

**MEDICAL DEVICES: ARE CURRENT REGULATIONS
DOING ENOUGH FOR PATIENTS?**

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BEFORE THE
SUBCOMMITTEE ON HEALTH
OF THE
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HOUSE OF REPRESENTATIVES
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THURSDAY, JUNE 18, 2009

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

The subcommittee met, pursuant to call, at 9:30 a.m., in Room 2322 of the Rayburn House Office Building, Hon. Frank Pallone Jr. [Chairman of the Subcommittee] presiding.

Members present: Representatives Pallone, Dingell, Green, Capps, Matheson, Barrow, Christensen, Castor, Sarbanes, Murphy, Space, Braley, Deal, Buyer, Pitts, Burgess, and Gingrey.

Staff present: Steve Cha, Professional Staff Member; Sarah Despres, Counsel; Elana Leventhal, Policy Advisor; Karen Nelson, Staff Director for Health; Alvin Banks, Special Assistant; Caren Auchman, Communications Associate; Karen Lightfoot, Communications Director; Clay Alspach, Counsel; and Chad Grant, Legislative Analyst.

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

Mr. PALLONE. The subcommittee is called to order, and I will recognize myself initially for an opening statement. Today's subcommittee is meeting to discuss the FDA's regulation of and authorities over medical devices. The goal of today's hearing is to determine if the current regulations are doing enough for patients while ensuring that these very important and sometimes life-saving devices are truly safe and effective.

We are here to hear about where the current system works well and where shortfalls might be. There is evidence of an approval system that is broken, that its standards, its procedures and its rules don't meet modern needs of getting medical devices to those in need with confidence in their safety.

We have made huge advances in medicine over the last few decades. Many illnesses that were once a death sentence are now preventable, curable or at least manageable through modern medical treatments. New and emerging technologies hold promises that our great-grandparents could never have imagined, and the medical device industry is one of the main drivers of this progress.

From pacemakers to artificial hips to tongue depressors, we can't enter the health care system without coming into contact with these devices. And we need an approval process that keeps pace

with new technologies, a modern process consistent with progress in medicine. We have to maintain the delicate balance between wanting to put these new technologies in the hands of patients who desperately need them and ensuring that the devices are actually safe for use in humans.

Now, last month this subcommittee held a hearing on the issue of preemption in the wake of the Regal versus Metronix Supreme Court decision. The Supreme Court ruled that patients could not receive compensation for their injuries, medical expenses, and lost wages caused by defective, pre-market approval or PMA devices or inadequate safety warnings.

While state product liability provides incentives for companies to make safe products, it should not be the only tool we have to ensure that the medical devices that are on the market today are safe. We need to know that the approval process and the regulatory standards are strong and enforceable and that the agency is empowered with the ability to ensure the safety of these products.

It is for this reason that we are here today at this hearing on the medical device approval process. I want a comprehensive overview of the major issues and potential problems that may arise in the regulation of medical devices. Of greatest importance to me is to find out what the FDA needs to ensure that the medical devices on the market are safe and effective.

In the FDA Amendment Act of 2007, I requested a GAO study to look specially at the 510(k) process and in particular focus on the pre-amendment devices that have never been through the FDA approval process.

The GAO is here today and will talk about that report in more detail. And I am interested to hear how the FDA is moving to review the high risk class three devices that have yet to ever be approved formally, as Congress instructed the FDA to do in the Safe Medical Device Act of 1990.

Why is it taking so long for the FDA to act, and what is the consequence of this inaction? Are there devices being cleared onto the marketplace that shouldn't be?

But beyond this particular study, the GAO has written other reports on medical devices. These studies have highlighted some of the successes and possible failures in FDA's ability to properly assess the safety and effectiveness of devices as well as maintain sufficient post-market surveillance and controls to ensure the devices patients are using continue to work the way they are supposed to.

And I am looking forward to hearing more about these findings as well. I also look forward to other witness testimony and hope that they give our committee members an in-depth look into how the process is working and where it may need to be fixed either through legislation or through increased and enhanced oversight at the FDA. At the end of the day, we are all talking about real people here, patients who need to know that these devices will do what they say, that they are supposed to do, and they won't cause them avoidable harm.

I want to thank particularly Dr. Marcia Crosse from the GAO and her team's tireless efforts to ensure that we are responding to the needs of patients. And now I would recognize Mr. Deal, our ranking member, for an opening statement.

OPENING STATEMENT OF HON. NATHAN DEAL, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF GEORGIA

Mr. DEAL. Thank you, Chairman Pallone. Thanks to our witnesses for being here today. Since we have several of you, I will not take too much time in my opening statement but simply to reiterate that all of us, I think, share a concern that in this area of medical devices that they be safe and that they do what they are supposed to do and that the approval process is adequate and that the approval process is not unduly delayed. So there is a delicate balance that has to be reached in terms of the approvals.

I am especially concerned in light of what this committee has placed on the FDA in recent weeks from tobacco regulation to yesterday an enhanced food safety bill. All of us understand the importance of all of these areas and support it. But I think one of the critical questions that always has to be asked is are we giving the FDA the resources and the abilities, legislatively or otherwise, to do what we are asking them to do.

Each of you share an insight into those questions, and I look forward to your testimony and I yield back my time. Thank you.

Mr. PALLONE. Thank you, Mr. Deal. Next is our subcommittee vice chair, Ms. Capps, from California.

OPENING STATEMENT OF HON. LOIS CAPPS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CALIFORNIA

Ms. CAPPS. Thank you, Chairman Pallone, and we have great witnesses here so I will be brief as well. But I am very pleased and I want to note that we are holding this very important hearing today.

I believe that members of Congress do have a duty to evaluate and reevaluate regulations to make sure that we are doing all we can to get safe and effective medical devices to American patients. However, safety and effectiveness are not the only things we need to keep in mind as we consider these regulations.

We must also ask do the rules in place pose any barriers to technological innovation, barriers that might hamper the improvement of prevention, diagnosis, and treatment of disease. Ultimately our evaluation must include assessing the pre-market and post-market processes for safety and effectiveness as well.

And I am glad that our committee takes seriously our role in the oversight on that process. I am eager to hear recommendations from our witnesses on what works, what doesn't, and how we can adequately address both. I yield back.

Mr. PALLONE. Thank you. The gentleman from Indiana, Mr. Buyer.

Mr. BUYER. I reserve my time.

Mr. PALLONE. Gentleman from Georgia, Mr. Barrow.

Mr. BARROW. I waive.

Mr. PALLONE. Gentleman from Pennsylvania, Mr. Pitts.

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

Mr. PITTS. Thank you, Mr. Chairman. Thank you for convening this hearing. More than 8,000 new medical devices come to market

in the U.S. each year ranging for syringes and surgical gloves to pacemakers and heart valves.

The medical device amendments of 1976 gave FDA the responsibility of ensuring that medical devices are safe and effective and provided a risk-based framework for FDA to evaluate the wide variety of devices seeking approval.

The majority of class two or moderate risk medical devices come to market through pre-market notification, also known as the 510(k) process. 510(k) submission must demonstrate that the new device is substantially equivalent to one or more similar devices legally marketed in the U.S. And this excludes pre-1976 grandfathered medical devices.

And the new device cannot be found substantially equivalent to a device that has been deemed misbranded or adulterated or removed from the market. To be substantially equivalent, the product must be at least as safe and effective as the legally marketed or predicate device, must have the same intended use and technological characteristics as the predicate, or if the intended use is the same but the technological characteristics differ, the technical differences must be shown to raise no new questions of safety and effectiveness.

510(k) submissions must include descriptive data or specifications, performance testing, and in approximately 10 percent of cases, clinical data. The 510(k) process has evolved over the last 30 years and has served the American public well. It provided FDA the discretion and flexibility to apply the proper amount of oversight to each device submission. It provides for timely product review, and it encourages technological innovation and evolution of device technology.

GAO released a report in January of this year. It said "shortcomings in FDA's pre-market review, post-market surveillance, and inspections of device manufacturing establishments" and I anticipate that Ms. Crosse will have more to say on the matter. But I believe the criticisms outlined in the report have more to do with FDA's actions and inactions its lack of resources than the statutory approval process for medical devices itself.

I look forward to hearing from the witnesses, and thank you. And yield back my time.

Mr. PALLONE. Thank you, Mr. Pitts. Chairman Dingell.

OPENING STATEMENT OF HON. JOHN D. DINGELL, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF MICHIGAN

Mr. DINGELL. Mr. Chairman, good morning. Thank you for holding this hearing on the current state of medical device regulation. I want to thank today's witnesses and look forward to their informative testimony. I also want to thank you for yesterday's work and my colleagues on the committee for what we did with regard to Food and Drug in the area of foods. This is a worthy successor for that undertaking, and I am delighted to see the way that you are leading on this matter. It is very important that we address the concerns that are developing with regard to the balance of the responsibilities at Food and Drug on pharmaceuticals, cosmetics, and devices.

In response to the question that you propose in the title of this hearing, I am convinced that more could be done to protect patients. This year alone, there have been nine class one recalls of medical devices. It is to be noted that these recalls are occurring in a very badly staffed, indeed understaffed, agency without the resources to properly monitor its responsibilities.

Class one recalls, as we know, are the most serious type of recall. It involves situations in which there is a reasonable probability that use of these products will cause serious injury or death.

I would note that the device industry is a responsible institution and is composed of responsible people. And I know they will want to work with us to make progress in terms of assuring safety of the American consumers and the competition in that particular portion of the medical services industry and is conducted in a way which does not constitute a race to the bottom.

Examining the regulatory framework that we currently confront for medical device approval, a few questions come to mind. First, is the current medical device approval standard “reasonable assurance of safety and effectiveness” rigorous enough? Second, does FDA rely on quality clinical studies during the medical device approval process? Third, is the current 510(k) review able to adequately ensure that devices that are marketed through this abbreviated approval process are safe and are being handled in a way consistent with the public interest? Last, is there too much discretion allowed to FDA in determining whether, through the 510(k) process, new device has the “safe intended use” or whether it has different technological characteristics?

This is a matter of no small importance. FDA premarket notification process for medical devices has been in place since 1976. Low-risk and moderate-risk devices are subject to abbreviated 510(k) process. With some exceptions, high-risk devices require premarket approval, PMA, process. Devices that were on the market prior to the Medical Device Amendments, MDA, were allowed to remain on the market with the assumption that FDA would later determine the product’s safety. We need to know whether this has been done, and I don’t think anybody can answer that question at this particular time.

Unfortunately, it appears that many of these products did not undergo rigorous review mechanisms, and unfortunately, we have other devices coming on the market using pre-MDA devices as a reference device. That is something that imposes substantial risk and peril on American consumers.

I also have concerns with the frequency of inspection of medical device establishments, and this is something we ought to listen to carefully. GAO estimated that FDA inspects foreign manufacturers of modest-risk devices only once every 27 years. And foreign high-risk manufacturers every six years despite the fact that there are more registered device manufacturers in China than any other foreign countries.

Chinese firms—listen to this—can expect FDA to visit them only once every 50 years. I don’t think anyone in this room can find that to be acceptable.

Yesterday, we were pleased that this committee unanimously passed the Food Safety Enhancement Act in a bipartisan fashion,

which will give FDA greater authorities and resources to protect our food supply. I intend to build on this bipartisan success as we turn our next focus to medical devices and pharmaceuticals. As you know, we worked on this matter in a bipartisan way, and we worked cooperatively with the industry. And I call on all of my colleagues to show the same extraordinary cooperation they did while we worked on this legislation and also on the industry to understand that we seek to see to it that they prosper but at the same time that the consumers are protected. We hope we will have their help.

Mr. Chairman, the FDA Globalization Act of 2009, legislation that you and I introduced earlier this year, will provide a solid foundation as we move forward to addressing the safety of medical devices and I will add also safety of pharmaceuticals and cosmetics.

I want to thank the witnesses for joining us today as we take a close look at this important topic. I want to thank you, Mr. Chairman, and I want to thank my colleagues for the good work we did yesterday. And I want you to know I look forward to working with all of you to try and see to it that we carry forward for the protection of the American consumers on the balance of Food and Drug's rather shabbily handled and rather under-financed resources and efforts. Thank you, Mr. Chairman.

Mr. PALLONE. Thank you, Chairman Dingell, and thank you for all you have done on this issue and others. Next is the gentleman from Texas, Mr. Burgess.

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

Mr. BURGESS. Thank you, Mr. Chairman. It is my firm opinion that this hearing should be about science and solutions, so I would just simply ask the question where is the Food and Drug Administration today? The Food and Drug Administration regulates more than 100,000 different medical devices manufactured by more than 15,000 companies. This number represents a spectrum of devices from all three medical device regulatory classes as defined by the Medical Device Amendments of 1976.

As often as I complain about how many times the Food and Drug Administration appears before the Energy and Commerce Committee, and it is no small investment of their funds that when we bring them up here. My complaint is aimed at wasting the Food and Drug Administration's resources to continue answering questions about competence when it is clear that resources are the real remedy.

If we are going to gavel in a hearing merely looking for a solution to any real or perceived gaps in the medical device approval process, then clearly I think we need to hear from the commissioner of the Food and Drug Administration or their surrogate so they can inform us what tools they need to address any gaps in regulatory authority to continue to ensure the safety of medical devices for all Americans.

When informed of the use and possible misuse of the 510(k) process, the previous commission of the Food and Drug Administration, Dr. Andrew Von Eshenbach, dramatically stated that the 510(k) system is "out of control." Has the approval process simply im-

proved with the change of administration, or are there still lingering issues? That is why we should have the presence of the Food and Drug Administration here today.

I am also noticing a troubling trend in our conversation about both devices and drugs. Last year, we held a hearing on biosimilars. And did we have the Food and Drug Administration present? No, we had the Federal Trade Commission. Now, I would like to think that is merely an oversight, but a pattern does seem to be developing which I think we should stop.

The Food and Drug Administration is not immune from interference. In the 1990s, it was noted the Food and Drug Administration took too long to approve devices, and we may have the opposite situation now. And none of us must forget that speed sometimes kills. The evidence points to the problem lying in the exceptions process to the device approval, known as the 510(k) application, which the Food and Drug Administration will grant for those devices which have substantial equivalents on the market. We want ingenuity and creativity in the marketplace, and we don't want the government to stand in the way of that process. But safety must always be our foremost concern. If safety is compromised, patients will never seek out the treatment which these devices—and I will tell you as a practicing physician for over 25 years, in today's medical legal climate, no doctor wants to place or implant a device which would be less than safe.

This is why the premarket approval process, as lengthy and arduous as it is, should not be overturned simply because the process is long. Safety cannot be timed. The device approval process is long for a reason. The science must rise to the level of trust Americans place in the stamp which says approved by the Food and Drug Administration.

There are questions that need to be answered, Mr. Chairman, which only the Food and Drug Administration can answer, and I hope we will take careful consideration of what the Food and Drug Administration has to say before we enact any laws or make changes to current authority. I will yield back the balance of my time.

Mr. PALLONE. Thank you. Next is the gentlewoman from the Virgin Islands, Ms. Christensen.

OPENING STATEMENT OF HON. DONNA M. CHRISTENSEN, A REPRESENTATIVE IN CONGRESS FROM THE VIRGIN ISLANDS

Ms. CHRISTENSEN. Thank you, Mr. Chairman. The approval process for medical devices is an important issue, and I thank you, Chairman Pallone, for holding this follow up hearing on it.

Any concerns with the approval process, application process needs to be resolved so that we can continue to bring these life-saving products quickly and safely to the American public.

In the practice of medicine, we are always taught to weigh the benefits of treatment versus the risk, and while this is true for devices as well as for pharmaceuticals, the approach to approval, both in the primary product and the secondary one, trying to use the pharmaceutical model for medical devices is perhaps worse than comparing apples to oranges and, in my opinion, should be avoided.

I also think it is important to recognize that we are having this hearing as we are emerging from the previous administration and that today we are in a different administration, a different place, a different mindset, a different vision. Between 2001 and 2009, we watched scientists and sound science be replaced or significantly influenced by industry special interests and political and even religious ideologues on several scientific panels. And it is my sense that from previous hearings and the examples raised in testimony that the problem has not been so much the use of the 510(k) application process but the failure to adhere to the process and the dictates of sound science.

