** inspection of medical-device maker Edwards Lifesciences identified six complaints of adverse events relating to use of mitral annuloplasty rings and pericardial prosthetic heart valves that were not reported to the FDA within the required 30-day window.

There is also room for improvement in the completeness of the data collected and reported by the FDA on approved devices. Our recent study published in *Circulation: Quality and Outcomes*, which reviewed Gender Bias in PMA cardiovascular devices, we found that nearly one-third of FDA studies did not report sex of the enrollees, and only 41% contained the required gender bias analysis confirming that data evaluated effectiveness in both men and women. A recent meta-analysis of implantable cardiac defibrillators (ICD) found that randomized trials showed no mortality benefit of ICDs in women, yet these devices have been routinely implanted in women for more than a decade despite the lack of evidence of benefit in women.

After FDA approval, Medicare and private insurance coverage often immediately follows and use generally expands. For example, drug coated stents, approved in 2003, meteorically shot to 90% of all stents used. The vast majority of usage was and remains off-label, e.g. not for FDA approved indications. A recent study found that use of such stents has added as much as $1.6 billion to Medicare costs since their introduction. Yet studies show that approximately one-third of these devices are implanted in persons who have never been shown to benefit from their use, such as persons without any symptoms.

The FDA is sorely underfunded for its enormous mission of protecting the public health by assuring food and drug and device safety. FDA device review is partially supported by industry user fees, Currently, device user fees are lower than pharmaceutical user fees even though drug trials are much more expensive to conduct than device trials. The FDA charged a standard fee of $4,007 for a 510(k) submission (and only half that amount for

small companies) and $217,787 for an original PMA (one-quarter that amount for small companies), compared to $702,750 to $1,405,500 for prescription drug applications according to 2010 data. The PMA user fees provide less than one-fourth of the $870,000 average cost of the review in terms of FDA staff and resources, creating a disincentive for FDA to select the PMA process. Increasing the budget of the Center for Devices and Radiologic Health would help to speed up device approvals by allowing more FDA staffers to review applications more expeditiously. But the process cannot and should not be speeded up by foregoing the requirement data of safety and effectiveness.

Technology is widely agreed to be the #1 reason for rapidly increasing health care costs and rapidly rising premiums, which threaten the stability of many US businesses. The medical device industry is over $100 billion per year. That is a good investment when such devices have been shown to be beneficial. But too often in the US we do not have this assurance of patient benefit before FDA approval.

The US device approval process often is compared to the European medical regulatory system. A recent review in the *BMJ* found that while European conditions may be more favorable for industry, they are not necessarily best for patients. The decision making process in Europe occurs "behind closed doors" and there is no publicly available summary for the reason for granting a CE mark. The BMJ editors contacted 192 manufacturers to request evidence of the clinical data used to approve their devices in Europe and every one denied access, stating "clinical data is proprietary information". The UK regulator expressed concerns about their current system, stating, "the evidence on safety and efficacy of new devices and new procedures at the time they are introduced into the UK practice is very variable," and noting that the evidence base for most devices was poor.

True innovations are welcomed, but cannot be recognized as such without clinical trial evidence to show that new technologies are beneficial for patients. Only high-quality clinical trials can assure safety and benefit, especially for invasive devices, from which patients incur risk of infection, bleeding and even death. It is well worth the time up front to gather data of safety and effectiveness so that my fellow cardiologists and I can confidently tell our patient that implantation of a device is in their best interest.

Mr. GOWDY. The chair would recognize the gentleman from Illinois Mr. Davis for his 5 minutes of questions.

Mr. DAVIS. Well, thank you very much, Chairman.

Mr. Lasersohn, I assume that you and your colleagues help people with all of these great ideas find the resources to develop some of the products that they manufacture and put together. Is that——

Mr. LASERSOHN. We certainly try to, yes, sir.

Mr. DAVIS. And every conversation almost that you have about health care, there's the whole issue of costs, the issue of liability, the issue of risk. If standards are altered, let's say, perhaps downward, would that pose a problem for the people in your business?

Mr. LASERSOHN. Well, we don't think the standards should be lowered, as a matter of fact. We support the safety and efficacy standard. The question—and I think this is the point Dr. Shuren was making—is—it's the question of how it is implemented and the how the agency manages it.

So we're not at all suggesting a reduction in the standard. We're recommending, in fact, what the agency does already in some cases when it works very well, which is to change the balances within the standard, the levels of evidence, for example, what is believed to be significant, what's meaningful, depending on the context and all—and other factors that may be relevant. The agency does this already in many, many cases. It is really the commonsense thing to do. I'm sure Dr. Shuren would agree. It's just a question of how do we make this a consistent practice within the FDA.

Mr. DAVIS. So, then, the higher the standards, the more comfort you and your colleagues have relative to the likelihood of trial lawyers getting involved in your business, lawsuits and all of those kinds of things.

Mr. LASERSOHN. You know, we think there really is value in the FDA setting a rational bar for approval. All of the points Dr. Shuren made we agree with in that respect. It's really a question of the internal balance in the last few years, we believe, has really gotten out of whack, and that the risk side of this equation has come to really dominate the culture of the FDA. And we don't suggest the basic risk-benefit idea should be abandoned in any sense or safety and efficacy. It's really just bringing it back into balance.

Mr. DAVIS. Dr. Gollaher, part of the discussion this afternoon has centered around some comparisons between what we do with our Food and Drug Administration, what's done in the European Union. Given the discussion, if you had to say let's maintain and perhaps even maybe intensify, would that be your position, or would it be, well, we probably could get away with becoming more like them?