Also from what I have read thus far, what I have seen is that there is a backlog in the work that FDA is already authorized and required to do. I am sure that does have something to do with prior staffing and funding levels. There may be some minor fixing of the medical device approval process that needs to be done, but for the most part, it seems sound. And if we adhere to science and use what is already provided for in the process, I think we will successfully protect the public's health and safety. I look forward to the testimony and dialogue with our panelists. Thank you. I yield back.

Mr. PALLONE. Thank you. Gentleman from Georgia, Mr. Gingrey.

OPENING STATEMENT OF HON. PHIL GINGREY, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF GEORGIA

Mr. GINGREY. Thank you, Mr. Chairman. Today as a result of advances in medical technology, we Americans enjoy access to a quality of health care that most nations do not. While some countries restrict or ration the types or amounts of drugs and devices that patients can access, American patients can receive the latest, the most advanced medical technology, such as an artificial hip or a knee or the latest cancer medication that will drastically improve and extend their lives. My 91-year-old mother, for example, recently had knee replacement surgery, and her quality of life has been dramatically improved over the last several months because of this surgery.

Mr. Chairman, ensuring the safety of medical devices is an absolute necessity for our continued access to quality health care. The FDA is charged with making certain that all medical devices have been thoroughly tested for safety and effectiveness before coming to the market. It is one of the FDA's primary responsibilities, and I support increased efforts in this area.

Unfortunately, there is an inherent risk associated with most modern medical procedures regardless of advances in technology or indeed effective oversight. It goes without saying that there are few absolutes in this world. Mr. Chairman, I am especially concerned with the GAO report submitted for testimony today, the report citing an FDA report in 2006 that cites "the agency's ability to understand the risks related to the use of medical devices is limited by the fact that the volume of submitted reports exceeded the FDA's ability to consistently enter or review the reports in a routine manner."

We have spent a few months in this committee examining ways to expand FDA's oversight of tobacco, a product that is, by all accounts, outside of the agency's core mission or it was. This new au-

thority will further burden an agency that, by GAO standards, has had shortcomings in other areas of its current oversight responsibilities.

With this thought in mind, I will look forward, of course, to hearing the testimonies of our witnesses today. Mr. Chairman, I thank you for calling the hearing. And with that, I will yield back my time.

Mr. PALLONE. Thank you, Mr. Gingrey. Gentleman from Ohio, Mr. Space.

Mr. SPACE. Thank you, Mr. Chairman. Very briefly, I appreciate you calling this hearing on what is obviously a very important issue, the safety of medical devices available on the market. I look forward to working with the committee as we continue to enhance a system that ensures that our consumers are safe while creating avenues for innovation and avenues to help consumers with their illnesses and afflictions and to strike that proper balance. I look forward to the testimony, and once again, thank you and Chairman Dingell for your work on this issue.

Mr. PALLONE. Thank you. Gentleman from Connecticut, Mr. Murphy.

Mr. MURPHY. Thank you, Mr. Chairman. I am looking forward to today's hearing as a new member of this subcommittee. In particular, I am looking forward to getting a better understanding particularly from our friends at the GAO, what they found as it relates to the FDA's current authorities to regulate varying classes of devices. Importantly, I believe we must determine whether the current processes that FDA uses, the 510(k) process and the PMA process, are adequate in their design but have been flawed in how aggressively the FDA uses its authority, or if the processes themselves need to be updated.

Often what Congress has found in a number of areas is that the regulations we intend and pass are only as good as the regulators and the agencies that are meant to enforce them. With a new administration in office, I believe that it is going forward to hear from them directly about their intentions as it relates to these processes and how they intend, if at all, to enforce current regulations differently than their predecessors.

Again, Mr. Chairman, I thank you very much for convening this hearing which is fundamentally about patient safety and improving our response to that but also about sustaining important advances in medical technology. I yield back the balance of my time.

Mr. PALLONE. Thank you. Gentleman from Texas, Mr. Green, is recognized for an opening statement.

**OPENING STATEMENT OF HON. GENE GREEN, A
REPRESENTATIVE IN CONGRESS FROM THE STATE OF TEXAS**

Mr. GREEN. Mr. Chairman, I want to thank you for holding the hearing on the regulation of medical device safety. In 1976, the FDA was given the authority to regulate medical devices by Congress. Congress directed the FDA to characterize the devices into three categories: class one, class two, and class three. In order for a manufacturer to market a device for sale and use, it must demonstrate to the FDA the device is safe and effective for its intended use.

The manufacturers can do this in a premarket application process or a process which is known as 510(k) clearance processes. 510(k) clearance is used to bring devices marketed that are substantially equivalent to a previous device that the FDA has already cleared for marketing. The premarket application process is more stringent than the 510(k) process. The premarket application can require clinical trials to demonstrate the safety of the device.

Much has been said by this committee over the past year with regard to safety and monitoring of our food and drug systems at the FDA. I could argue that the device section of FDA has a good system in place to monitor the safety of medical devices compared to food and drugs. This is one of the few sectors the FDA has the ability to issue mandatory recalls in the instance of an adverse event, and they can require the reporting of adverse events by hospitals, nursing homes, and clinical labs.

Additionally, the FDA requires manufacturers to identify and monitor significant adverse events in the manufacture and user facility device experience database. I am looking forward to hearing from the witnesses today on the current state of the medical device safety at the FDA.

I would also like to say we have a new FDA commissioner, and I am sure the new team at the FDA will be making some changes in all sectors of the FDA. I would think we could identify the issues in this hearing today that need to be addressed, and I hope this new team will certainly consider it. And again thank you for the hearing. I yield back my time.

Mr. PALLONE. Thank you, Mr. Green. Gentleman from Maryland, Mr. Sarbanes.

OPENING STATEMENT OF HON. JOHN P. SARBANES, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF MARYLAND

Mr. SARBANES. Thank you, Mr. Chairman. I am looking forward to the testimony here today from the panel. This is another hearing that goes under the heading of the FDA is back or the FDA is coming back, however you want to look at it.

We have had a number of hearings and markups of legislation designed to make sure that the FDA has the sufficient regulatory authority it needs to ensure that Americans have the confidence that these kinds of devices are safe and other things that are safe. That is essentially all the average person is looking for, that government is looking out for them in the way that they expect.

I have been impressed, I guess is the word, maybe struck by discovering the things that the average person out there would assume are in place are not in place. So a lot of what we are doing is getting back to meeting the expectation of the consumer out there, that these protections are available.

So this hearing, as others have done, is looking at whether there is, as I have said, the sufficient regulatory authority, whether the resources are in place at the FDA to do the job that they need to do, whether the talent is there. I believe that talent pool is becoming deeper and deeper by the day. And whether this attitude of vigilance that needs to be part of the agency's approach is in place. So we are very encouraged by the direction things are moving, and

your testimony today will help shed even further light on that. And I yield back my time.

Mr. PALLONE. Thank you. Gentlewoman from Florida, Ms. Castor.

OPENING STATEMENT OF HON. KATHY CASTOR, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF FLORIDA

Ms. CASTOR. Thank you, Mr. Chairman, very much for calling this important hearing on medical devices and the FDA. In reading the GAO report on the current status of the FDA regulation of medical devices, I am concerned about the efficacy of the practices used to approve devices, particularly those that may impose life-or-death consequences on the patients that use them.

I am also concerned that the FDA has thus far been unable to implement the more stringent premarket review of certain devices as intended by the 1976 law. FDA has not been able to review all of the reports of adverse events caused by devices released into the market, and this lack of oversight in the market poses a heightened risk for consumers.

Now Americans certainly appreciate the lifesaving medical devices and the great innovations over the past decades. But with these innovations, we have seen many more advance products entering the market that require scrutiny and attention. And while we want to ensure that product review is completed in a timely manner, we do not want to allow under-reviewed devices into the market that may impose risks that could be avoided with a more responsible review.

Thank you to the witnesses for being here today. I look forward to your testimony and recommendations. I yield back.

Mr. PALLONE. Thank you. The gentleman from Iowa, Mr. Braley.

OPENING STATEMENT OF HON. BRUCE L. BRALEY, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF IOWA

Mr. BRALEY. Thank you, Mr. Chairman, for holding this hearing on medical device regulations. The safety of American patients is a matter of utmost importance to me and every member of this committee, and the issue before us today is truly a matter of life and death.

The January 2009 GAO study of the 510(k) premarket notification process was eye-opening to say the least. As many here are aware, the report made the recommendation that the FDA expeditiously take steps to issue regulations for class three device types currently allowed to enter the market through the 510(k) process by requiring premarket approval or reclassifying them to a lower class.

It is astonishing to me that the 94th Congress envisioned that the FDA would approve class three devices through the PMA process, and here we sit in the 111th Congress wondering why this hasn't happened. Since the GAO report, FDA did take the step of requesting information on the safety and effectiveness of these devices. However, there are few details available and no timeframe that I am aware of outlining FDA's next steps to help ensure the safety of those devices.

In addition, it is my understanding that the FDA has struggled with its postmarket surveillance of devices, and it is not meeting statutory requirements for inspecting certain manufacturers. This is not a good record of oversight of medical devices by the FDA. Amazingly, despite the limitations on FDA's ability to keep Americans safe, we have seen other efforts here in Washington undermine the only other check on the safety of medical devices: judicial recourse for injured patients. For decades Congress has recognized the importance of keeping American patients safe by maintaining complementary systems to protect consumers through the FDA and American courts.

Those who oppose ensuring patient safety through judicial accountability often make the argument that the FDA approval—

Mr. PALLONE. I am just afraid that your mike is not on. What is going on? Did you press a button?

Mr. BRALEY. I did.

Mr. PALLONE. It is not working.

Mr. BRALEY. Is it on now? The light is lit.

Mr. PALLONE. Does that mean you can't record it or—you want to move to another—we don't want you not to be recorded.

Mr. BRALEY. Where would you like me to begin?

Mr. PALLONE. Start there.

Mr. BRALEY. You want me to start over? I apologize to everyone in the room for having to go through this again.

Thank you, Mr. Chairman, for holding the hearing today on medical device regulations.

Mr. PALLONE. You can just continue where you were.

Mr. BRALEY. All right, I think where I was right at the time of the interruption was talking about the importance of maintaining our complementary system of accountability to protect consumers through both the FDA and American courts.

Those who oppose ensuring patient safety through judicial accountability often make the argument that FDA approval of a medical device is enough to ensure the safety of the device, yet here we sit in a hearing about FDA shortcomings, and the evidence is clear that we should not be betting lives on the efficacy of the FDA.

That is why, in addition to ensuring a stringent medical device approval process through the FDA, we must pass H.R. 1346, The Medical Device Safety Act. This legislation is needed to ensure that every American patient has the ability to hold manufacturers of defective medical devices accountable for injuries and deaths caused by unsafe products.

And, yes, many of these unsafe products did receive FDA approval yet still resulted in recalls, injuries, and deaths. The Medical Device Safety Act clarifies the intention of Congress to keep American patients safe by maintaining our complementary systems to protect patients through the FDA and American courts.

Many medical safety experts agree that patient safety is compromised when we allow the FDA to have the final say on device safety, and the examination today of the FDA's shortcomings is only further evidence of this. Strong state laws are critical to maintaining accountability for device manufacturers, and allowing the FDA to preempt these state laws is a surefire way to place sales over safety and profits over people.

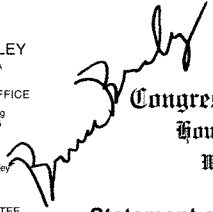
When it comes to patient safety, we must now lose sight of the fact that the single most important priority that all of us share is saving lives. So thank you, Mr. Chairman, for holding the hearing. I thank the witnesses, my colleagues, and the audience here today for recognizing the importance that this issue has on individual Americans' health and safety.

[The prepared statement of Mr. Braley follows:]

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Congress of the United States
House of Representatives
Washington, DC 20515

**Statement of Congressman Bruce Braley
Energy and Commerce Committee
Subcommittee on Health
Hearing on "Medical Devices: Are Current Regulations Doing
Enough for Patients?"
June 18, 2009**

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Thank you, Mr. Chairman, for holding this hearing today on medical device regulations. The safety of American patients is of the utmost importance to me, and the issue before us today is truly an issue of life or death.

The January 2009 Government Accountability Office study of the 510(k) premarket notification process was eye-opening. As many here are aware, the report made the recommendation that FDA expeditiously take steps to issue regulations for class III device types currently allowed to enter the market via the 510(k) process, by requiring pre-market approval or reclassifying them to a lower class. It is astonishing to me that the 94th Congress envisioned that FDA would approve class III devices through the PMA process, and here we sit in the 111th Congress, wondering why that isn't happening.

Since the GAO report, FDA did take the step of requesting information on safety and effectiveness of these devices. However,

there are few details available, and no timeframe that I'm aware of, outlining FDA's next steps to help ensure the safety of those devices. In addition, it's my understanding that FDA has struggled with its post-market surveillance of devices, and that it is not meeting statutory requirements for inspecting certain manufacturers. This is not a good record of oversight of medical devices by the FDA.

Amazingly, despite the limitations of FDA's ability to keep Americans safe, we have seen other efforts here in Washington to undermine the only other check on the safety of medical devices: judicial recourse for injured patients. For decades Congress has recognized the importance of keeping American patients safe by maintaining complementary systems to protect consumers through the FDA and American courts. Those who oppose ensuring patient safety through judicial accountability often make the argument that FDA approval of a medical device is enough to ensure the safety of the device. Yet here we sit – in a hearing about FDA's shortcomings. The evidence is clear that we should not be betting lives on the efficacy of the FDA.

That's why, in addition to ensuring a stringent medical device approval process, we must pass HR 1346, the *Medical Device Safety Act*. This legislation is needed to ensure that every American patient

has the ability to hold manufacturers of defective medical devices accountable for injuries and deaths caused by unsafe products. And yes, many of these unsafe products did receive FDA approval, yet still resulted in recalls, injuries, and deaths. The Medical Device Safety Act clarifies the intention of Congress to keep American patients safe by maintaining our complementary systems to protect patients through the FDA and American courts.

Many medical safety experts agree that patient safety is compromised when we allow the FDA to have the final say on device safety, and the examination today of FDA's shortcomings is only further evidence of this. Strong state laws are critical to maintaining accountability for device manufacturers, and allowing the FDA to preempt these state laws is a surefire way to place sales over safety and profits over people. When it comes to patient safety, we must not lose sight of the single most important priority: saving lives.

Again, thank you for holding this hearing, Mr. Chairman. I hope that the witnesses, my colleagues, and the audience here today all recognize the importance that this issue has on individual American's health and safety. Thank you.

Mr. PALLONE. Thank you, and I would ask unanimous consent that Mr. Braley's entire statement be included in the record. Without objection, so ordered. And I believe that concludes our opening statements by members of the subcommittee. So we will now turn to our witnesses, and I obviously want to welcome all of you. Let me introduce each of you. Starting on my left is Dr. Marcia Crosse, who is with the GAO. I don't have your title. What is your title?

Ms. CROSSE. Director of health care.

Mr. PALLONE. Director of health care. Okay, thanks. And then we have Dr. William Maisel, who is director of the Medical Device Safety Institute, Department of Medicine at Beth Israel Deaconess Medical Center in Boston and also Harvard University, I believe. And then we have Phillip J. Phillips who is independent consultant and Dr. Peter Lurie who is deputy director of Health Research Group for Public Citizen.

And what we do is we have five-minute opening statements, and I think you know that. They become part of the hearing record, and then we may give you some written questions afterwards, hopefully within 10 days after the hearing, that we would ask you to respond to as well. And I will start with Dr. Crosse.

STATEMENTS OF MARCIA CROSSE, DIRECTOR OF HEALTH CARE, GOVERNMENT ACCOUNTABILITY OFFICE; WILLIAM H. MAISEL, M.D., PH.D., DIRECTOR, MEDICAL DEVICE SAFETY INSTITUTE, DEPARTMENT OF MEDICINE AT BETH ISRAEL DEACONESS MEDICAL CENTER; PHILLIP J. PHILLIPS, INDEPENDENT CONSULTANT; AND PETER LURIE, M.D., M.P.H., DEPUTY DIRECTOR, HEALTH RESEARCH GROUP, PUBLIC CITIZEN

STATEMENT OF MARCIA CROSSE

Ms. CROSSE. Mr. Chairman and members of the subcommittee, I am pleased to be here today as you consider issues related to the regulation of medical devices. Americans depend on FDA to provide assurance that medical devices sold in the United States are safe and effective.