Mr. GOLLAHER. I think that the idea of the FDA being the gold standard is what we should aspire to. I think that regulation can be a competitive tool, as it has been in the past in the United States, and that our goal should be to make the regulatory process the best in the world, which also means the most efficient and the highest performing. I think the industry's goal is exactly that; in other words, to have clear communications on standards between industry and the agency, and to see a process in which those standards are clearly applied and implemented.

The comments earlier about changing goalposts, about not knowing what's required, is something that bothers many, many companies. I think there are enormous opportunities for performance improvements, many of which Dr. Shuren in his comments focused upon.

Mr. DAVIS. Dr. Redberg, you expressed a great deal of affinity for innovation and for being able to come up with new approaches, new techniques, new technology, but pretty much it seems to me that you're saying at the end of the day that we really need to have as much assurance as we can possibly have that whatever it is that we've come up with is going to work in the best interests of the patient, and that they are going to be able and should be able to feel safe, secure and comfortable with what we've got. Is that an interpretation of what you were saying?

Dr. REDBERG. That's correct, Mr. Davis, absolutely. As I said, innovation—we've had great advance in medical care, but a new technology, just because something is new doesn't mean it's good for patients. And so every new—and we've gotten to an era where we have a lot more devices and a lot more complex technology, but that means there's a lot of down side. We're now mostly talking about implanted devices that are going inside someone's body. And so it's really incumbent upon us to know that before I recommend that device to be implanted in my patient, that I have clinical data, high-quality clinical data, showing safety and effectiveness. And really it's effectiveness, because we don't need to talk about safety if there is no benefit to implanting that device. As Dr. Shuren pointed out, the EU's standard does not include effectiveness.

We all know, I mean, we've heard about the metal on metal recall, the ICD lead recalls; there was just the Boston Scientific recall a few days ago. I mean, these devices have been implanted and lead to serious adverse events, including death. And so I do embrace innovation, but it has to be shown to be beneficial.

Mr. DAVIS. Well, let me thank all three of you for sharing your expertise with us, your willingness to come and testify.

I thank you very much and yield back, Mr. Chairman.

Mr. GOWDY. I thank the gentleman from Illinois.

Mr. Lasersohn, if you're going to change the risk structure, are you also advocating changing the litigation structure that we have in this country?

Mr. LASERSOHN. Wow, that's a hard one. I think that litigation absolutely does contribute to excess use of a lot of medical technology, and I think that is a factor that we really have to consider. So I think reasonable litigation reform is something to think about.

In terms of the risk side of it, I don't think that the view is at all to accept greater risk in the sense that a device has no—that the risk-benefit has become undesirable. The argument is that you accept a higher level of risk only if there is a higher level of benefit to balance it out. So obviously——

Mr. GOWDY. How do you know——

Mr. LASERSOHN. Sorry.

Mr. GOWDY [continuing]. That balancing?

Mr. LASERSOHN. That's the job of the FDA and then ultimately the medical community. It's a decision that a physician makes

every day. Every decision a physician makes involves some level of risk averseness.

Mr. GOWDY. But the physician doesn't do it for devices. Physicians aren't well equipped to go do their own research, I would not imagine. So how do you suggest that physicians who wind up using these products and devices, how do they balance risk with efficacy?

Mr. LASERSOHN. So they don't do it across the board. First of all, the FDA really does make that decision ultimately, right? And we believe in that system. So the FDA is ultimately responsible for deciding that a particular device, the risk-benefit is favorable. That's why it's approved.

But what a physician does is when that approval happens, it's approved for a very broad population of patients, it may not actually be an appropriate use of a device in a particular patient. And that's really what the physician does. It decides—a physician might decide that the use of the drug-eluting stent, even though it is technically for a particular use in a particular patient with a particular set of comorbidities and risk factors, perhaps age, perhaps diabetes, other unfavorable factors, that in that particular case the risk-benefit is not worthwhile to use it.

So even though the FDA is primarily responsible for this, putting a device onto the market, ultimately a physician really exercises fine-tuned judgment about whether to use a particular device in a particular patient.

Mr. GOWDY. I'm with you, and I have to confess, I'm just a prosecutor in South Carolina that made very poor grades in math and science. So say it slow for me to get it. The FDA doesn't do their research, though, correct?

Mr. LASERSOHN. No, but it relies on the research provided.

Mr. GOWDY. All right. To Dr. Redberg's point, what in your paradigm eliminates physicians who have a fiscal stake in the outcome of the research? Where would you factor that into it?

Mr. LASERSOHN. First of all, it has to be disclosed. The industry has taken a very, very strong position on this that any conflicts of interest must be disclosed. If they are not disclosed, that's, I think, a mistake. I think they should be disclosed so that people like the FDA can weigh that in their analysis of the validity of the data that's being provided to them. In certain cases is may be completely inappropriate for a physician to conduct, for example, a clinical trial if they are the inventor of the technology and there are other alternatives, and they very well may not be appropriate in that case.

Mr. GOWDY. Dr. Gollaher, let me see if I can qualify you as an expert in contrasting our system with the European system. Are you aware of any studies that suggest the recall rate is higher in Europe than in the United States?

Mr. GOLLAHER. No.

Mr. GOWDY. Are you aware of any studies that indicate the bad outcome rate is higher in the European Union than in the United States?

Mr. GOLLAHER. No.

Mr. GOWDY. Is the litigation rate higher in the European Union than in the United States?

Mr. GOLLAHER. No.

Mr. GOWDY. Is there anything about the U.S. system that you think is superior to the European system?

Mr. GOLLAHER. Yes.

Mr. GOWDY. What is it?

Mr. GOLLAHER. I think that on balance the centralized approach with a stronger publicly funded science base is a better system than a completely distributed system. However, I think that there is some balance to be struck, and that there are lessons that we can learn from the European system in addition to that.

Mr. GOWDY. If Dr. Shuren were to go on vacation for 2 weeks and appoint you the head of FDA for this section, what are the first three things you would do before he got back?

Mr. GOLLAHER. We'd all be in trouble, but I think one of the things that would be interesting to know is much—to gain a deeper understanding of what's happening in Europe. Quite clearly there has been a major migration of medical technology companies, technologies invented in America that are being introduced first in Europe. There is an economics of that, and we understand part of it.

What we don't understand nearly well enough is the taxonomy of the European system. We need more information. That would be a high priority, because right now Europe is outcompeting us with respect to the regulatory process, and it's exerting an economic cost in terms of jobs and innovation in the United States.

The second thing is to decide which things can be done immediately from a managerial perspective in the agency to improve its performance. And the third thing is a corollary to that, which is what needs legislation. Right now we're in the MDUFA negotiation process. There's some things that Congress needs to legislate in order to promote agency improvement, and we need a better understanding of what's managerial, and what the leaders can do, and what needs congressional support. And, of course, part of that, which Dr. Shuren mentioned, is providing adequate resources for the agency. I think all of us believe that's a fundamental principle.

Mr. GOWDY. Dr. Redberg, your passion and advocacy for your patients is palpable, and I would commend you for that. But I think you would agree that patients who either die or get sicker because they're waiting on the approval process to work, that's not any more fair to them if the delay is unnecessary than patients who are subjected to devices that are either unsafe or just don't work.

So how do you strike the balance between the risk, which is—I would imagine is impossible to zero it out, but what level of risk is acceptable given the fact that for lots of patients time is the greatest risk that they face?

Dr. REDBERG. Sure. I agree that we do have to strike a balance. And so certainly I want some clinical data, human data of benefit, particularly for a high-risk implanted device.

But I think it is possible, you know, to have a sort of followup period for studies, because obviously the longer the followup, the longer for the time to approval. I think a shorter period is fine, assuming that we have actual postmarketing data, because frequently the FDA mandates postmarketing data means we're going to follow that device for the next year to 3 years, but that data actually is not ever coming. So then if we had a more robust postmarketing system, I think that there's less onus on getting every-

thing up front preapproval to FDA. And so I think we can strengthen the evidence both premarket and postmarket, kind of like the accelerated approvals for drugs that we do, to have that system with a real postmarketing registry where we follow. We have so many new carotid stents and defibrillators, but we have very little data on how patients are doing 1, 2, 3, 4 years later.

Mr. GOWDY. In your testimony you stated, and others, I think, have stated today, that the European model does not include efficacy as part of the analysis, which, again, those of us that don't practice medicine and are not experts, that was surprising, because I wouldn't know what else you would consider. I guess safety. I guess it can be safe and still a placebo. Is that what you meant by that?

Dr. REDBERG. That's right. And actually unfortunately, especially with devices, there is a lot of placebo effect. For example, recently vertebroplasty is the spinal procedure for back pain that has been FDA approved on the basis of a trial that did not have a sham control. A year or 2 after FDA approval, the New England Journal of Medicine published two randomized trials where they did vertebroplasty and they did a sham control, and there was no difference in the outcomes of those patients certainly. And some insurance companies then reevaluated their approval.

Medicare spends over a billion dollars on vertebroplasty, for this procedure that has never been shown to be more beneficial than a sham control. So it is an excellent point. In order to see benefit, especially for a device, you have to have an adequate control group. But once you've established benefit, then the level of risk is going to depend on the patient, the population, and I think that can be better determined after FDA approval when you have widespread use.

The other point about legal is for PMA approval. As you know better than I do, the Supreme Court by *Riegel* v. *Medtronic,* that is the only patient protection for patients that have PMA devices. They cannot sue in State court for *Riegel* v. *Medtronic* for devices.

Mr. GOWDY. I think we all agree we don't want our capital, our jobs, our companies fleeing the United States because our system is second-rate. Nor do we want to trade safety for expediency. So thank you for helping educate the committee, the subcommittee, and we look forward to hearing from you again. I appreciate, again, your patience as we had to vote and go through two other panels. And I applaud your knowledge, your acumen, your professionalism, and your civility toward one another and to the subcommittee.

Anything else, Mr. Davis?

Mr. DAVIS. No, sir.

Mr. GOWDY. With that, the subcommittee hearing is adjourned, and I will come down there and thank you. The hearing is adjourned.

[Whereupon, at 3:55 p.m., the subcommittee was adjourned.]

[Additional information submitted for the hearing record follows:]

Medical Technology Company Case Studies

to accompany the testimony of

Congressman Erik Paulsen, Member of Congress

before the House Committee on Oversight and Government Reform

June 2, 2011

1. **Ocular Therapeutix**

Ocular Therapeutix, maker of the ReSure™ Adherent Ocular Bandage, has been interacting with the FDA since 2007. FDA's guidance to the company has been ever changing and untimely. After completing a 450 patient study in an effort to obtain a 510k approval, Ocular Therapeutix was informed that a PMA path was required and that another 450 patient study was necessary. The company is now seeking IDE approval to initiate this pivotal study. The delays, however, continue as new rounds of questions surface time and time again. Commercialization in the U.S. remains more than two years away. At the same time, the device was approved in Europe under a CE Mark in 2008 and was hailed as one of the five most promising innovations for ophthalmology by the ASCRS. Having already completed a round of layoffs, if these delays continue, the team is considering abandoning the product altogether.