FDA's responsibilities span premarket review of devices, postmarket surveillance, and inspections of manufacturing establishments. We have done work to examine aspects of all these areas and have identified a number of concerns and made recommendations for improvements.

Earlier this year, GAO added FDA's oversight of medical products including medical devices to its list of high-risk areas warranting attention by Congress and the executive branch. Today I will provide some general background and touch on the findings from a number of GAO reports.

As you know, FDA classifies medical devices into three classes with class one including devices with low risk to patients, such as bandages, and class three, including devices with high risk such as pacemakers. About two-thirds of medical devices are exempt from any FDA premarket review. These are mostly low-risk class one devices and some class two devices. FDA does little to monitor these devices including rarely inspecting their manufacturing facilities. I

will focus my remarks on the remaining one-third of devices, which require greater regulation and oversight.

Almost all of these devices, mostly class two, are reviewed by FDA through its premarket notification process known as the 510(k) process. The remaining one percent of medical devices are class three devices that are subject to FDA's premarket approval or PMA process.

Medical device regulation follows a least burdensome approach. The 510(k) process is less stringent than the PMA process. For 510(k) submissions, the manufacturer must demonstrate that the new device is substantially equivalent to a device legally on the market. Clinical data are generally not required, and substantial equivalents will normally be determined based on comparative device descriptions including performance data.

For the more stringent PMA process, the manufacturer must supply evidence providing reasonable assurance that the device is safe and effective. Manufacturers typically submit clinical data for a PMA application, but FDA does not always require clinical data even for implantable devices. FDA may approve a class three device solely on the basis of engineering data. FDA clears or approves the vast majority of both 510(k) and PMA submissions. Some 90 percent of the class one and class two 510(k) submissions are cleared for marketing, and roughly 80 percent of PMA applications for class three devices are approved by FDA.

In January 2009, we reported on a key area of concern regarding FDA's premarket reviews. When Congress established FDA's premarket review system for medical devices in 1976, it envisioned that all class three devices would be subject to the more stringent PMA process. Nonetheless, we found that more than 30 years after Congress acted, FDA had still not completed the regulatory steps necessary to require PMA reviews for some two dozen types of class three devices, including certain hip joints and other implantable devices.

In the five-year period we reviewed, almost one-quarter of the class three device submissions that were cleared went through the less stringent 510(k) process. We recommended that FDA move expeditiously to address this issue, and in response, in April 2009, FDA began the necessary steps. However, the agency has not specified a timeframe for how quickly it will act on these devices.

The least burdensome approach relies on postmarket studies to identify problems. However, FDA also faces challenges in postmarket surveillance of medical devices. For example, the agency's ability to understand the risks related to the use of medical devices is limited because the volume of adverse event reports submitted has exceeded FDA's ability to consistently review the reports.

We have also found shortcomings in FDA's monitoring of manufacturers' compliance with postmarket study and reporting requirements.

Finally, we have found that FDA has not conducted required inspections of manufacturing establishments which are FDA's primary means of assuring that the safety and effectiveness of devices are not jeopardized by poor manufacturing practices. In 2008, we reported that FDA has not inspected domestic establishments on

schedule, and inspections of foreign establishments greatly lagged domestic inspections.

FDA has begun to take steps to address shortcomings related to inspections including opening foreign offices and hiring additional inspectors. However, FDA has stated that it will be several years before inspectors are sufficiently trained to conduct foreign inspections.

Taken together, our work raises concerns about the current pre-market and postmarket activities that are necessary for ensuring the safety and effectiveness of medical devices. Mr. Chairman, this concludes my prepared remarks. I would be happy to answer any questions that you or other members of the subcommittee may have.

[The prepared statement of Ms. Crosse follows:]

United States Government Accountability Office

GAO

Testimony
Before the Subcommittee on Health,
Committee on Energy and Commerce,
House of Representatives

For Release on Delivery
Expected at 9:30 a.m. EDT
Thursday, June 18, 2009

MEDICAL DEVICES

Shortcomings in FDA's Premarket Review, Postmarket Surveillance, and Inspections of Device Manufacturing Establishments

Statement of Marcia Crosse
Director, Health Care



June 18, 2009



Highlights of GAO-09-370T, a testimony before the Subcommittee on Health, Committee on Energy and Commerce, House of Representatives

Why GAO Did This Study

Americans depend on the Food and Drug Administration (FDA) to provide assurance that medical devices sold in the United States are safe and effective. FDA classifies medical device types into three classes, with class I including those with the lowest risk to patients (such as forceps) and class III including those with the greatest risk (such as pacemakers). FDA's responsibilities include premarket and postmarket oversight—spanning, for example, both premarket review of devices and postmarket surveillance (the collection and analysis of data on marketed devices). These responsibilities apply to all devices marketed in the United States, regardless of whether they are manufactured domestically or overseas. In 2009, GAO added FDA's oversight of medical products, including devices, to its list of high-risk areas warranting attention by Congress and the executive branch.

GAO was asked to testify on recent work related to FDA's responsibilities for medical devices, including premarket review, postmarket surveillance, and inspection of manufacturing establishments. This statement is based on a recent GAO report, *Medical Devices: FDA Should Take Steps to Ensure That High-Risk Device Types Are Approved through the Most Stringent Premarket Review Process* (GAO-09-190, January 15, 2009) and on other GAO reports and testimonies related to FDA oversight.

View GAO-09-370T or key components. For more information, contact Marcia Crosse at (202) 512-7114 or crossm@gao.gov.

MEDICAL DEVICES

Shortcomings in FDA's Premarket Review, Postmarket Surveillance, and Inspections of Device Manufacturing Establishments

What GAO Found

GAO found that FDA does not review all class III devices through its most stringent premarket review process. Unless exempt by regulation, new devices must clear FDA premarket review through either the 510(k) premarket notification process, which is used to determine if a new device is substantially equivalent to another legally marketed device, or through the more stringent premarket approval (PMA) process, which requires the manufacturer to supply evidence providing reasonable assurance that the device is safe and effective. In 1976, Congress envisioned that FDA would eventually approve all class III devices through the more stringent PMA process, but this process remains incomplete. GAO found that in fiscal years 2003 through 2007, FDA cleared 228 submissions representing 24 types of class III devices through the 510(k) process. GAO recommended in its January 2009 report that FDA expeditiously take steps to issue regulations requiring PMAs for or reclassifying class III device types currently allowed to enter the market via the 510(k) process. In response, in April 2009, FDA required manufacturers to submit information on the safety and effectiveness of the types of devices. However, FDA did not specify a time frame for how quickly it will reclassify them or require PMAs for those device types that remain in class III.

FDA also faces challenges in postmarket surveillance of medical devices. In 2008, GAO reported that the number of adverse event reports associated with medical devices increased substantially from 2000 to 2006. Both GAO and FDA, however, have identified shortcomings in FDA's postmarket oversight. For example, in 2006 FDA reported that the agency's ability to understand the risks related to the use of medical devices is limited by the fact that the volume of submitted reports exceeded FDA's ability to consistently enter or review the reports in a routine manner. In 2008, FDA officials told us that while they have a number of strategies to prioritize their reviews of adverse event reports, they still cannot review all the reports they receive.

Finally, GAO has found that FDA has not conducted required inspections of manufacturing establishments, another key FDA responsibility for medical devices marketed in the United States. In 2008, GAO reported that FDA has not met a statutory requirement to inspect certain domestic manufacturing establishments every 2 years. Instead, FDA officials estimated that the agency has inspected domestic establishments every 3 years (for class III devices) or 5 years (for class II devices). There is no comparable requirement to inspect foreign establishments, and FDA officials estimate that they have been inspected every 6 years (for class III devices) or 27 years (for class II devices). GAO reported that FDA has taken some steps to address shortcomings related to inspections of foreign establishments, but GAO has not evaluated whether these changes will improve FDA's inspection program.

Taken together, these shortcomings in both premarket and postmarket activities raise serious concerns about FDA's regulation of medical devices.

Mr. Chairman and Members of the Subcommittee:

I am pleased to be here today as you examine issues related to the regulation of medical devices. Americans depend on the Food and Drug Administration (FDA), an agency within the Department of Health and Human Services (HHS) responsible for ensuring that medical devices and other medical products sold in the United States are safe and effective.¹

FDA's responsibilities for medical devices begin before a new device is brought to market and continue after a device's clearance or approval, and these responsibilities apply to devices marketed in the United States regardless of whether they are manufactured domestically or overseas. FDA reviews submissions for thousands of new devices filed each year to decide whether they should be allowed to be marketed in the United States and is also responsible for oversight of thousands of devices already on the market. As part of both premarket and postmarket oversight, the agency inspects manufacturing establishments to ensure they are in compliance with the good manufacturing practices specified in FDA's quality system regulation as well as other statutory and regulatory requirements.

Recently, concerns have been expressed about FDA's ongoing ability to fulfill its mission of ensuring the safety and efficacy of medical products, including drugs, biologics, and devices. Reports issued by FDA's Science Board in 2007 and the Congressional Research Service in 2008 point out that the demands on the agency have soared in recent years for a variety of reasons, including the complexity of new products submitted to FDA for premarket approval and the globalization of the industries that FDA regulates. The Science Board also found that FDA's resources had not increased in proportion to the growing demands placed on it, putting public health at risk. In its fiscal year 2007 and 2008 reports, the HHS Office of Inspector General identified the oversight of drug and device safety as one of HHS's top management challenges. In January 2009, we added FDA's oversight of medical products, including devices, to GAO's

¹Generally, medical devices include items used for the diagnosis, cure, mitigation, treatment, or prevention of a disease. See 21 U.S.C. § 321(h). Throughout this statement, the term *device* refers to a medical device that is not being regulated as a drug or a biological product.

list of high-risk areas warranting attention by Congress and the executive branch.²

Medical devices range from simple tools like bandages and surgical clamps to complicated devices like pacemakers. FDA classifies each type of device into one of three classes—class I, II, or III—based on the level of risk it poses and the controls necessary to provide reasonable assurance that it is safe and effective.³ According to FDA, the risk the type of device poses to the patient or the user is a major factor in the class it is assigned: class I includes devices with the lowest risk and class III includes devices with the highest risk. Examples of types of devices in each class include the following:

- class I: tongue depressors, elastic bandages, reading glasses, and forceps;
- class II: electrocardiographs, powered bone drills, and mercury thermometers; and
- class III: pacemakers and replacement heart valves.

²See GAO, *High-Risk Series: An Update*, GAO-09-271 (Washington, D.C.: Jan. 2009).

³Throughout this statement, we refer to *type of device* or *device type* to indicate a generic category of device, which has a particular intended use (for example, a scalpel is intended to cut tissue) and which may include a variety of models made by different manufacturers. FDA's classifications of device types are codified in parts 862 through 892 of title 21 of the *Code of Federal Regulations*. Class I devices are those for which compliance with general controls, such as good manufacturing practices specified in FDA's quality system regulation, are sufficient to provide reasonable assurance of their safety and effectiveness. Class II devices are subject to general controls and may also be subject to special controls, such as postmarket surveillance. For class II devices intended to support or sustain human life, FDA must examine, identify, and describe the special controls necessary to provide assurance of their safety and effectiveness. Class III devices are those (1) for which insufficient information exists to determine whether general and special controls are sufficient to provide reasonable assurance of their safety and effectiveness and (2) that support or sustain human life or are of substantial importance in preventing impairment of human health, or that present a potential unreasonable risk of illness or injury. See 21 U.S.C. § 360c.

In general, unless exempt under FDA regulations,⁴ devices are subject to one of two types of FDA premarket review before they may be legally marketed in the United States.⁵

- **Premarket approval (PMA):** The manufacturer must provide evidence, typically including clinical data, providing reasonable assurance that the new device is safe and effective. The PMA process is the most stringent type of premarket review. A successful submission results in FDA approval.
- **Premarket notification (510(k)):** The manufacturer must demonstrate to FDA that the new device is *substantially equivalent* to a legally marketed device that does not require a PMA.⁶ A successful submission results in FDA clearance.

My remarks today will discuss shortcomings we have identified in FDA's premarket review of medical devices, FDA's postmarket surveillance activities, and FDA's inspections of manufacturing establishments. My statement includes findings from our recent report on FDA's premarket review of medical devices.⁷ My statement also draws from several other GAO reports and testimonies on FDA inspections of domestic and foreign

⁴Under federal regulations, many types of devices are exempt from FDA premarket review. Although FDA does not track the number of devices that are actually sold or marketed in the United States, manufacturers are required to register with FDA and provide a list of devices intended for commercial distribution, including device types that are exempt from premarket review. See 21 U.S.C. § 360(j)(2)(A); 21 C.F.R. § 807.21 (2008). About 67 percent of the more than 50,000 separate devices that manufacturers listed with FDA during fiscal years 2003 through 2007 were exempt from premarket review. Of the exempt devices that manufacturers listed with FDA, about 95 percent were class I devices, for example reading glasses and forceps. About 5 percent were class II devices, for example wheeled stretchers and mercury thermometers.

⁵A small percentage of devices enter the market by other means, such as through the humanitarian device exemption process that allows market entry, without adherence to certain requirements, for devices benefiting patients with rare diseases or conditions. See 21 U.S.C. § 360(m), 21 C.F.R. pt. 814, subpart H (2008).

⁶*Substantial equivalence* or *substantially equivalent* means that the device has the same intended use as another legally marketed device and the same technological characteristics, or different technological characteristics and submitted information demonstrates that the device is as safe and effective as the legally marketed device and does not raise different questions of safety or effectiveness. See 21 U.S.C. § 360c(i)(1)(A).

⁷See GAO, *Medical Devices: FDA Should Take Steps to Ensure That High-Risk Device Types Are Approved through the Most Stringent Premarket Review Process*, GAO-09-190 (Washington, D.C.: Jan. 15, 2009).

device manufacturing establishments and other aspects of FDA's oversight of devices that we have issued since 2007,⁸ as well as ongoing work we are conducting related to FDA.

For this body of work, we analyzed information from FDA databases,⁹ interviewed FDA officials; and reviewed pertinent statutes, regulations, guidance, and reports. For the report on FDA's premarket review of devices, we examined the premarket review processes—the 510(k) premarket notification process or the premarket approval (PMA) process—FDA used in fiscal years 2003 through 2007 and reviewed a sample of FDA files related to submissions for new devices. Our analysis included traditional and abbreviated 510(k) submissions, original PMA submissions, and submissions for two types of supplemental PMAs: panel-track PMA supplements (which are supplements requesting approval for a significant change in design or performance, or a new use of a device, for which clinical data are generally necessary to provide reasonable assurance of safety and effectiveness) and 180-day PMA supplements (which are supplements requesting approval for a significant change in components, materials, design, specification, software, color additives, or labeling).¹⁰

To assess FDA's program for inspecting establishments that manufacture medical devices, we analyzed information from three FDA databases¹¹ and interviewed officials from FDA's Center for Devices and Radiological Health and Office of Regulatory Affairs, which each have responsibilities for managing the medical device inspection program. We also obtained updated information from FDA on the status of FDA's programs for third-party inspections in June 2009. Specifically, we obtained data from FDA on the number of inspections conducted by accredited third parties since March 11, 2004—the date when FDA first cleared an accredited organization to conduct inspections.

⁸See "Related GAO Products" at the end of this testimony.

⁹The databases we used included FDA's 510(k) and premarket approval (PMA) databases, Device Nomenclature Management System, Device Registration and Listing System (DRLS), Field Accomplishments and Compliance Tracking System (FACTS), and Operational and Administrative System for Import Support (OASIS).

¹⁰Our analysis did not include certain types of device submissions, for example, special 510(k) submissions, which are requests for clearance of minor modifications to devices that have already been cleared through the 510(k) process.

¹¹The FDA databases we used were DRLS, FACTS, and OASIS.

We conducted our work in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

Background

FDA's responsibilities related to medical devices include premarket and postmarket oversight—spanning, for example, both premarket review of devices and postmarket surveillance (the collection and analysis of data on marketed devices). As part of both premarket and postmarket oversight, FDA is responsible for inspecting certain foreign and domestic establishments to ensure they meet required manufacturing standards.

Premarket Review

Relative to the PMA process, the 510(k) premarket review process is generally:

- **Less stringent.** For most 510(k) submissions, clinical data are not required and substantial equivalence will normally be determined based on comparative device descriptions, including performance data. In contrast, in order to meet the PMA approval requirement of providing reasonable assurance that a new device is safe and effective, most original PMAs and some PMA supplements require clinical data.
- **Faster.** FDA generally makes decisions on 510(k) submissions faster than it makes decisions on PMA submissions. FDA's fiscal year 2009 goal is to review and decide on 90 percent of 510(k) submissions within 90 days and 98 percent of them within 150 days. The comparable goal for PMAs is to review and decide upon 60 percent of original PMA submissions in 180 days and 90 percent of them within 295 days.¹²
- **Less expensive.** The estimated cost to FDA for reviewing submissions is substantially lower for 510(k) submissions than for PMA submissions. For fiscal year 2005, for example, according to FDA the estimated average cost for the agency to review a 510(k) submission was about \$18,200, while the estimate for a PMA submission was about \$870,000. For the applicant, the standard fee provided to FDA at the time of submission is also significantly lower for a 510(k) submission than for a PMA submission. In

¹²FDA's goals for original PMAs included panel-track PMA supplements.

fiscal year 2009, for example, the standard fee for 510(k) submissions is \$3,693, while the standard fee for original PMA submissions is \$200,725.

In general, class I and II device types subject to premarket review are required to obtain FDA clearance through the 510(k) process, and class III device types are required to obtain FDA approval through the more stringent PMA process. With the enactment of the Medical Device Amendments of 1976, Congress imposed requirements under which all class III devices would be approved through the PMA process before being marketed in the United States.¹³ However, certain types of class III devices that were in commercial distribution in the United States before May 28, 1976¹⁴ (called preamendment device types) and those determined to be substantially equivalent to them may be cleared through the less stringent 510(k) process until FDA publishes regulations requiring them to go through the PMA process or reclassifies them into a lower class.¹⁵ Prior to 1990, FDA issued regulations requiring some class III device types to go through the PMA process but many class III device types continued to be reviewed through the 510(k) process.¹⁶ The Safe Medical Devices Act of 1990 required FDA (1) to reexamine the preamendment class III device types for which PMAs were not yet required to determine if they should be reclassified to class I or II or remain in class III and (2) to establish a schedule to promulgate regulations requiring those preamendment device types that remain in class III to obtain FDA approval through the PMA process.¹⁷ Accordingly, all class III devices are eventually to be reviewed through the PMA process.

¹³See Pub. L. No. 94-295, 90 Stat. 539, 552-53 (codified at 21 U.S.C. § 360e).

¹⁴May 28, 1976, is the date of enactment of the Medical Device Amendments of 1976, which established the three device classes. Pub. L. No. 94-295, 90 Stat. 539.

¹⁵Based on new information respecting a device, FDA may, upon its initiative or upon petition of an interested person, by regulation change the classification of a device from class III to (1) class II if it determines that special controls would provide reasonable assurance of the safety and effectiveness of the device and that general controls alone would not provide reasonable assurance of the safety and effectiveness of the device or (2) class I if FDA determines that general controls alone would provide reasonable assurance of the safety and effectiveness of the device. 21 U.S.C. § 360c(e).

¹⁶In August 1988, GAO reported that FDA had called for premarket approval applications for only 9 of approximately 150 types of preamendment class III device types. See GAO, *Medical Devices: FDA's 510(k) Operations Could Be Improved*, GAO/PEMD-88-14 (Washington, D.C.: Aug. 17, 1988).

¹⁷Pub. L. No. 101-629, § 4(b), 104 Stat. 4511, 4515-17 (codified at 21 U.S.C. § 360c(i)).

Postmarket Surveillance

In addition to its responsibilities for premarket review of devices, FDA's postmarket activities to help ensure that devices already on the market remain safe and effective include collecting and analyzing reports of device-related adverse events and reviewing annual reports required from manufacturers.¹⁸ FDA's reporting framework for device-related adverse events includes both mandatory and voluntary components. Under FDA's Medical Device Reporting regulation,

- manufacturers are required to report device-related deaths, serious injuries, and certain malfunctions to FDA and
- user facilities, such as hospitals and nursing homes, are required to report device-related deaths to FDA and to the device manufacturer and to report serious injuries to the manufacturer (or, if the manufacturer is unknown, to FDA).

Manufacturers and user facilities, as well as health professionals and consumers, may also voluntarily report less serious device-related events to FDA. FDA maintains databases that include both mandatory and voluntary reports of device-related adverse events, which agency officials can search to conduct research on trends or emerging problems with device safety. FDA scientists review these reports, request follow-up investigations, and determine whether further action is needed to ensure patient safety. Such action may include product recalls, public health advisories to notify health care providers and the public of potential device-related health and safety concerns, or requiring a manufacturer to change the instructions in its device labeling.

¹⁸FDA approves some devices conditionally, meaning that as a condition of approval, manufacturers must comply with specific terms specified by FDA, such as conducting postmarket surveillance studies. Manufacturers report to FDA on their compliance with these conditions through annual reports.

Inspections of Device Manufacturing Establishments

Finally, as part of both premarket and postmarket oversight of medical devices, FDA is responsible for inspecting certain foreign and domestic establishments to ensure they meet required manufacturing standards.¹⁹ Such inspections are FDA's primary means of assuring that the safety and effectiveness of devices are not jeopardized by poor manufacturing practices. Requirements governing domestic and foreign inspections differ. Specifically, FDA is required to inspect domestic establishments that manufacture class II or III devices every 2 years.²⁰ There is no comparable requirement to inspect foreign establishments.

In 2002, in response to concerns about FDA's ability to meet its responsibilities for inspecting device manufacturing establishments, Congress included certain provisions in the Medical Device User Fee and Modernization Act of 2002 (MDUFMA).²¹ These provisions were designed to (1) increase the number of inspected device manufacturing establishments and (2) help device manufacturers meet the inspection requirements of both the United States and foreign countries in a single inspection. Specifically, MDUFMA required FDA to accredit third-party organizations to conduct inspections of certain foreign and domestic establishments. In response, FDA implemented its Accredited Persons Inspection Program, which permits certain establishments to voluntarily request inspections from third-party organizations to meet inspectional requirements. Additionally, in September 2006, in partnership with Health Canada,²² FDA established another program for inspection by accredited third parties—the Pilot Multi-purpose Audit Program—that allows accredited organizations to conduct a single inspection to meet the regulatory requirements of both countries.

¹⁹FDA regulations define an establishment as a place of business under one management at one general physical location at which a device is manufactured, assembled, or otherwise processed. 21 C.F.R. § 807.3(c) (2007). Device manufacturers may have more than one establishment. We use the term *manufacture* to refer to activities including manufacturing, preparing, and processing devices.

²⁰21 U.S.C. § 360(h). There is no statutory requirement for inspection of class I device manufacturing establishments, and FDA does not routinely inspect them. However, FDA periodically inspects establishments manufacturing surgeon's gloves and patient examination gloves, which are both class I devices, due to ongoing problems with leakage. FDA also periodically inspects manufacturers of randomly selected class I devices.

²¹See Pub. L. No. 107-250, § 201, 116 Stat. 1588, 1602-09 (2002) (codified as amended at 21 U.S.C. § 374(g)).

²²Health Canada is the governmental entity that regulates medical devices marketed in Canada.

FDA Has Not Ensured That All Class III Devices Are Approved through the Most Stringent Premarket Review Process

Although Congress envisioned that all class III devices would eventually be approved through the more stringent PMA process, we found that this was not always the case. In January 2009, we reported that in fiscal years 2003 through 2007, FDA reviewed all submissions for class I and II devices through the 510(k) process, and reviewed submissions for some types of class III devices through the 510(k) process and others through the PMA process.²¹

- FDA reviewed all 13,199 submissions for class I and class II devices through the 510(k) process, clearing 11,935 (90 percent) of these submissions.
- FDA also reviewed 342 submissions for class III devices through the 510(k) process, clearing 228 (67 percent) of these submissions.
- In addition, the agency reviewed 217 original PMA submissions and 784 supplemental PMA submissions for class III devices and approved 78 percent and 85 percent, respectively, of these submissions.

Table 1 summarizes the FDA review decisions, by class of device, in fiscal years 2003 through 2007 for 510(k) and PMA submissions.

²¹See GAO-09-190.

Table 1: FDA 510(k) and PMA Decisions by Class, Fiscal Years 2003 through 2007

| Submission type | Device class | Determined substantially equivalent or approved (percentage of row) | Determined not substantially equivalent or denied (percentage of row) | Other decision* (percentage of row) | Total (percentage of row) |
|---------------------------|--------------------|---|---|-------------------------------------|---------------------------|
| 510(k) | Class I | 1,265 (84) | 40 (3) | 204 (14) | 1,509 (100) |
| | Class II | 10,670 (91) | 373 (3) | 647 (6) | 11,690 (100) |
| | Class III | 228 (67) | 100 (29) | 14 (4) | 342 (100) |
| | Other [†] | 476 (33) | 27 (2) | 955 (66) | 1,458 (100) |
| PMA | | | | | |
| Original | Class III | 170 (78) | — [‡] | 47 (22) ^c | 217 (100) |
| Supplemental [§] | Class III | 664 (85) | — [‡] | 120 (15) ^c | 784 (100) |

Source: GAO analysis of FDA data.

Notes: Data represent 14,999 traditional and abbreviated 510(k) submissions, 217 original PMA submissions, and 784 supplemental PMA submissions for which FDA made review decisions in fiscal years 2003 through 2007. Percentages may not sum to 100 because of rounding.

*Other decisions include submissions that were withdrawn, were exempted by regulation, were non responsive to FDA's requests within a specified time frame, were forwarded to another FDA center (e.g., drugs or biologics), were duplicates, or were for products determined not to be devices.

[†]Other device class includes submissions for which a device class was not recorded in FDA's 510(k) database.

^cAccording to FDA data, all PMA decisions during fiscal years 2003 through 2007 were approved or withdrawn. FDA did not deny approval of any PMA submissions during this period. According to FDA officials, when a PMA was seriously deficient, FDA issued a "not approvable" letter under 21 C.F.R. § 814.44(f) and placed the submission on hold. A company may withdraw a submission voluntarily. FDA also considers submissions to be withdrawn voluntarily if the applicant is unable to provide the information necessary to support approval within 180 days.

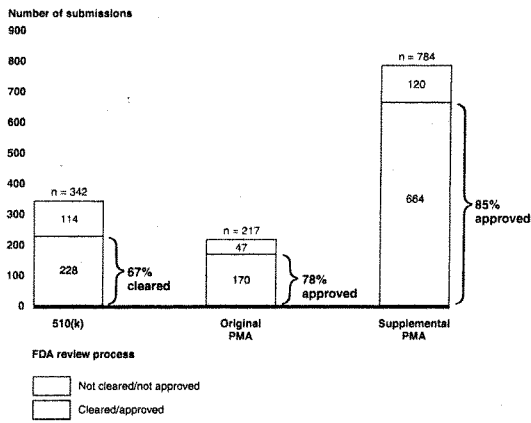
[§]Supplemental PMA submissions include 180-day (user-fee) and panel-track PMA supplements. The numbers in this row do not include other types of PMA supplements.

With respect to class III devices, in fiscal years 2003 through 2007, FDA reviewed submissions for some types of class III devices through the 510(k) process, and other types of class III devices through the PMA process. Specifically, FDA reviewed 342 submissions for new class III devices through the 510(k) process, determining 228 (67 percent) of these submissions to be substantially equivalent to a legally marketed device.²⁴

²⁴Consumer advocates have raised questions regarding 510(k) clearance of devices that may utilize new technologies that are different than those in the marketed devices to which they are compared. In our review of a representative sample of 510(k) submissions for which FDA reached a review decision of substantially equivalent or not substantially equivalent in fiscal years 2005 through 2007, we found that FDA determined 23 percent of cleared class III device submissions had new technological characteristics. This compares to 14 percent of cleared class II submissions.

During the same time period, FDA reviewed 217 original PMA submissions and 784 supplemental PMA submissions for class III devices and approved 78 percent and 85 percent of them, respectively. (See fig. 1.)

Figure 1: Class III Device Submissions with FDA Review Decisions in Fiscal Years 2003 through 2007, by FDA Review Process and Review Decision



Source: GAO analysis of FDA data.

Notes: Figure represents FDA review decisions made between October 1, 2002, and September 30, 2007, for class III device submissions reviewed through the 510(k) and PMA processes. 510(k) includes traditional and abbreviated 510(k) submissions; supplemental PMA includes panel-track supplements and 180-day (user-fee) supplements.

Not cleared/not approved includes (1) for 510(k) submissions, those submissions FDA found to be not substantially equivalent or withdrawn and (2) for PMA submissions, those submissions that were withdrawn. According to FDA data, all PMA decisions during fiscal years 2003 through 2007 were approved or withdrawn. FDA did not deny approval of any PMA submissions during this period. According to FDA officials, when a PMA is seriously deficient, FDA issues a "not approvable" letter and places the submission on hold. An applicant may then withdraw a submission voluntarily. FDA also considers submissions to be withdrawn voluntarily if the applicant is unable to provide the information necessary to support approval within 180 days.

The 228 class III device submissions FDA cleared through the 510(k) process in fiscal years 2003 through 2007 were for devices such as artificial hip joints, implantable blood access devices, and automated external defibrillators. Class III 510(k) submissions were more likely than other 510(k) submissions to be for device types that were implantable; were life sustaining; or pose a significant risk to the health, safety, or welfare of a patient. Of the 228 510(k) submissions for class III devices that FDA cleared in fiscal years 2003 through 2007, FDA's databases flagged 66 percent as being for device types that are implantable, life sustaining, or of significant risk. This compares to no 510(k) submissions for class I devices and 25 percent of 510(k) submissions for class II devices.

Although the Medical Device Amendments of 1976 imposed requirements under which all class III devices would be approved through the PMA process, and the Safe Medical Devices Act of 1990 required that FDA either reclassify or establish a schedule for requiring PMAs for class III device types, this process remains incomplete. The 228 class III device submissions cleared by FDA through the 510(k) process in fiscal years 2003 through 2007 represented 24 separate types of class III devices. As of October 2008, 4 of these device types had been reclassified to class II, but 20 device types could still be cleared through the 510(k) process. FDA officials said that the agency is committed to issuing regulations either reclassifying or requiring PMAs for the class III devices currently allowed to receive clearance for marketing via the 510(k) process, but did not provide a time frame for doing so.

We recommended that the Secretary of Health and Human Services direct the FDA Commissioner to expeditiously take steps to issue regulations for each class III device type currently allowed to enter the market through the 510(k) process. These steps should include issuing regulations to (1) reclassify each device type into class I or class II, or require it to remain in class III, and (2) for those device types remaining in class III, require approval for marketing through the PMA process. In commenting on a draft of our report, HHS agreed with our recommendation, noting that since 1994 (when FDA announced its strategy to implement provisions of the Safe Medical Devices Act of 1990) FDA has called for PMAs or reclassified the majority of class III devices that did not require PMAs at that time. The department's comments, however, did not specify time frames in which FDA will address the remaining class III device types allowed to enter the market via the 510(k) process, stating instead that the agency is considering its legal and procedural options for completing this task as expeditiously as possible, consistent with available resources and competing time frames. Given that more than 3 decades have passed since

Congress envisioned that all class III devices would eventually be required to undergo premarket review through the more stringent PMA process, we believe it is imperative that FDA take immediate steps to address the remaining class III device types that may still enter the market through the less stringent 510(k) process by requiring PMAs for or reclassifying them.