2. **Visiogen**

Visiogen, which is developing an accommodating intraocular lens and was acquired by Abbott/AMO in 2009, has been seeking FDA approval of its product since 2009. After successfully completing its pivotal clinical study, the company submitted its PMA application to the FDA in Quarter two of 2009. Currently, 23 months have passed, multiple rounds of questioning have occurred, and Visiogen is still awaiting a panel date. In a striking comparison, CE Mark approved the device over five years ago, in Quarter two of 2006.

3. **GI Dynamics**

GI Dynamics, which is developing the Endobarrier™ Gastric sleeve to treat obesity and Type II diabetes (a growing epidemic in the US), received its CE Mark in November 2008. Since receiving its CE Mark, the company has been commercializing its device in Europe and has successfully treated over 500 patients worldwide. Approval for a US pilot study was received in June 2010. The company had originally planned to initiate this study by the end of last year, but a competing company's failure with the FDA, and subsequent closure, has caused GI Dynamics to rethink its strategy. As a result, GI Dynamics has since put its U.S. plans on hold. Furthermore, these regulatory challenges have made it more difficult to access the U.S. capital markets and GI Dynamics is actively pursuing an IPO on an overseas exchange.

4. **Luminous Medical**

Case Study: Luminous Medical Inc. and the FDA

Background:
Luminous Medical was founded in November 2005 to serve the emerging clinical need for improved methods to control glucose levels in patients who are critically ill. It has long been known that critically ill patients, whether diabetic or not, often lose the ability to control their glucose levels. However, it was not until a landmark study was published in 2001 that it was believed that this was a harmful condition. Prior to that study only the most extreme glucose levels were actively treated. Since 2001, clinical practice has been moving toward normalizing glucose levels with intravenous insulin and frequent glucose monitoring. This is a challenging undertaking and it has proven to be very difficult, if not dangerous, to accomplish with the existing tools for patient management. Recognizing that the hand-held glucose meters used to measure glucose on a regular basis were part of the problem, Luminous set out to provide something better.

Product Requirements:
Intravenous insulin is a very powerful, fast acting drug that when used improperly can change glucose levels too quickly and too severely. While hyperglycemia is the condition that is being treated, it is not difficult to create iatrogenic hypoglycemia by giving too much insulin. Since the patient's response to insulin is not a constant, the first requirement is that glucose must be checked frequently, typically on an hourly basis. It is also important to determine the glucose concentration in circulating blood as this is the medium that distributes this important fuel source to the body's cells. Other body fluids are either not in equilibrium with circulating blood or significantly lag in detecting changes in glucose. A means to frequently sample circulating blood without injuring the patient or exposing them to infection risk is also a requirement. Finally, since the glucose measurement is used to determine the infusion rate of insulin, the accuracy of the measurement must be very high and not subject to influence by the patient's critically ill physiology or medications.

Summary:
1. Frequent measurements
2. Sample from circulating blood
3. Safe access to blood samples
4. Accurate measurements

Luminous Product Development:
November 2005-First Generation Development
Luminous began its development efforts using a glucose measurement method that was innovative and novel. The blood access method was fully automated and required a dedicated venous catheter for its operation. After considerable development effort a working model of the product was demonstrated and a pre-IDE meeting was requested with FDA to discuss the clinical and regulatory path. The meeting was granted and Luminous representatives traveled to FDA on September 24, 2008.

September 2008-First Meeting with FDA

After a thorough presentation and discussion of the new technology FDA provided feedback that helped guide future product development. In that meeting the following information was provided:

1. FDA was leaning toward a PMA for the product due to the novel glucose measurement method. FDA later modified their position saying that there was no *a priori* reason why the product could not follow the 510k path but it was clear that there was a preconceived idea that a PMA was likely.
2. A higher level of control will likely be required compared to handheld meters used by patients with diabetes. No clarification on the level of control that would be required was available.
3. Handheld meters currently used to measure glucose in the ICU are not cleared for that purpose and are contraindicated for this use. This was not generally known to meter manufacturers prior to this time and there are no cases where product labeling explicitly indicates that these products should not be used in the ICU. It was FDA's interpretations that some meters have limitations that make them unsuitable for use in the ICU and this was the reasoning for their position.

September 2008 to March 2009 2nd Generation Development

Following this meeting, Luminous Medical management revisited its strategy for product development. Realizing that an uncertain FDA path made for an impossible investment situation, the first of two major re-development efforts was undertaken. Rather than push uphill with a novel glucose measurement method, the company abandoned the original approach and planned to license an existing sensor that used traditional technology for glucose measurement. Luminous approached Radiometer, a leading manufacturer of blood gas monitors, for opportunities for licensing. The sensor for Radiometer's ABL80 FLEX monitor included a suitable glucose sensor that could be retrofitted to the original Luminous product. The ABL80 FLEX is a point of care *in vitro* diagnostic system that is designed for use in the near patient environment, including the ICU. By using a sensor with traditional glucose oxidase measurement technology that is already cleared for use in the ICU, Luminous believed it could avoid the difficult path encountered at the first meeting. A licensing deal with Radiometer was subsequently completed.

Luminous proceeded to redevelop the product using the ABL80 FLEX sensor. The product retained the fully automated blood withdrawal and return features of the original product but changed the measurement technology and calibration methodology. When the product reached a sufficient level of development a request for another pre-IDE meeting with FDA was submitted. In that document our proposed clinical studies were outlined, including a study to be conducted with ICU patients. Luminous again traveled to FDA for a meeting on March 2, 2009.