In April 2009, FDA took what it termed “the first step towards completing the review of Class III device types predating the 1976 law, as was recommended by the U.S. Government Accountability Office (GAO) in a January 2009 report to Congress.” Specifically, FDA announced that it was requiring manufacturers of 25 types of class III medical devices marketed prior to 1976 to submit safety and effectiveness information to the agency by August 7, 2009, so that it may evaluate the risk level for each device type. In the *Federal Register* notice announcing the requirement,³⁵ FDA stated that once the safety and effectiveness information was submitted, the agency would be able to determine which device types would be required to undergo the agency’s most stringent premarket review process. FDA’s requirement that manufacturers submit safety and effectiveness information is an essential initial step toward implementing our recommendation and fully implementing the law. However, FDA did not specify a time frame for how quickly it will review the submitted information, determine whether to reclassify the device types, and require PMAs for those that remain in class III.

It should be noted, however, that while the PMA process is more stringent than the 510(k) process, FDA can approve a device through the PMA process without clinical data demonstrating the safety and effectiveness of the device. For example, in our review of FDA’s approval of PMAs for certain temporomandibular joint (jaw) implants, FDA managers overruled their review staff to approve one of the devices, despite the review staff’s concern over the sufficiency of the clinical data.³⁶ The review decision stated that either good engineering data or good clinical data—not necessarily both—were acceptable to approve a device and accepted the engineering data as a basis for approving an implanted device for which the review staff had determined that the clinical data were inadequate.

³⁵See 74 Fed. Reg. 16214 (Apr. 9, 2009).

³⁶See GAO, *Medical Devices: FDA’s Approval of Four Temporomandibular Joint Implants*, GAO-07-996 (Washington, D.C.: Sept. 17, 2007).

FDA Faces Challenges in Postmarket Surveillance

In our recent high-risk report, we noted that FDA's monitoring of postmarket safety of approved products, including medical devices, has been questioned by numerous groups.²⁷ In 2008, we reported that the number of adverse event reports associated with all devices increased substantially from about 77,000 reports in 2000 to about 320,000 reports in 2006.²⁸ FDA's review and analysis of these reports provides information about trends such as infection outbreaks or common user errors caused by inadequate instructions and may result in actions such as device recalls. During fiscal year 2006, FDA initiated 651 recall actions involving 1,550 medical devices. This included 21 recall actions in which FDA determined that it was likely that the use of the medical device would cause serious health problems or death.

We and FDA have identified shortcomings in FDA's postmarket surveillances. In 2006, FDA reported that the agency's Center for Devices and Radiological Health's ability to understand the risks of adverse events related to the use of medical devices—whether used in the in the home of a patient, in a hospital, in a laboratory, or in the office of a private practitioner—is limited both by a lack of informative, validated adverse event reports and by a lack of quality epidemiologic information.²⁹ FDA specifically reported:

- One major constraint is the lack of objective data about device use and device-related problems.
- Underreporting of adverse events continues to be a problem.
- FDA's medical device reporting system is a passive system—that is, the reports are entered as reported by manufacturers, facilities, practitioners, or patients—and, as a result, some reports are incomplete or difficult to understand.

²⁷See GAO-09-271, 18.

²⁸FDA officials told us that the vast majority of reports involve a device malfunction that has the potential to cause a death or serious injury if the malfunction were to recur, even though there was no death or serious injury in the reported event. See GAO, *Reprocessed Single-Use Medical Devices: FDA Oversight Has Increased, and Available Information Does Not Indicate That Use Presents an Elevated Health Risk*, GAO-08-147 (Washington, D.C.: Jan. 31, 2008).

²⁹See Food and Drug Administration, *Ensuring the Safety of Marketed Medical Devices, CDRH's Medical Device Postmarket Safety Program* (Jan. 18, 2006).

- The volume of submitted reports exceeded the center's ability to consistently enter or review the data in a routine manner.

In its 2006 report, FDA identified areas for improvement in postmarket problem assessment for the center. In 2008, FDA officials told us that while they have a number of strategies to prioritize their reviews, they still cannot review all the reports they receive.

We have also found shortcomings in FDA's monitoring of manufacturers' compliance with requirements following device approval. In 2007, we found that manufacturers do not always submit their required annual reports in a timely manner. For example, FDA was missing five annual reports from the manufacturer of one device we were examining, but it was not until we requested these reports that FDA contacted the manufacturer to obtain the missing information.³⁰ Without these annual reports, FDA cannot adequately monitor manufacturers' compliance with postmarket requirements.

FDA Has Not Conducted Required Inspections of Manufacturing Establishments

Our work has also identified challenges faced by FDA in terms of inspecting establishments that manufacture medical devices. In January 2008, we testified that FDA has not met a statutory requirement to inspect certain domestic manufacturing establishments every 2 years.³¹ FDA officials estimated that the agency has inspected these establishments every 3 years (for establishments manufacturing class III devices) or every 5 years (for establishments manufacturing class II devices). There is no comparable requirement to inspect foreign establishments, and agency officials estimate that these establishments have been inspected every 6 years (for class III devices) or 27 years (for class II devices).

We also testified that FDA faces additional challenges in managing its inspections of foreign device establishments. We found that two databases that provide FDA with information about foreign device establishments and the products they manufacture for the U.S. market contain inaccuracies that create disparate estimates of establishments subject to FDA inspection.³² Although comparing information from these two

³⁰GAO-07-996.

³¹See GAO, *Medical Devices: Challenges for FDA in Conducting Manufacturer Inspections*, GAO-08-428T (Washington, D.C.: Jan. 29, 2008).

³²These two databases are DRLS and OASIS.

databases could help FDA determine the number of foreign establishments marketing devices in the United States, these databases cannot exchange information and any comparisons must be done manually. Moreover, inspections of foreign device manufacturing establishments pose unique challenges to FDA, such as difficulties in finding translation services and in extending trips if the inspections uncover problems. FDA has taken some steps to address shortcomings related to inspections of foreign establishments, including changes to its registration database to improve the accuracy of the count of establishments and initiatives to address unique challenges related to inspections of foreign manufacturers, but we have not evaluated whether these changes will improve FDA's inspection program.

In addition, FDA's accredited third-party inspection programs may be unable to quickly help FDA fulfill its responsibilities. In January 2007, we reported on the status of the Accredited Persons Inspection Program, citing, among other things, concerns regarding its implementation and potential incentives and disincentives that may influence manufacturers' participation.³⁴ We found that several factors may influence manufacturers' interest in voluntarily requesting an inspection by an accredited organization. According to FDA and representatives of affected entities, there are potential incentives and disincentives to requesting an inspection, as well as reasons for deferring participation in the program. Potential incentives include the opportunity to reduce the number of inspections conducted to meet FDA and other countries' requirements and to control the scheduling of the inspection. Potential disincentives include bearing the cost for the inspection and uncertainty about the potential consequences of making a commitment to having an inspection to assess compliance with FDA requirements in the near future. Some manufacturers might be deferring participation. For example, manufacturers that already contract with a specific accredited organization to conduct inspections to meet the requirements of other countries might defer participation until FDA has cleared that organization to conduct independent inspections. In both our January 2008 and May 2008 testimonies, we reported that few inspections of device manufacturing establishments had been conducted through FDA's two

³⁴See GAO, *Medical Devices: Status of FDA's Program for Inspections by Accredited Organizations*, GAO-07-157 (Washington, D.C.: Jan. 5, 2007).

accredited third-party inspection programs.³⁸ As of June 12, 2009, FDA reported that a total of 21 inspections—8 inspections of domestic establishments and 13 inspections of foreign establishments—had been conducted under these programs. The small number of inspections completed by accredited third-party organizations raises questions about the practicality and effectiveness of these programs to quickly help FDA increase the number of establishments inspected.

Taken together, these shortcomings in both premarket and postmarket activities raise serious concerns about FDA's regulation of medical devices.

Mr. Chairman, this completes my prepared statement. I would be happy to respond to any questions you or the other members of the subcommittee may have at this time.

Contacts and Acknowledgments

For further information about this statement, please contact Marcia Crosse, at (202) 512-7114 or crossem@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this statement. Kim Yamane and Geraldine Redican-Bigott, Assistant Directors; Susannah Bloch; Matt Byer; Sean DeBlicek; Helen Desauiniers; and Julian Klazkin made key contributions to this report.

³⁸See GAO-08-428T and GAO, *Medical Devices: FDA Faces Challenges in Conducting Inspections of Foreign Manufacturing Establishments*, GAO-08-780T (Washington, D.C.: May 14, 2008).

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Mr. PALLONE. Thank you, Dr. Crosse. Dr. Maisel.

STATEMENT OF WILLIAM MAISEL

Dr. MAISEL. Thank you. Chairman Pallone, Ranking Member Deal, distinguished members of the committee, my name is Dr. William Maisel. I am a practicing cardiologist at Beth Israel Deaconess Medical Center and assistant professor of medicine at Harvard Medical School in Boston. I also direct the Medical Device Safety Institute, an industry-independent, non-profit organization dedicated to improving the safety of medical devices. I have served as a consultant to the FDA's Center for Devices and Radiologic Health since 2003, and I have previously chaired the FDA's postmarket and heart device advisory panels.

Thank you for the opportunity today to speak about medical device regulation and to discuss areas where improvements can be made to the benefit of millions of Americans who utilize medical devices every day.

Recently several high-profile device safety issues have raised concerns about the FDA's ability to properly evaluate and monitor the safety and effectiveness of medical devices. FDA has been criticized for taking too long to identify medical device safety concerns and for failing to implement robust scientific standards for device clearance and approval.

FDA device physicians and scientists have alleged serious wrongdoing at FDA, including the alteration and distortion of scientific and technological findings and conclusions. Unfortunately, these allegations divert attention from the many superb FDA engineers, physicians, scientists, and public servants who work tirelessly to ensure that only safe and effective medical devices reach the American public.

We are fortunate to have the preeminent medical device regulatory system in the world. The U.S. Food and Drug Administration regulates more than 100,000 different medical devices manufactured by more than 15,000 companies. They annually receive several thousand applications for new and modified devices, and they are mandated by Congress to complete their premarket evaluations in a timely fashion.

Unlike drugs, the medical device product life cycle from conception to obsolescence is short. While a drug may remain on the market essentially unaltered for decades, rapid technological device advances offer the potential to improve medical device performance, reduce patient suffering, improve health, and sometimes treat previously untreatable conditions.

Unnecessarily slowing the device regulatory approval process would be akin to leaving medical device patients with an outdated antique telephone in an iPhone world. Nevertheless, it is evident that to best protect the health of American medical device users, the FDA must promote and enforce a higher scientific standard for device clearance and approval, particularly for higher risk devices whose abnormal performance is likely to have adverse effects on patient health.

Unfortunately, due to the current FDA premarket evaluation process, unanswered questions regarding device safety and effectiveness often remain at the time of FDA clearance or approval.

This creates the potential for a large number of patients to be rapidly exposed to a newly approved product in the absence of long-term follow-up data.

For example, close to 268,000 patients have been implanted with the Medtronic Sprint Fidelis implantable defibrillator lead before it was recalled in October 2007 after it was determined that the wire was prone to fracture. A fracture of the lead which connects the implantable defibrillator to the heart may result in serious health consequences including painful electrical shocks or death.

Mr. Sidney Engler, a patient of mine, was one of the unfortunate people to receive this lead when he had an implantable defibrillator placed in February 2006. Mr. Engler is a decorated World War II veteran, having served in Europe from 1943 to 1945, and on the evening of August 14, 2008, while preparing to retire for the evening, the simple act of removing his shirt over his head caused his defective defibrillator lead to fracture. Mr. Engler suffered a cardiac arrest in front of his wife. He required CPR and received numerous unnecessary painful shocks from his defibrillator. Fortunately due to the prompt response of his local EMTs, Sidney survived. Despite a prolonged hospital stay and months of rehabilitation, he has still not fully recovered.

The FDA approved the Medtronic Sprint Fidelis defibrillator lead, the one in Mr. Engler's heart, as a PMA supplement in 2004 on the basis of no human clinical data. The original Medtronic defibrillator lead PMA was submitted in 1992. More than 30 supplements had been submitted in the interim, and the Fidelis lead bears little resemblance to its original counterpart.

In addition to a lack of human clinical performance data, the FDA failed to require a postmarket study to monitor the device's performance. The result was the widespread distribution of a defective product to hundreds of thousands of patients.

Medical devices have enriched and extended the lives of countless people. The safety and performance of medical devices must be improved, and the frequency of medical device malfunctions and adverse events must be reduced. Additional consumer safeguards are needed. By demanding more thorough scientific device evaluations, the FDA can reestablish consumer confidence and improve its ability to protect the public's health. Thank you.

[The prepared statement of Dr. Maisel follows:]

**STATEMENT OF
WILLIAM H. MAISEL, MD, MPH
DIRECTOR, MEDICAL DEVICE SAFETY INSTITUTE
BETH ISRAEL DEACONESS MEDICAL CENTER
HARVARD MEDICAL SCHOOL**

**BEFORE THE
HOUSE COMMITTEE ON ENERGY AND COMMERCE
SUBCOMMITTEE ON HEALTH**

**MEDICAL DEVICES:
ARE CURRENT REGULATIONS DOING ENOUGH FOR PATIENTS?
JUNE 18, 2009**

Maisel WH – Medical Devices: Are Current Regulations Doing Enough for Patients?

INTRODUCTION

Chairman Pallone, Ranking Member Deal, Distinguished Members of the Committee. My name is Dr. William Maisel. I am a practicing cardiologist at Beth Israel Deaconess Medical Center and Assistant Professor of Medicine at Harvard Medical School in Boston. I am also Founder and Director of the Medical Device Safety Institute (www.medicaldevicesafety.org), an industry-independent, non-profit organization dedicated to improving the safety of medical devices. I have served as a consultant to the FDA's Center for Devices and Radiological Health (CDRH) since 2003 and I have previously chaired the FDA's Post Market and Heart Device Advisory Panels. Thank you for the opportunity today to speak about medical device regulation and to discuss areas where improvements can be made to the benefit of millions of Americans who utilize medical devices every day.

Recently, several high-profile device safety issues have raised concerns about the FDA's ability to properly evaluate and monitor the safety and effectiveness of medical devices. FDA has been criticized for taking too long to identify medical device safety concerns and for failing to implement robust scientific standards for device clearance and approval. FDA device physicians and scientists have alleged "serious wrongdoing" at FDA, including the alteration and distortion of scientific and technological findings and conclusions¹. Unfortunately these allegations divert attention from the many superb FDA engineers, physicians, scientists, and public servants who work tirelessly to ensure that only safe and effective medical devices reach the American public.

We are fortunate to have the preeminent medical device regulatory system in the world. The U.S. Food and Drug Administration regulates more than 100,000 different medical devices manufactured by more than 15,000 companies². They annually receive several thousand applications for new and modified devices and they are mandated by Congress to complete their premarket evaluations in a timely fashion³.

When Congress drafted the Medical Device Amendments of 1976, they recognized that medical devices differ from drugs in a number of important ways. Typically, premarket evaluation of drugs includes clinical trials involving thousands of patients. During the premarket evaluation and the postmarket phase, much is learned about the drug, including its pharmacology, its biological effects, and its potential for adverse reactions.

Medical devices are different. Thorough, science-based evaluations of medical device performance can be challenging due to the variability of device types and risks, the

¹ Letter to President Barack H. Obama, April 2, 2009. Accessed 6/26/09 at: <http://finance.senate.gov/press/Gpress/2009/prg040209a.pdf>.

² Maisel WH. Medical device regulation: An Introduction for the practicing physician. *Ann Intern Med* 2004; 140: 296-302.

³ U.S. Department of Health and Human Services. Food and Drug Administration. Center for Devices and Radiological Health. Office of Device Evaluation: Annual Report – Fiscal Year 2006 and Fiscal Year 2007. Accessed May 10, 2009 at: <http://www.fda.gov/cdrh/annual/fy2007/ode/report.pdf>.

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difficulty in conducting well-designed clinical trials (for example, the difficulty in conducting blinded or placebo-controlled studies), the heavy reliance on bench testing as a surrogate for clinical performance, and the difficulty in distinguishing device-related adverse events from “expected” procedural or disease-related complications. Perhaps most importantly, unlike drugs, the medical device product life cycle—from conception to obsolescence—is short. While a drug may remain on the market essentially unaltered for decades, rapid technological device advances offer the potential to improve medical device performance, reduce patient suffering, improve health, and sometimes treat previously untreatable conditions. Unnecessarily slowing the device regulatory approval process would be akin to leaving medical device patients with an outdated, antique telephone in an iPhone world.