March 2009-Second Meeting with FDA

After an update on the product development changes and a briefing on the ABL80 FLEX measurement technology a productive discussion with FDA ensued. At this meeting the following information was conveyed:

1. Since the clinical studies, including the studies to be conducted in the ICU use venous access they are likely to be determined to be "non-significant risk" (NSR) and would not require an IDE.
2. Although an IDE was necessary for the proposed clinical trials, Luminous would need to submit all clinical protocols to FDA before proceeding with the trials.
3. Since the company was planning to demonstrate performance compared to a laboratory analyzer, no comparison to a predicate device would be necessary.
4. FDA expects to see performance that demonstrates accuracy of ±6 mg/dL or ±10% whichever is greater. FDA stated that the performance criteria would be expected for measurements of clinical samples when compared with an established reference instrument such as YSI. This is substantially more stringent than the current ISO 15197 standard which requires ±15mg/dL or ±20% whichever is greater.
5. FDA declined to provide guidance on whether the regulatory path would be 510k or PMA but the Luminous impression was that it was likely to be a 510k.
6. FDA had many questions about the blood access method and its safety. Although the method is the same as with the original product, the questions were not raised in the first meeting.

March 2009 to July 2010-Third Generation Development

Over the following year a number of market conditions developed that required a reassessment of the approach Luminous had taken to develop the product. A major clinical study was published which refuted the original premise on the importance of glucose control in the ICU, the healthcare bill was passed and the economy significantly declined. Hospitals began to delay their purchases of capital equipment and became less aggressive in controlling patient glucose levels. While insulin use remained common, the target glucose concentration range was relaxed reducing the demand for a fully automated glucose monitor.

In a final attempt to develop a product that was responsive to customer needs and that could pass over the US regulatory hurdle, Luminous undertook a second major redesign of its product. While retaining the very accurate ABL80 FLEX sensor, the automated blood withdrawal system was abandoned in favor of a manual method that uses components that are already cleared for that purpose. The sensor was also relocated from inside the device to an existing arterial catheter that is present in many ICU patients. This resulted in a substantially cost reduced product that still met the current needs of the customers. As it now used a blood access method that is already cleared for that use, it was hoped that it would serve to reduce FDA's concern over blood access.

July 2010-Third Meeting with FDA

Luminous once again approached FDA by submitting a pre-IDE meeting request for the final product. That meeting was held on July 22, 2010 but days before the meeting the Agency provided a written response to some of the questions raised in the pre-IDE document. In that document, Luminous learned:

1. The proposed clinical studies are automatically considered significant risk because in one trial, a hypoglycemic clamp procedure is conducted on healthy subjects and in another trial the study includes ICU patients. Previously, FDA had stated that the ICU trials were

likely to be non-significant risk and it was the Agency that suggested we perform the hypoglycemic clamp study.
2. FDA considers that the intended use of the Luminous product and the ABL80 FLEX are not the same even though they are both used to determine glucose on patients at the bedside, including ICU patients and the intended use statements are very similar.
3. FDA does not consider the measurement technology of the Luminous product and the ABL80 FLEX to be the same, even though they use the exact same sensor and calibration method.
4. Although FDA had previously communicated that the current ISO 15197 standard would not be appropriate, they reiterated that a much tighter standard would be required but could not comment on what the standard would be.

Luminous proceeded with the in-person meeting on July 22, 2010. During that meeting, FDA modified, but did not reverse, their position on points 1&2 above. The Agency agreed to reconsider the intended use issue when the 510k is submitted and stated that they had a much better understanding of the technologies following the meeting. The Luminous interpretation of these events was that FDA had a preconceived idea that they wanted this product to go through the PMA path and were going to make their interpretations with that as an objective.

It was also clearly confirmed that FDA wanted to see the Luminous clinical protocols before they were conducted and Luminous committed to provide them. FDA agreed that an additional pre-IDE meeting would be appropriate before the final IDE submission was made.

December 2010-Fourth Meeting with FDA (teleconference)

Prior to this meeting Luminous submitted its clinical protocols but had a number of questions it posed to the Agency for clarification and comment. At this meeting FDA began taking positions that were considered extreme by the Luminous team. After further discussion FDA modified its positions and became more reasonable in many cases. Members of the FDA team seemed confused about the product and how it operates even though very detailed explanations had been previously reviewed. A few examples of the strangest requests were:

1. FDA stated that in the ICU trials it would be necessary that the ICU patient glucose levels be managed using a laboratory reference method during the study. This was a rather bizarre requirement as it would necessitate that the hospital convert from its current standard of care to a laboratory method for the duration of the study. Since the Luminous study was designed as a blinded study that would not interfere with patient management it seemed to be an extraordinarily intrusive requirement for the Agency to make. This requirement was eventually reversed
2. FDA also asked Luminous to conduct a study in healthy volunteers using venous access before an arterial access study was conducted. Since the Luminous product uses a blood access method that is already cleared for arterial use in the ICU, it seemed overly burdensome to require this. Also, the Luminous product had been optimized for arterial access so it wasn't clear how such a study would be conducted or what its value would be. The Agency agreed to reconsider this position and eventually reversed themselves on this requirement.

Other questions were not addressed at the meeting and FDA agreed to provide a response after further internal review. The lead reviewer closed the meeting by saying that the pre-IDE was now closed, although there were outstanding obligations by the Agency to respond to Luminous.

January 2011-Fifth and Final Meeting with FDA (teleconference)

After letting a few weeks go by, Luminous followed up with FDA on the outstanding issues. At that time the reviewer said that since the pre-IDE was closed there could be no further response from the Agency. It was stated that no one could work on the responses if there was no open pre-IDE to charge their time to. If Luminous wanted additional feedback, an additional pre-IDE meeting request would need to be submitted.

A final pre-IDE meeting was requested and a phone call was scheduled for January 25, 2011. The main objective of this meeting was to resolve the final issues from the prior meeting but a number of new issues were raised by the Agency.

1. FDA stated that they were currently deciding the best way to evaluate these "continuous monitoring devices". During the phone call the Luminous product was described in this way multiple times by FDA and it was indicated that the Agency now thought that the Luminous product, although manually operated, was similar to continuous glucose monitors that measure glucose interstitial fluid and are worn outside the body. An attempt to clarify this issue was abruptly cut off by the Agency in the interest of time.
2. FDA stated that this new category may require a panel review before it could be approved.
3. FDA stated that the study protocol previously submitted would now have to be split into two separate study protocols subject to two sequentially reviewed IDE applications. The first study in healthy subjects, proposed for 12 volunteers, would need to be 50 subjects, a number that had no statistical justification but is "what we are more used to".
4. The second study in ICU patients could not be submitted at this time since there is no standard of performance that can be used to calculate an appropriate sample size. The Agency suggested that Luminous conduct the healthy subject study first and that the standard may have been determined by the time that is complete. An IDE for the ICU study could then be submitted at that time.

There were many other issues raised about the details of the proposed studies, some of which were resolved in favor of the Luminous position but that indicated an Agency with a strong pre-disposition toward more studies, more subjects, more arduous conditions, all under the name of patient safety with no regard for the burden placed on the company.

The final revelation that the standard of performance not only remains unknown but that there is no guidance on when it will be available was, by itself, devastating. It is very difficult to persuade investors to continue to support a venture that has such an uncertain performance requirement. Moreover, the inability to determine the timing or the size of the final clinical trial added sufficient uncertainty that Luminous investors determined that they could not provide the additional capital that the company desperately required. The decision reached by the Luminous

investors was that the Luminous product needed to be placed in a larger company that could better tolerate the uncertainty and cost of dealing with the Agency. Luminous has now laid-off all of its employees and is currently in the process of selling its assets to a larger company.

5. Acorn Cardiovascular, lnc. Case Study (10 December 2010)

Heart failure is the only cardiovascular disease in the US which is increasing in both incidence and prevalence. It has been characterized by the US government as a health care epidemic, and treatment of heart failure is the largest single cost in the Medicare system. Drug therapies have reached the limits of their efficacy, and there has not been a new class III heart failure device or drug approved in the US for over a decade. Patients worsening from heart failure suffer from severely limited quality of life and high rates of hospitalization.

In response to this overwhelming need, Acorn Cardiovascular, Inc. has developed the CorCap cardiac support device, a Class III(PMA) implantable medical device for heart failure patients who are worsening despite optimal medical management. The CorCap is a highly reliable technology with no leads, batteries, anti-coagulation, or post-surgical support required. Using S105M in venture capital investment, Acorn has compiled an impressive list of accomplishments with respect to the CorCap, including the following:

1. A 300 patient randomized trial in the US, designed collaboratively with FDA over a 2 year period, met all pre-specified success criteria (P=0.02). This study showed statistically significant reductions (>4O%) in the use of transplant and ventricular assist devices, significant reductions in heart size, significant improvements in heart shape, and significant improvement in quality of life for the patients.
2. Patients from this pivotal trial were followed-up for 5 years (by far the longest follow-up period of any heart failure device therapy ever evaluated), and the results showed no mitigation of benefit or safety issues.
3. The CorCap received CE marking in Europe in September 2000, and more than 650 CorCap devices have been implanted worldwide.
4. There have been 87 peer-reviewed manuscripts and 83 abstracts on the CorCap.
5. Acorn has 66 granted US patents on the CorCap and an additional 20 patents pending.
6. Acorn has developed a minimally invasive surgical technique which allows device delivery in less than 45 minutes skin-to-skin, with no need to cut the sternum or place the patient on cardio-pulmonary bypass.

Yet, despite the CorCap's significant data demonstrating safety and efficacy, the CorCap has not
been approved by the FDA, and Acorn is now in the throes of insolvency as a result. FDA's review of the CorCap has been characterized by gross inconsistency, personnel turn-over, and personal bias -the sum of which has kept an important and innovative therapy from the American public and destroyed a small business. A summary follows:

A.FDA Inconsistency

i. In November }OOL, the incoming Director of the Division of Cardiovascular Devices (DCD) unilaterally voided an agreement which had been carefully negotiated between Acorn and the previous DCD Director and staff over a period of 6 months. The resulting delay added 120 patients, 24 months in time, and $25 M in additional costs.

ii. In March 2004, DCD forced Acorn to significantly change their study design after enrollment was already complete. During a June 2005 Circulatory System Advisory panel meeting, this change was roundly criticized by the panel. DCD took no responsibility, stating that "ultimately, the trial design is the sponsor's responsibility."

iii. In August 2005, DCD sent Acorn a not approvable letter which specifically defined three options for making the PMA approvable. In a January 20O6 meeting between Acorn and FDA, the DCD Director stated that they "really did not mean to allow two of these options and that only the third was acceptable."

iv. In March 2006,the Director of the Office of Device Evaluation (ODE) wrote to Acorn to inform them that the primary basis for not approving their PMA in August 2005 was, after further review, acceptable after all. However, ODE would still not approve the PMA without Acorn repeating the panel review process.

v. In February 2010, DCD voided a three-trial agreement that had been carefully negotiated between Acorn and DCD in 2007. Although there had been no safety issues and Acorn was entering the third and final trial of the agreement, DCD simply stated that "their position had evolved."

vi. In March 2OI0, the DCD Branch Chief personally called Acorn and specified a trial design to Acorn which had been reviewed internally by DCD and deemed acceptable. Acorn subsequently modified their trial design to meet this recommendation and re-submitted it for DCD review. In April 2010, this application was again rejected. Once again, DCD stated that their position had evolved.