Nevertheless, it is critical that the safety and performance of medical devices be improved, that the frequency of medical device malfunctions and adverse events be reduced, and that patients and physicians be adequately informed about device clinical effectiveness and risks in a timely fashion. In short, FDA needs to improve its science-based device assessments and decision-making.

PREMARKET EVALUATION

To gain marketing clearance or approval from the FDA for a medical device, a manufacturer must demonstrate reasonable assurance of safety and effectiveness. The specific data required by the FDA to determine safety and effectiveness depend on the type of device, its intended use, and the perceived risk to the patient’s well-being². A device designed to treat a life-threatening condition for which no alternative therapy exists should have a higher acceptable risk than a device designed to treat a benign condition.

Premarket evaluation is designed to confirm the safety, quality, reliability, and predicted clinical performance of the medical device. Data to support safety and effectiveness may include device design verification and validation studies, reliability and engineering analyses, bench and manufacturing tests, statistical risk analyses, animal studies, and human clinical studies. The FDA is required by Congress to use the “least burdensome” approach, meaning that manufacturers are required to provide only data that are necessary to demonstrate safety and effectiveness. In fact, most FDA device marketing reviews do not include human clinical data.

Three medical device regulatory classes (I, II, and III) were defined by the Medical Device Amendments of 1976 depending on the perceived risk of the device². In general, class I and II device types subject to premarket review are required to obtain FDA clearance through the 510(k) process, and class III device types are required to obtain FDA approval through the more stringent PMA process^{2,4}.

⁴Government Accountability Office. Medical Devices: FDA Should Take Steps to Ensure That High-Risk Device Types Are Approved through the Most Stringent Premarket Review Process. January 2009. Accessed June 16, 2009 at: <http://www.gao.gov/new.items/d09190.pdf>.

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510(k) Process

The 510(k) process requires a device manufacturer to notify FDA before it intends to market a device and to establish that the device is “substantially equivalent” to a legally marketed “predicate” device that does not require a PMA². The FDA’s premarket review of 510(k) submissions is less stringent than that for PMA submissions. For most 510(k) submissions, clinical data are not required and substantial equivalence is determined based on comparative device descriptions and other non-clinical data⁴. The less stringent premarket review also extends to other aspects of FDA’s 510(k) review⁴.

Notably, although Congress intended that higher risk class III devices would be approved through the more stringent PMA process, the Government Accountability Office (GAO) reported in January 2009 that certain types of class III devices continue to be cleared for the U.S. market through the 510(k) process – despite the fact that The Safe Medical Devices Act of 1990 (SMDA) required FDA to reexamine these devices and reclassify them either to class I or II or to have them remain in class III and obtain FDA approval through the PMA process⁴. Nearly two-thirds of the 228 class III 510(k) device submissions that FDA cleared in fiscal years 2003 through 2007 were implantable, life sustaining, or significant risk devices⁴.

One of the class III device types that is still cleared via the 510(k) process is the automated external defibrillator (AED). AEDs are small computers that provide automated heart rhythm analysis, voice commands, and shock delivery to rescue victims of cardiac arrest. The increasingly widespread distribution of AEDs in public places has been an important public health development that has resulted in improved survival of cardiac arrest victims – a leading cause of mortality in the United States accounting for nearly 330,000 deaths annually⁵. Earlier this month, on June 2, 2009, the House passed HR 1380 – the Josh Miller HEARTS Act - sponsored by Representative Betty Sutton (D-OH). The Act is intended to establish a grant program for automated external defibrillators in elementary and secondary schools⁶. Congress certainly recognizes the importance of these devices.

While easy to use, AEDs are technically complex devices. Their life-saving function has prompted their FDA class III designation. However, the 510(k) clearance process for these devices has failed to protect American consumers. According to FDA data from 1996 to 2005, fatal AED-related device malfunctions occurred in 370 patients⁵. In addition, there were 52 FDA recalls and safety alerts affecting nearly 386,000 AEDs and AED accessories. In total, more than 20% - or 1 in 5 - of the nearly 1 million AEDs in circulation have been recalled by the FDA – most often due to electrical or software problems⁵.

⁵ Shah JS, Maisel WH. Recalls and Safety Alerts Affecting Automated External Defibrillators. JAMA 2006;296:655-660.

⁶ Text of H.R. 1380: Josh Miller HEARTS Act. Accessed June 16, 2009 at: <http://www.govtrack.us/congress/billtext.xpd?bill=h111-1380>.

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The shortcomings of the 510(k) process, however, run deeper than simple reclassification of class III 510(k) devices. A recent case involving the Edwards Lifesciences Myxo ETlogix annuloplasty ring highlights a concerning reliance by FDA on the medical device industry to police themselves - this despite an inherent conflict of interest sometimes measured in billions of dollars. Annuloplasty rings are implanted via open heart surgery and are used to treat leaky heart valves. The Edwards device was on the U.S. market for two and a half years and implanted into numerous unsuspecting patients despite never being formally cleared by the FDA⁷.

The FDA does permit manufacturers to make a modification to a device without filing a new 510(k) if the manufacturer concludes that the change does not significantly affect the safety or effectiveness of the device or constitute a major change in the intended use of the device^{8,9}. Edwards claimed the device was legally marketed because it incorporated only minor changes to a previously 510(k) cleared device, the Geoform Ring 4200⁷. However, the FDA determined that the company made "the wrong decision" when it marketed its product without FDA clearance⁷. The company recalled the device last fall and formally filed a 510(k) application that resulted in FDA clearance for marketing on April 10, 2009 for the dETlogix annuloplasty ring 5100 (a change in name only from the Myxo ETlogix)⁷. According to the FDA, Edwards will not face any sanctions for having inappropriately marketed the valve⁷.

Remarkably, although manufacturers are required to maintain documentation of their self-conducted regulatory analyses, they are not required to submit documentation to FDA or even to notify the Agency that device modifications have been made⁸. It is apparent that manufacturers have performed numerous other device modifications without the FDA's knowledge and without the Agency's ability to track these changes or their impact on device safety.

Premarket Approval (PMA) Process

The PMA process is the most stringent type of FDA premarket review. Although only 1% of devices listed with the FDA are evaluated via the PMA process, these high-risk devices are implanted into tens of millions of patients and include products such as coronary stents and implantable defibrillators⁴. For fiscal years 2003-2007, FDA reviewed 217 original PMA submissions and 784 supplemental PMA submissions for class III devices (in contrast to the more than 13,000 510(k) submissions during the same time period)⁴.

⁷ Wood S. FDA clears Myxo ETlogix valve ring under new name but disagrees with earlier decision by Edwards that device did not need 510(k). April 14, 2009. Accessed June 16, 2009 at: <http://www.theheart.org/article/960385.do>.

⁸ Grassley calls on FDA to explain letting device maker off hook. Accessed June 16, 2009 at: http://grassley.senate.gov/news/Article.cfm?customel_dataPageID_1502=20502.

⁹ U.S. Food and Drug Administration. Deciding When to Submit a 510(k) for a Change to an Existing Device (K97-1), January 10, 1997. Accessed June 16, 2009 at: <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080235.htm>.

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While original PMA submissions typically require clinical data to support device approval, there is no absolute requirement for it to support PMA supplement applications. Indeed, many device modifications for high risk, life sustaining devices occur via the PMA supplement route without supporting clinical data¹⁰. Many medical devices undergo frequent design and manufacturing iterations. Proposed alterations may be brought about by the desire to improve device performance, reliability, ease of manufacturing, or by more practical issues such as contracting with a new supplier of a device component. Even some substantial device alterations may be approved in the absence of clinical data. For example, design changes to a ventricular assist device intended to provide temporary mechanical circulatory support for patients awaiting a cardiac transplant were approved on the basis of only mechanical tests¹⁰. Similarly, FDA approved graft material modifications for a vascular stent system designed to treat peripheral arterial disease in the abdominal aorta on the basis of bench and animal testing without human clinical data¹⁰.

Although there is nothing inherently wrong with bench and animal testing and while many bench tests are designed to satisfy and exceed international standards, bench testing alone cannot account for all patient attributes, physician techniques, or clinical scenarios and may not identify effects that only occur in humans. Bench and animal testing may occasionally identify underperforming devices or device designs that subsequently undergo modifications, although few studies have validated that the results of these tests accurately predict long-term device clinical performance. Premarket clinical device studies can be useful for assessing acute or subacute device performance – although they tend to be underutilized by the FDA. Longer-term premarket clinical device studies are seldom used by FDA to assess long-term premarket device performance as this may substantially slow innovative products from reaching patients in a timely fashion. Notably, premarket clinical testing is typically not useful for identifying rare device failures or unusual device-related adverse events; however, it can identify important safety concerns before unnecessarily exposing large numbers of patients to an underperforming product.

There are a number of reasons why a manufacturer and the FDA would favor evaluation of a device via the 510(k) route rather than the PMA route – most notably the lower cost and lower resource utilization. For fiscal year 2005, for example, the estimated average cost for FDA to review a 510(k) submission was about \$18,200, compared to \$870,000 for a PMA submission⁴. Applicants also pay a substantially lower fee for a 510(k) submission (\$3,693 in fiscal year 2009) compared to an original PMA submission (\$200,725), or PMA supplement (\$30,109-\$150,544)⁴.

It is evident that to best protect the health of American medical device users, the FDA must promote and enforce a higher scientific standard for device clearance and approval – particularly for higher risk devices whose abnormal performance is likely to have adverse effects on patient health. This may best be accomplished by not only clarifying

¹⁰ U.S. Food and Drug Administration. Guidance for Industry and FDA Staff: Modifications to Devices Subject to Premarket Approval (PMA) – The PMA Supplement Decision-Making Process. December 15, 2008.

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the status of 510(k) class III devices, but also by closing the loophole that permits many modified devices to be approved via the less stringent PMA supplement route. Additional efforts directed at promoting more robust, scientifically sound, clinically predictive bench testing will minimize product clearance and approval delays and improve overall device safety.

POSTMARKET SURVEILLANCE

During the premarket evaluation, several factors may limit the ability of the FDA to identify and predict which products will perform safely after clearance or approval. There may be questions that cannot be answered in the premarket stage, or an issue may arise after the device is marketed. FDA may require manufacturers to perform post-approval studies as a “condition” of approval to provide on-going evaluation of the device’s safety, effectiveness, and reliability after initial marketing approval. These post-approval studies are most often used to: 1) monitor device performance and safety during the transition from clinical trial to real-world use, 2) assess the long term safety, effectiveness, and reliability of the device, and 3) look for infrequent but important adverse events. These studies may also be initiated to evaluate an emerging public health concern in response to reported adverse events.

In all, the FDA annually receives reports of more than 200,000 device-related injuries and malfunctions, and more than 2000 device-related deaths¹¹ and it is challenging for the Agency to identify patterns of device malfunction among the deluge of adverse event reports. FDA initiatives to better integrate the premarket and postmarket workforces, to develop novel methods of surveillance such as the Medical Product Surveillance Network (MedSun), and to improve tracking of required manufacturer postmarket studies will help.

Although the FDA can theoretically order a product recall in response to observed adverse events or device malfunctions, the vast majority of recalls are voluntarily initiated by the manufacturer. Because of the manufacturers’ inherent financial conflict of interest, the timing and extent of the product recalls are often controversial. FDA often takes weeks or months to officially classify these regulatory actions. During fiscal year 2006, 651 recall actions were initiated involving 1,550 products – again reminding us that FDA product clearance or approval does not ensure device reliability and performance⁵.

Medtronic Sprint Fidelis Implantable Defibrillator Lead Recall

Unfortunately, it is not uncommon for unanswered questions regarding device safety and effectiveness to remain at the time of FDA approval. This creates the potential for a large number of patients to be rapidly exposed to a newly approved product in the absence of long-term follow-up data. For example, close to 268,000 patients had been implanted with the Medtronic Sprint Fidelis implantable defibrillator lead before it was recalled in

¹¹ Center for Devices and Radiologic Health. CDRH FY 2006 highlights. Accessed June 16, 2009 at: <http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDRH/CDRHReports/ucm129258.pdf>.

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October 2007 after it was determined that the wire was prone to fracture¹². A fracture of the lead, which connects the implantable defibrillator to the heart, may result in serious health consequences, including painful electrical shocks or death.

Mr. Sidney Engler, a patient of mine, was one of the unfortunate 268,000 people to receive this lead when he had an implantable defibrillator placed in February 2006. Mr. Engler is a decorated WWII veteran, having served in Europe from 1943 to 1945. On the evening of August 14, 2008 while preparing to retire for the evening, the simple act of removing his shirt over his head caused his defective defibrillator lead to fracture. Mr. Engler suffered a cardiac arrest in front of his wife. He required CPR and received numerous unnecessary painful shocks from his defibrillator. Fortunately, due to the prompt response of his local EMTs, Sidney survived. Despite a prolonged hospital stay and months of rehabilitation, he has still not fully recovered.

The FDA approved the Medtronic Sprint Fidelis implantable defibrillator lead as a PMA supplement in 2004 on the basis of no human clinical data¹². The original Medtronic defibrillator lead PMA was submitted in 1992; more than 30 supplements had been submitted in the interim and the Fidelis lead bears little resemblance to its original counterpart. In addition to a lack of human clinical performance data, the FDA failed to require a postmarket study to monitor the device's performance. The result was the widespread distribution of a defective product to hundreds of thousands of patients.

Although the FDA does utilize its authority to implement postmarket monitoring strategies, effective postmarket surveillance is undermined by: 1) the lack of uniform criteria for determining which devices require postmarket studies; 2) the repeated inability to get manufacturers to implement these studies in a timely fashion; and 3) the lack of criteria for determining what safety actions FDA should take and when they should take them in response to observed adverse events and product malfunctions.

CONCLUSIONS

Medical devices have enriched and extended the lives of countless people. With the aging of the U.S. population and exponential growth of the medical device industry, device-related malfunctions, adverse events, and patient injuries can be expected to grow. In the wake of high-profile device safety issues and concerns about the FDA's ability to properly evaluate and monitor the safety and effectiveness of medical devices, it is apparent that additional consumer safeguards are needed. Only by demanding more thorough, scientific device evaluations can the FDA hope to reestablish consumer confidence in its ability to protect the public's health.

¹² Maisel WH. Semper Fidelis – Consumer Protection for Patients with Implanted Medical Devices. *N Engl J Med* 2008; 358: 985-987.

Mr. PALLONE. Thank you, Dr. Maisel. Mr. Phillips.

STATEMENT OF PHILLIP J. PHILLIPS

Mr. PHILLIPS. Mr. Chairman, Mr. Ranking Member, subcommittee members, thank you for the opportunity to share my testimony with the subcommittee today. For the record, I am here as an independent consultant. I am not representing any companies, trade associations, or any special interests, and I receive no compensation from any source connected with any related to my appearance today.

As I understand it, I am here simply to express my views of FDA regulation of devices based upon my 28 years of experience dealing with the regulation of medical devices. 24 years of that was with the Food and Drug Administration, and since then, I have had four years with the private sector.

Keep in mind it was just a mere 33 years ago that devices were not subject to the regulations that they are subject to today. There was no FDA premarket authorization 33 years ago. No premarket authorization, registration listing, GMP inspections, and there was very little postmarket surveillance or postmarket vigilance.

The 94th Congress did actually a remarkable job in designing the Medical Device Amendments of 1976. They created a three-tiered classification system for medical devices where the level of FDA regulation is commensurate with the risks associated with the devices. The system appears complex, but from my vantage point, it is actually very simple.

Under the 1976 authorities, the simplest of devices were placed into class one subject to general controls. General controls include prohibitions against adulteration, misbranding, good manufacturing practices, labeling, registration listing, and a few others.

Devices that were of greater complexity were put into class two subject to, at that time, it was required to meet performance standards. The distinction between class two and class three devices was that the agency has confidence that they knew sufficiently enough about the technologies and the use to conclude that performance standards could be developed to assure safety and effectiveness.

The most complicated devices or complex devices, the higher-risk devices, where they did not have the confidence that general controls and special controls would assure safety and effectiveness were to be placed into premarket approval where a device-by-device demonstration of safety and effectiveness would be required.

Lastly, under the medical device authorities, Congress provided the agency the ability to adjust classification over time based upon the experience and knowledge gained from the use of medical devices. And that was through reclassification processes.

Initially there were 16 expert advisory panels that looked at over 1,600 generic types of devices. A generic type of device could include dozens of manufacturers and literally hundreds of individual models, not to mention components and accessories. The recommendations of these committees fueled the rule-making process and FDA-generated classification regulations for each and every one of these generic types of devices. Today I believe that there are over 1,800 generic types of classification regulations in the Code of Federal Regulations.

The original framework exists; although, it has expanded to accommodate the diverse nature of medical technologies and also the rapidly advancing technology.

What is a 510(k)? We have all talked about 510(k). It is a means for FDA to classify devices. It is not an approval. In fact, there is a prohibition for industry to refer to a clearance through a 510(k) as an approval of a device. The device is found substantially equivalent to go to market subject to the requirements that are associated with the generic class in which they are assigned.

In 1981, I was a review scientist with FDA. I can remember my first 510(k)s. I looked at them. They were very simple submissions. We did side-by-side comparisons of descriptive data, one device versus an old device. It was actually very simple in the earlier days, but as technology evolved, we realized we had to have a greater framework and structure in which to render substantial equivalence determinations.

Today's 510(k)s are replete with performance data on the new devices. Simply examine any 510(k) or look at FDA guidance document, and you will see what FDA's scientific expectations are for new devices. Reviewers get largely what they demand, and again, simply look at the number of additional information requests and look at the responses. You will find industry provides the reviewers exactly what they need in order to be able to support their clearances.

The PMA process is very rigorous and demanding. It is not only high standards to get to market, but it is almost like a mortgage on a home. Once you are successful and you get your PMA application, it is actually a significant burden to stay on the market because of the filing of voluminous reports and supplements to the Food and Drug Administration.

It is sort of an interesting dichotomy that I will bring to your attention because innovations come from generally small entrepreneurial companies, and those are the least able to comply with the rigorous PMA requirements. With rare exception, only the large companies are able to play in the PMA arena. My bottom line is I think that there is a place for the PMA process, and it should be used whenever it is warranted.

As far as my recommendations, I will leave you with just simply four. We have new administration at the Food and Drug Administration, and I think that we should empower Dr. Hamburg and Dr. Sharpstein to look at the medical device program, identify any gaps that exist and formulate a strategy for dealing with those gaps.

The class three devices, I agree completely with the General Accounting Office. They need to be dealt with either through reclassification or premarket approval, one or the other.

There is another interesting issue that I will bring to your attention, which I think is also a gap. It is a deficit in the way that devices are regulated. For class two devices, they were supposed to be performance standards. The agency has never promulgated performance standards, actually one dealing with the safety of leads associated with electrical products that come in contact with patients. But by and large, there are no performance standards, and there are a relatively small number of special controls. Special con-

trols replaced performance standards with the Safe Medical Devices Act of 1990.

I believe that the agency should develop special controls for everything that is in class three, just like there should be premarket approval for everything that is—excuse me. There should be special controls for everything in class two just like there should be premarket approval for every class three medical device.

The last thing I will say is that the reclassification process needs to be vitalized, not revitalized because it has never been a really functional system. The agency and consumers need to have the ability to adjust the classification of devices based upon new information. With that, that is the end of my remarks, and I look forward to questions.

[The prepared statement of Mr. Phillips follows:]

Testimony of Philip J. Phillips before the Subcommittee on Health

Hearing - Medical Devices: Are Current Regulations Doing Enough for Patients?

Thursday, June 18, 2009

Rayburn House Office Building, Washington, D.C.

Mr. Chairman, Mr. Ranking Member, thank you for the opportunity to share my testimony with the Committee. It has been a little over 34 years since the 94th Congress drafted the Medical Device Amendments of 1976 to the Federal Food, Drug, and Cosmetic Act thereby creating the framework for device regulation that still exists today. Before this time, the medical device industry was largely unregulated. Therefore, Congress had little experience in dealing with the industry and, understandably, an uncertainty about the breadth and complexity of their undertaking. Despite this handicap, Congress drafted an enormously successful statutory framework that protects the American public from unsafe and ineffective medical devices.

The 1976 amendments created a “classification system” for devices that applies a level of FDA regulation commensurate with the risks associated with devices. While the law has been amended a half dozen times since 1976, the original framework exists and continues to accommodate not only the diverse nature of medical devices, but also rapidly evolving device technology.

Under the US regulatory system, general controls; controls including good manufacturing practices, labeling, and registration and listing, assure the safety and effectiveness of class I devices that pose the least amount of risk. Class I includes devices such as bandages, manual surgical instruments, and eyeglasses. For more complex and riskier class II devices, “special controls”, in addition to the general controls, may apply. For class II devices such as powered wheel chairs, infusion pumps and many orthopedic implants, special controls provide FDA tremendous flexibility and include, but are not limited to, performance standards, agency guidelines and clinical testing. For class III devices; the most complex and riskiest devices including implantable defibrillators, artificial organs, and sophisticated lasers for vision correction, general controls, any applicable special controls, and “premarket approval” all apply. Perhaps most important, but too often neglected, our system of device regulation allows for adjustments in classification over time based on increasing knowledge and experience. Thus, through “reclassification” FDA can titrate the level of regulation that is needed to meet evolving public health priorities.

In accordance with the statutory framework, FDA designed and implemented a premarket review program responsible for the regulation of all medical devices. Serving as the foundation of this program was the premise that the lowest level of regulatory control sufficient to provide a reasonable assurance of safety and effectiveness should be applied.

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This was the mandate of the 16 expert advisory panels that made recommendations to FDA on the proper classification of all devices in existence at the time. It also led to the premarket notification (510(k)) process becoming the predominant path for new devices to enter the domestic market.

What is 510(k); other than perhaps the most misunderstood premarket review program in FDA? It is the means by which FDA classifies new devices. When FDA reaches a determination that a new device is “substantially equivalent” to a legally marketed device, the new device can go to market only after satisfying the requirements associated with its assigned class.

When I entered FDA in 1981 as a review scientist, “substantial equivalence” had not yet been defined. For most 510(k) submissions this was not a problem, but as devices changed and their use and technology evolved, it became apparent that guidance was needed if consistency and the goals of the program were to continue to be achieved. From an internal agency task force convened to look at the 510(k) program, came the needed guidance, elements of which just 4 years later became codified in law through the Safe Medical Devices Act of 1990. The definition of substantial equivalence and the basic process by which it is determined still exists today, but continuous improvements have occurred along the way to strengthen the program to ensure that it focuses on the important issues of device intended use and technology to maximize the program’s contribution to public health.

At one time, most 510(k)s involved side-by-side comparisons between a new device and an old one. Since the earliest days of the program, there has been a shift away from clearances based on simple comparisons to requirements for performance data on new devices. Today’s 510(k)s are replete with performance data on new devices. Testing routinely involves biocompatibility, sterilization, electrical safety, software validation and engineering analyses, but also includes clinical data when warranted. To get a sense of FDA’s expectations one need only review one of the many device specific guidance documents that exist. To see how intent FDA is on ensuring that all of the necessary data is available for decision-making, examine the number of 510(k)s that are placed on hold to get the data that review scientists demand.

To see how a more progressive risk-based approach to 510(k) clearance works, I urge you to examine any of the class II special controls guidance documents. With the risk-based approach, the agency identifies the risks associated with devices and the measures capable of mitigating the risks. Rather than simply showing similarities to other devices, special controls place a greater emphasis on documenting device safety.

Turning to class III devices, the premarket approval (PMA) process remains the most rigorous and demanding path to market and is rightfully reserved for the riskiest and least understood devices. Large clinical trials, exhaustive preclinical testing, preapproval inspections and voluminous submissions over the entire life of the device translate into a process that should be applied only to those devices demanding this degree of regulation.

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Quite simply, most of the creativity in the device industry originates from small entrepreneurial companies that are the least prepared to satisfy these demanding requirements. Please do not misunderstand me; PMAs are often warranted and should be required. My point is that “new” or “different” should not automatically translate into class III status and any misunderstanding over the capability of the 510(k) program should not result in a shift toward requiring more PMAs.

Independent of the actual paths to market, we must preserve the ability to change regulatory requirements based on the knowledge and experience that is gained with any technology over its lifetime. The existing regulatory system is designed to permit these changes in classification, but the “reclassification” program has been less than successful. Risk-based classification, or *de novo* classification, has enjoyed some success in preventing new or different devices from automatically being placed in class III, but by and large, FDA has not established a viable means to change the classification of a device based on new information. Perhaps changing the thought “once a PMA, always a PMA” would reduce the fear associated with being determined to be class III.

In summary, the flexibility of FDA’s approach to device regulation has served the US healthcare community and consumers well through the years. It has permitted numerous devices to enter the marketplace in an efficient manner, thus keeping down the costs to consumers and the healthcare community. In this way, it has facilitated technological innovation, while permitting FDA to responsibly regulate the rapidly progressing medical device industry.

Perceptions that the 510k program is inadequate to ensure the safety and effectiveness of today’s medical technology foster the opinion that more devices currently found substantially equivalent should be subject to PMA requirements. Before drawing such a conclusion, I urge the Committee to examine the facts, as such an action will have a significant impact on FDA resources, as well as the future investment in new medical technology. Any changes that would result in more devices being subject to PMA requirements should be supported by both a sound public health and scientific rationale.

Finally, the 510(k) program should not be judged on dissatisfaction expressed over a relatively small number of agency decisions. There have been over ¼ million devices cleared through section 510(k) since 1976 while the examples cited by the critics in support of changing the program are extremely few.

Before introducing new legislation, I recommend that FDA be given the time required to deal with the preamendment class III devices that were the subject of the recent GAO report. Furthermore, I believe that it is important that the agency development special controls in a priority manner for all class II devices. These efforts will require Congressional support and additional FDA resources, but in the end the effort expended will result in great public health impact. Whatever the future holds, I urge you to do your part to ensure that FDA has the necessary resources to meet expectations.

Mr. PALLONE. Thank you, Mr. Phillips. I want to hear from Dr. Lurie, and we will right now. But I did want to mention unfortunately that that bell was for 26 amendments that we will be—28 amendments that we will be voting on. So we are going to hear from Dr. Lurie. Then we are going to go to the floor. It says right now that the first is 15 minutes, and each of them are five. I am hoping that when we get there, they will reduce it to two. But we are talking probably at least an hour and a half.

So we are going to hear from Dr. Lurie and then we will go vote. Hopefully be back by around noon, maybe earlier. I doubt it. And then we will take questions. Dr. Lurie.

STATEMENT OF PETER LURIE

Dr. LURIE. Chairman Pallone, members of the committee, thank you for the opportunity to address you. Our comments this morning are primarily about the premarket review of medical devices and not about postmarket issues at all.

I can summarize my comments as follows. The bad news is that device review, particularly with respect to effectiveness at the FDA is severely damaged. But the good news is that actions that the FDA could take today without any additional regulatory or statutory authority, in addition to the powers that could be granted by this committee and by the Congress, could make an enormous difference in improving the quality of medical device review.

We are going to look at three separate problems in medical device review and give examples from recent regulatory proceedings to illustrate each of those. Problem one, the standard for approval of medical devices is lower than the standard of approval for drugs. By statute, the approval standards for devices is—for drugs, I am sorry—is “substantial evidence of effectiveness.” Whereas the sponsor of a new device need only demonstrate “a reasonable assurance of safety and effectiveness.”

What this means is that whereas you might get two clinical trials for a drug to be approved, a single study, if you even get that, is the norm for devices. In fact, FDA regulations even permit the absence of well-controlled investigations under PMA.

In practice for consumers what this means is that data that would never be considered sufficient to support the approval of a drug can result in the approval of a device and thus to treat the very same condition as my example will show, thus potentially diverting patients from effective and well-proven devices to less effective and less—excuse me—from diverting patients from effective and well-proven drugs to less effective and less well-proven devices.

Consider the Cyberonic’s vagus nerve stimulator. It is a surgically implanted device for depression. A randomized control trial was done, and it failed to demonstrate any significant impact upon depression. However, the company was allowed to rely upon the kind of data that the drug division at the FDA would not even look at. They were allowed to look at follow-up data at a year using a control group that was not randomized. It was not blinded, using patients that were recruited at different times, and in which the patients were allowed to modify the antidepressant drugs and even get electroshock therapy.

An expert at the FDA's drug center told the device center that with similar data for an antidepressant drug, that the drug center would not even have allowed the filing of an NDA. Yet instead what happened was the center for devices, the director consulted with more than 20 FDA scientists and officials, not one of whom recommended approval of the device. And he overruled all of them, and the product got approved.

Fortunately, CMS has taken the position that the product is in fact not effective and is not reimbursing. So it has not been widely used.

Now, the second two problems that I want to talk about deal with the 510(k). We have already heard a lot about them. We have heard already how, according to the GAO, the 510(k) process is generally less stringent, less expensive, and faster. We have heard how only a small minority of 510(k) submissions contain any clinical data.

In fact the FDA says "it does not attempt to address all of the issues that would be answered in a PMA in its review of 510(k)s." Now, the 510(k) pathway itself is not the problem. The problem is that there are two ways to get into the 510(k) process, and in practice, in part because of legislation and in part because of FDA practice, these are not interpreted in a rigorous way. And so products that ought to be going through PMA instead go through 510(k).

So that leads to problem two, permissive interpretation of same intended use. That is one of the two elements that can get you into 510(k). The best example here is ReGen's Menaflex Collagen Scaffold, which is a device implanted during arthroscopic surgery to replace damaged knee cartilage.

Now, after consulting with the FDA, ReGen began a trial to support a PMA, which was a well-done, two-year, randomized trial comparing partial meniscus removal to partial meniscus removal with the product, the MCS. Only problem was this study was stone cold negative. Absolutely no evidence of benefit whatsoever.

Now, after the trial was complete, the FDA allowed the company to shift courses and submit a 510(k). Why were they able to do this? Because current agency practices provide for permissive interpretations of same intended use. They say "our scientific expertise enables us to exercise considerable discretion in construing intended uses."

Now, the first two 510(k)s were rejected, and in a third one, ReGen said that the predicate device, the device to which it needs to be shown to be substantially similar, were surgical meshes, surgical meshes that do not plainly seem to be for the same intended use at all. Rotator cuff mesh in the shoulder, anal fistula plug, and hernia repair graft. These don't sound like devices that belong in the knee.

In fact, an FDA reviewer pointed out that none of these meshes that the company had cited was implanted in a weight-bearing joint or intended to facilitate the regrowth of articular cartilage. So the result was these plainly dissimilar devices counted as "same intended use."

Of course, the company downplayed the results from the randomized control trial. It said that the bench testing data, like whether or not you could pull the cartilage replacement apart, or whether

it could hold sutures well, should provide the primary basis even though it had already done a well-done randomized control trial that showed that the product had no public health benefit whatsoever.

And it made this point before an advisory committee saying that the decision for the advisory committee should be based upon the function of this device as a surgical mesh and not the ultimate clinical outcome. Let me tell you, as a doctor, this is really very painful even to think about. The clinical outcomes are ones that matter to us, and we hear Dr. Hamburg in particular talking about putting the agency on a public health footing, this is what, I think, she must be talking about.

Subsequently a number of irregularities in the advisory committee review of this product came to light. It turned out that ReGen was permitted early input into the questions posed to the advisory committee, into who made the FDA presentation at the meeting, people who were not the original reviewers of the product, and even standing advisory committee members who were available to attend the meeting were replaced by clinicians thought more likely to favor the device. And all of the positive votes for this device came from the replacement advisory committee members. So there really were very large irregularities here. FDA is looking into this, and we hope that some of this will be explored further.

The third problem which might get you into 501(k) if not properly enforced is different technological characteristics. The 1990 amendments to the Food, Drug, and Cosmetic Act provide for products with different technological characteristics to be predicates as long as no new issues of safety or effectiveness are raised.

The problem is that this has led to predicates which are plainly different from the device up for approval, and thus products go through 501(k) when they should instead be going through PMA. The example here is transcranial magnetic stimulation, or TMS, also a device intended to treat depression. The agency permitted TMS to be reviewed under 501(k) with electroshock therapy as the predicate device, even though electroshock is toxic involves the administration of the electrical currents to produce a generalized seizure, whereas TMS simply applies a magnetic field to a specific region of the brain.