B. Personnel Turn-over

It is near impossible for a sponsor to get predictability from the FDA when the FDA personnel associated with the review are turned-over at a high rate. Acorn has been subjected to the following FDA personnel changes during the course of the review of the CorCap: 6 primary reviewers, 4 ODE Directors, 2 DCD Directors, 4 Medical Officers (plus an additional 2 consulting MD's),3 CDRH Directors, and 5 FDA Commissioners.

C. Personal Bias

a. Acorn has been negatively affected by a number of individuals involved in the CorCap review who clearly had personal bias issues that affected their judgment:

i. In August 2005, the Branch Chief of DCD (the primary FDA manager on the project) refused to sign the not approvable letter sent to Acorn because she vehemently disagreed with the decision, FDA's basis for the decision, and the due process accorded Acorn. She was subsequently transferred to another location in FDA by the DCD Director, and within one year, her career at FDA was over.

ii. In fall 2006, a consulting MD assigned to the Acorn project attempted to coerce a physician to end his involvement and support of Acorn. This physician had

previously sent a letter to FDA stating that the consulting MD had severely misinterpreted and misquoted one of his operative reports, resulting in an unfair and incorrect assessment of the CorCap. The CDRH Director investigated this incident, and subsequently removed the individual from any further involvement with the Acorn review.

iii. During the period 20Ot-2006, another consulting MD assigned to the CorCap review forced Acorn (and other companies in the heart failure space) to use a clinical endpoint for its studies that significantly increased study costs and risk to the patient - despite the fact that the scientific basis for this endpoint was not clearly substantiated and had been pointedly criticized by key scientists within the Heart Failure Society of America (the medical professional society for heart failure specialists, similar to the Society of Thoracic Surgeons). in fact, this individual had spent her entire career in heart failure conducting research on this endpoint, with the result being that she had an intractable conflict of interest on the subject. To make matters worse, the NIH eventually conducted a large scale study to analyze this endpoint. The study failed and, as previously predicted by key HF scientists in the heart failure community, showed no correlation between this endpoint and heart failure outcomes in patients. It is inexplicable that the DCD Director did not recognize this potential conflict of interest and intervene.

In summary, FDA failed the American public in its review of the CorCap. The macro result is that for 10 years US patients have been denied a life-saving therapy that is available to the population of the European Union, $105 M in dedicated capital has been frivolously wasted by FDA, and the opportunity for hundreds of jobs associated with producing and marketing the CorCap technology has been obviated. The micro result is that patients who had been previously enrolled in the last 4 CorCap trials will be denied standard follow-up (even though there have been no safety issues associated with the CorCap), and providers are left with even less options for treating heart failure patients who are out of therapeutic options.

Respectfully provided by,

Steven M. Anderson
President
Acorn Cardiovascular, Inc.

6. Disc Dynamics

I recently have had the opportunity to be the medical director of an encouraging emerging technology spine company, Disc Dynamics, Inc. Unfortunately, as of January of 2010, this company discontinued operations because of failure to achieve adequate funding. This failure to receive adequate funding was directly related to the inconsistent and excessive requirements by the FDA. The final issue was a request that our feasibility patients be followed for two years rather than the initial agreed to three months prior to beginning a pivotal study. As you are well aware, for a nonrevenue company that is venture based, to extend the runway for this length of time makes financial viability extremely unlikely.
This technology was directed at treating patients for whom we currently do not have an ability to treat in a less invasive and disruptive fashion. One of the patients that was treated in the feasibility study is a young gentleman who runs his own cement company. He is in his early 30s and had had intractable back pain for some time. He had failed multiple attempts at nonoperative treatment, yet was to the point that he was going to have to discontinue working in his occupation if other treatment was not available. Unfortunately the current treatment would entail an extensive fusion which likely would not allow him to
return to this heavy laboring type position. We elected to do a minimally invasive ASCOR procedure.

This procedure took approximately 2 hours in length to perform. He has had an excellent response to this treatment and has returned at six weeks to his previous job in cement finishing. This afforded a dramatic opportunity for this gentleman over and above any others that are currently in the market place. Conversely, an additional young woman who I have treated for many years recently undenvent a fusion because of the lack of availability of a viable nucleus replacement technology. This is a young woman who is college educated and has been very active in sporting activities and yet was to the point where
even sitting for short periods of time provoked significant pain. She has had to put her graduate degree in occupational therapy on hold to gain better control of her painful disc degeneration. Because of the lack of a less invasive nucleus replacement device, I ultimately performed a fusion in her lumbar spine, permanently eliminating all motion through this motion segment. Thankfully she has had a good clinical result. However, a less invasive, more physiologic solution would have been much more appealing.

Unfortunately as the FDA continues to make these inconsistent decisions relative to the regulatory stance of new technology, it is likely that promising opportunities will continue to go by the wayside. I hope you find this information useful and should you have further questions, please feel free to contact me.
Sincerely,

John E. Sherman, M.D.

7. ATS Medical

The THV PMA submission was a modular submission, comprised of the following modules, submitted around the time listed below:

- Module 1—Device Description, risk analysis, materials testing and sterilization—ESD: Mid October, 2005
- Module 2—Animal and in vitro testing—ESD: End of January, 2006
- Module 3—Manufacturing—ESD: End of October, 2005
- Module 4—Clinical Studies—ESD: End of September, 2006

This schedule was discussed and agreed during August 2005, with who was the first main reviewer and contact assigned to our PMA.

The main reviewer and contact changed two times through-out the first two years.

Responses to any questions or requests received from the FDA, went back to the agency within thirty days following receipt of the FDA letter.

It was then in the filing letter received from the agency dated October 30, 2006, that FDA immediately requested us to update the pending PMA, three months after the filing date with new safety and effectiveness information (per 21 CFR 814.20 e)) and requesting a new Clinical Update, which we turned around in January 2007.

It wasn't then until the end of July, 2008, seven months later, that we then heard about the next steps to complete prior to approval (SSED, Labelling/IFU, etc). Finally, the PMA was approved October 30, 2008, exactly two years after the original filing letter received on October 30, 2006.

Important Facts:

- Under MDUFMA the first PMA of small companies is at no cost (free). This was the case of this PMA originally submitted under the first start-up company.
- Changes in reviewers severely affected the progress of this PMA.

8. Minneapolis Heart Institute Foundation

A pleasant, spry 88-year-old lady had a severe narrowing of her Aortic Heart Valve (called aortic stenosis). This condition occurs in about 2% of the general population, and is increasingly frequent in the Elderly. It is progressive, relentless, and eventually fatal if not treated, with patients dying a very uncomfortable death due to heart failure since the heart cannot expel blood properly though this narrowed valve. Definitive therapy is to replace the valve with an artificial valve, which allows for complete resumption of a normal life and normal life expectancy. However, this patient was deemed too high of a surgical risk due to her age. She had already had one open heart operation, bypass surgery many years previously, for coronary artery disease. Open heart surgery, especially a second operation in the elderly is risky for the kidney failure, lung failure, and serious stroke or heart attack. She did not wish to take a chance on these potentially debilitating and fatal outcomes to surgery.

Instead, a procedure developed years ago was offered to her, consisting of inserting a balloon into the valve, inflating it under high pressure, and creating a larger opening. This procedure is done through a small wound in the leg, with the balloon advanced though the arterial system to her heart. When successful, patients do well, and go home within a few days, avoiding the need for surgery. However, when the balloon is used, scar forms and the valve re-narrows typically within 6 months, leaving the patient in the same condition as before the procedure, though at least the 6 month period after the procedure, patients typically have an excellent quality of life.

The patient underwent the balloon-valve opening procedure, quite successfully, but as expected it lasted less than 1 year. She chose to undergo a second balloon procedure, (October 2010) which this time lasted less than 2 months before the valve renarrowed. She became increasingly short of breath at home. She couldn't walk more than a few feet, couldn't sleep, and needed to sleep sitting upright in a recliner chair. She developed a bad cough, and suddenly developed severe heart failure about 6 weeks after her second procedure. She needed immediate intubation and ventilation by machine.

She is not a candidate for further balloon procedures as they are increasingly likely to fail, and remains too high risk for open heart valve replacement. She has spent more than 1 week in a Cardiac Intensive care unit, where costs can exceed $10,000.00 per day for critically ill patients. She is doomed to a downhill course of progressive shortness of breath, chest pain and likely an eventual painful death, with her only treatment being palliative. This is despite a well preserved mind, mental status, and body other than her aortic valve.

A therapy for this unfortunate lady is available in Europe, approved, and on the market, performed every day many times. Though conceived, developed, financed, and now manufactured in the USA, she cannot receive the new device and procedure because of US regulatory delays.

A New Therapy: Transcatheter Aortic Valve Implant

The problems experienced by our patient drove a small group of American scientists and Engineers to invent and build a heart valve that can be inserted though the skin into an artery, and advanced to the heart where it is implanted. This technology was conceived and funded here

in the USA by a small startup company. It was tested initially in France, and refined there (see figure). The technology works very well. The startup company was acquired by an American company, and is now approved, sold, and reimbursed for implant across Europe. Many Europeans are routinely receiving these valves (manufactured in California) in a life saving procedure. Many Americans are reportedly flying to Europe for implantation since it is not available here. A second valve startup company was also acquired by a different American cardiovascular company, and is similarly available in Europe and across the world. More than 20,000 such valves have been implanted this way across the world, and the procedure is comparatively safe, very effective, and eminently useful in the elderly and/or high risk patient. Moreover, it is cheaper than the open-heart technique since a full operation is unnecessary. A clinical trial of the valve was performed and reported as part of the FDA approval process. This trial was markedly positive for both quantity and quality of life, and has received widespread acclaim in the Medical community. Yet at a recent Cardiology meeting where the valve and its study was discussed, FDA staff were less than enthusiastic about rapid approval.

'....after praising the trial and the investigators, he pointed out that the responsibility of the FDA is to analyze the trial and other evidence. He pointed to the variably controlled use outside the U.S., the short-term follow-up, and the complex engineering required to consistently provide a safe and durable product as reasons that careful evaluation is needed.' (see Reference 4)
Many prominent Cardiologists were visibly upset by this implication that approval will likely be delayed.
The other valve that has been developed and placed through the skin without major surgery is widely used with success. After lengthy delays, in November 2010 this valve received FDA approval to initiate a Clinical Trial. This process took more than 5 years of effort, despite the fact that over 12,000 devices worldwide had been implanted, with satisfactory results.
In summary, a now-proven, life saving, cost saving, and quality of life improving technology that was conceived and developed by American Scientists and Engineers and now owned by a major US medical company is widely available in Europe and across the world, yet will likely be years before available in this country.
Robert S. Schwartz, MD, FACC, FAHA

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