They did a randomized control trial. The results showed that the effectiveness of this product was statistically nonsignificant and clinically minor. I am not going to get into the details here, but this product was eventually approved through a process called the de novo process, which is not the subject of my testimony today. But suffice it to say they couldn't have got to de novo had they not got to 510(k). And they could not have got to 510(k) without invoking the different technological characteristics provision. So one thing leads to another, and now we have this device that barely works that is on the market.

Let me conclude with two contextual matters and then the final conclusion. The two contextual matters are that the matter of the least burdensome means of showing effectiveness for devices that I believe Dr. Crosse referred to.

Mr. PALLONE. Mr. Lurie, I just want the members to know there is only about three minutes left. I want to hear the rest of it, but just so you know there is only three minutes left.

Dr. LURIE. I will certainly finish well within that time.

Mr. PALLONE. OK.

Dr. LURIE. This gives the industry recourse to challenge many requests that it regards as onerous. Indeed, ReGen evoked this very language when the FDA was considering the unfavorable findings of its randomized trial. So that is the first contextual issue.

The second is that in general the FDA has permitted scientific approaches that fall well short of rigorous, and we have listed a number of things just from the examples cited in this testimony are really unacceptable from a scientific point of view.

Depending on the specific case, these lax scientific standards can be the result of any combination of the lower standard for device approval, the inappropriate routing of devices through 510(k) instead of PMA, the least burdensome requirement, or simply the lack of rigor at the agency level.

Now, each of the issues that have been identified in this testimony can be remedied by a combination of agency practice, regulation, and legislation. And to the former, even today under existing authority, the agency can require greater scientific rigor. It can send more devices through the PMA, and it can tighten the same intended use requirements.

But legislation could also make a difference. It could address all three of the problems that I focused on today: the lower approval standards for devices than for drugs, the permissive interpretation of same intended use, and the different technological characteristics loophole. We call on the Congress to pass exactly those three kinds of legislation. Thank you.

[The prepared statement of Dr. Lurie follows:]

**Medical Devices: Are Current Regulations Doing Enough for Patients?
Testimony of Peter Lurie, MD, MPH and Jonas Hines
Health Research Group at Public Citizen
before the Subcommittee on Health
Committee on Energy and Commerce
United States House of Representatives
June 18, 2009**

Chairman Pallone and members of the committee, thank you for the opportunity to present our concerns about current problems with the regulation of medical devices by the Food and Drug Administration (FDA). Several serious weaknesses in the existing premarket review process impede the FDA's ability to ensure the effectiveness of devices and adequately protect American patients.

In our testimony today, we will focus on three problems in the review process, each illustrated by a paradigmatic case from recent regulatory proceedings. Other aspects of medical device regulation, such as postmarketing surveillance and compliance are beyond the scope of this testimony. Our testimony will also not address certain other premarket review issues including high-risk devices that the agency has not fully reviewed, despite a congressional mandate.¹ Furthermore, we will not discuss a group of over 200 overlooked devices that continue to reach the market through less-stringent review procedures.² We would be happy to provide the committee with more details on these subjects upon request.

Problem 1: Lower Approval Standard for Medical Devices than for Drugs

By statute, the approval standard for devices is lower than for drugs, regardless of how the device is reviewed. Before a new drug can be marketed, the sponsor must show "substantial evidence [of effectiveness],"³ whereas the sponsor of a new device need only demonstrate a "reasonable assurance of ... safety and effectiveness."⁴ In practice, new drug applications (NDAs) typically contain two or more well-controlled clinical studies,⁵ whereas, even under the most stringent review process for devices, a single study is the norm.⁶ Furthermore, the FDA accepts lower-quality studies for devices compared to drugs; while for drugs, agency regulations state that "uncontrolled studies or partially controlled studies are not acceptable as the sole basis for the approval of claims of effectiveness,"⁷ for devices, even those reviewed under the most stringent review procedures, the regulations permit "reliance upon other valid scientific evidence ... even in the absence of well-controlled investigations."⁸ Thus, data that would never be sufficient to support the approval of a drug can result in the approval of a device used to treat the same condition, potentially diverting patients from effective drugs to less-effective devices.

This concern is not merely theoretical. Consider Cyberonics's vagus nerve stimulator (VNS), a surgically implanted device for treatment-resistant depression. In the only randomized, controlled trial, the device did not

demonstrate a statistically significant benefit on the primary depression measurement at ten weeks ($p=0.25$).⁹ However, the company relied on less-rigorous follow-up data at one year in which a group of VNS-treated patients improved more than a control group ($p<0.001$). Moreover, the control group was not randomized (patients were not assigned to their treatments at random); the study was unblinded (patients and doctors knew which patients were receiving VNS); patients in the treated and control groups were recruited at different times; and both groups were permitted to modify their antidepressant medications and to receive electroconvulsive therapy (ECT).¹⁰ An expert in the FDA's drug center advised the Center for Devices and Radiological Health (CDRH) that, with similar data for an antidepressant drug, the center would not have permitted even the filing of an NDA.¹¹ While CDRH initially issued a non-approvable letter, the director of CDRH reversed this decision and approved the device, overruling more than 20 FDA scientists and officials.¹¹ The Centers for Medicare and Medicaid Services subsequently declined reimbursement for the device under Medicare, saying that it did "not believe there is a treatment benefit directly attributable to VNS."¹²

In order to remedy this approval-standard inconsistency, Congress should raise the standard for device approval to that required for drugs: sponsors of devices that claim to treat diseases should produce "substantial evidence," rather than merely "reasonable assurance," of effectiveness. Such devices would have to

meet the same requirements as drugs, including more than one well-controlled trial.

Reliance upon Less-rigorous Review Mechanisms

As the committee is well aware, there are two general premarket review procedures for devices: the "premarket approval" (PMA) application and the "premarket notification" submission, often referred to as a "510(k)" submission. A PMA application, which is reserved for high-risk and novel devices, is analogous to a NDA. Sponsors must submit valid scientific evidence that directly establishes safety and efficacy, although, as we have seen in the VNS case, this need not be a randomized, controlled trial. In contrast, in a 510(k) submission, a sponsor need demonstrate only that the new device is "substantially equivalent" to an existing ("predicate") 510(k) device.¹³

Compared to the PMA process, 510(k) review is "generally less stringent ... less expensive ... [and] faster."¹⁴ The average time until a decision on 510(k) submissions in fiscal year 2006 was 54 days, compared to 283 days for PMA applications.¹⁴ Only 10-15% of 510(k) submissions contain any clinical data.¹⁵ Instead, 510(k) submissions primarily contain performance characteristics comparing the new device to the predicate. In considering a PMA application, the FDA may consult with an advisory committee comprised of non-government

experts; this option is rarely pursued for 510(k) submissions. As the FDA acknowledges, it “does not attempt to address all of the issues [that] would be answered in a PMA in its review of 510(k)s.”^{13,*}

In the 510(k) pathway, new devices are compared to predicate devices with respect to their “intended uses” and “technological characteristics.”¹⁶ Less-rigorous interpretation of either element, and resultant review under 510(k), can permit manufacturers to evade the more-demanding requirements of PMA applications.

Problem 2: Permissive Interpretation of “Same Intended Use”

ReGen’s Menaflex Collagen Scaffold (MCS) is a device implanted during arthroscopic surgery to replace damaged knee cartilage (meniscus). After consulting with the FDA, which determined that the MCS was a novel device requiring a PMA,¹⁷ ReGen began a trial to support such an application^{18,19} – a two-year randomized, controlled trial comparing partial meniscus removal to partial meniscus removal with MCS. On all three primary clinical endpoints, however, the trial showed no benefit for the MCS.^{20,21}

* In addition, whereas the FDA has explicit authority to recall or temporarily suspend marketing of PMA-approved devices, corresponding statutory language for 510(k)-cleared devices does not exist.

With the trial complete,²² the FDA allowed the company to shift courses and submit a 510(k). ReGen was able to make this switch because current agency practices provide for permissive interpretations of "same intended use." The FDA asserts that its "scientific expertise enables it to exercise considerable discretion in construing intended uses."¹³

The company's first two 510(k)s were rejected. In a third 510(k) submission, ReGen claimed that the MCS was a surgical mesh and that the intended use - to repair and reinforce soft tissue - was similar to other surgical meshes (e.g., rotator cuff mesh, anal fistula plug, and hernia repair graft). However, an FDA reviewer²⁰ pointed out that none of the twenty-two meshes cited by the company was implanted in a weight-bearing joint or intended to facilitate the regrowth of articular cartilage, both crucial aspects of the MCS.

The company downplayed the results of the randomized, controlled trial and argued that it was entitled to the less-rigorous review given to the MCS's predicate devices. It claimed that bench testing data (e.g., suture retention strength and tensile strength) should provide the primary basis for establishing substantial equivalence.²³ Articulating this point before an FDA advisory committee, the company asserted that the committee's decision should be based upon "the function of this device as a surgical mesh ... and not the ultimate

clinical outcome.”²⁴ The committee voted to endorse the MCS and the agency cleared it for commercial distribution in December 2008.

Subsequently, a number of irregularities in the advisory committee review of this device have come to light. Departing from usual agency practices, ReGen was permitted input into the questions posed to the advisory committee and into who made the FDA presentation at the meeting. Moreover, at the company’s request, standing advisory committee members were replaced by clinicians thought more likely to favor the device.¹⁸ Currently, the FDA is reviewing the procedural and substantive aspects of this case.²⁵

To correct this problem, the agency could immediately tighten its working definition of “same intended use,” and begin directing novel devices with weak “same intended use” claims such as the MCS to the PMA pathway. This change in practice should also be formalized in either a regulation or statute.

Problem 3: “Different Technological Characteristics”

The second element of 510(k) review relates to the technological characteristics of the new device and its predicate. The 1990 amendments to the Food, Drug, and Cosmetic Act permit a new device to have “different technological characteristics” from its predicate as long as no new issues of safety or

effectiveness are raised.²⁶ Indeed, 14% of cleared 510(k) submissions have “different technological characteristics” from their predicates.¹ This provision has led to devices acting as predicates for devices from which they are plainly dissimilar, thus permitting use of the 510(k) pathway by devices that otherwise would have been reviewed as PMAs.

For example, transcranial magnetic stimulation (TMS) is a device intended to treat depression. The agency permitted TMS to be reviewed under the 510(k) process with ECT as the predicate device, even though ECT involves the administration of electrical currents to induce a generalized seizure and TMS applies a magnetic field to a specific region of the brain. The manufacturer, Neuronetics, conducted a nine-week randomized, controlled trial comparing TMS to a placebo.[†] The difference in depression severity between patients treated with TMS and those receiving a placebo was clinically minor (1.7 points on a 60-point scale) and statistically non-significant ($p=0.057$);²⁷ only the improper, after-the-fact exclusion of six patients yielded statistical significance ($p=0.038$).²⁸ An advisory committee concluded that, “the clinical effect was perhaps marginal, borderline, questionable, and perhaps a reasonable person could ask whether there was an effect at all.”²⁹

[†] Although the company claimed that TMS was substantially equivalent to ECT, it conducted no studies directly comparing the two devices and relied instead on less-rigorous historical data for ECT, which were mostly more than two decades old and used a different scale for depression.

The FDA ultimately determined that TMS was not substantially equivalent to ECT. But this debate (and the device's subsequent clearance as described in the footnote[‡]) would have been foreclosed if Congress were to repeal the "different technological characteristics" provision and thereby steer more devices like TMS toward the PMA route.

Conclusions

Advances in medical device technologies have translated into significant improvements in the health of patients. Yet cracks in the premarket device review system threaten to undermine this progress. In our testimony, we have focused on three specific problems in the review process for medical devices. But two overarching issues provide the context in which these deficiencies occur.

First, the 1997 amendments direct the agency, in certain circumstances, to consider the "least burdensome" means of showing effectiveness for devices,^{30,31}

[‡] TMS ultimately reached the market via a relatively obscure premarket review procedure, called the *de novo* process (21 USC §360c(f)(2)), reserved for devices rejected in the 510(k) pathway. Created in the FDA Modernization Act of 1997, the sponsor of a product rejected under 510(k) may use this process to request clearance without identifying a predicate device, thus circumventing another 510(k) or even a PMA. Here, the company requested clearance for a modified indication identified by another after-the-fact analysis of the negative randomized controlled trial (Lisanby, et al. *Neuropsychopharmacology*. 2009;34(2):522-34; Hines, et al. *Neuropsychopharmacology*. 2009;34(8):2053-4.). Such a statistical maneuver is typically regarded with considerable skepticism by most statisticians. Instead, for TMS it formed the basis for clearance by the FDA.

Importantly, Neuronetics could not have used the *de novo* process without the initial 510(k) designation, which itself was only made possible by the provision permitting technologically dissimilar devices to use the 510(k) pathway.

giving the industry recourse to challenge many requests it regards as onerous. For example, ReGen invoked this language when the FDA considered the unfavorable findings of its randomized, controlled trial, asserting that the agency was "required to consider the least burdensome information necessary to demonstrate substantial equivalence."^{32,5}

Second, the FDA has permitted scientific approaches that fall well short of the rigorous. Approaches drawn from the examples in this testimony include a host of unacceptable practices as basic as failure to randomize,³³ after-the-fact looks at data,³⁴ comparing groups studied at different points in time,³⁵ failure to adjust for multiple statistical tests.²⁸ Depending on the specific case, these lax scientific standards can be the result of any combination of the lower standard for device approval, the inappropriate routing of devices through 510(k) instead of PMA, the "least burdensome" requirement, and lack of rigor at the agency level.

Thus, each of the issues identified in this testimony can be remedied by the combination of agency practice, regulation and legislation unique to that issue. Under the former, the agency can exercise its existing discretionary powers to require greater scientific rigor by sending more devices through PMA and by tightening the "same intended use" requirements. But legislation could also address all three of the problems identified in this testimony: the lower approval

⁵ However, even this assertion was incorrect. The "least burdensome" language relevant to 510(k) submissions is only applicable to the "different technological characteristics" situation (21 USC §360c(i)(1)(D)), which did not apply to ReGen.

standards for devices than for drugs, the permissive interpretations of "same intended use," and the "different technological characteristics" loophole. Most fundamentally, to reclaim its tarnished reputation for rigor, CDRH must place its decisions on a firm scientific base.

¹ Government Accountability Office. Medical devices: FDA should take steps to ensure that high-risk device types are approved through the most stringent premarket review process. Washington, DC: Government Printing Office, January 2009. Publication No. GAO-09-190. <http://www.gao.gov/new.items/d09190.pdf>. Accessed June 11, 2009.

² Center for Devices and Radiological Health. Medical device classification database [searched 'unclassified' under 'Device Class' field; searched '510(k)' under 'Submission Type' field]. Rockville, MD: Food and Drug Administration, Last June 8, 2009. <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPCD/classification.cfm>. Accessed June 9, 2009.

³ 21 USC § 355(d).

⁴ 21 USC § 360c(a).

⁵ Center for Drug Evaluation and Research. Providing clinical evidence of effectiveness for human drug and biological products. Rockville, MD: Food and Drug Administration, May 1998. <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072008.pdf>. Accessed June 9, 2009.

⁶ 60 Fed Reg 39180-1 (August 1, 1995).

⁷ 21 CFR § 314.126(e).

⁸ 21 CFR § 860.7(e)(2).

⁹ Rush AJ, Marangell LB, Sackeim HA, et al. Vagus nerve stimulation for treatment-resistant depression: a randomized, controlled acute phase trial. *Biol Psychiatry*. 2005;58(5):347-54.

¹⁰ Center for Devices and Radiological Health. FDA clinical review memorandum for Neurological Devices Panel for the Vagus Nerve Stimulator. Rockville, MD: Food and Drug Administration, June 15, 2004.

http://www.fda.gov/ohrms/dockets/ac/04/briefing/4047b1_00_FDA%20Clinical%20Review%20Memo.htm. Accessed June 11, 2009.

¹¹ United States Senate, Committee on Finance. Review of the FDA's approval process for the vagus nerve stimulation therapy system for treatment-resistant depression. Washington, DC: Government Printing Office, February 2006. Publication No. S. Prt. 109-45.

http://finance.senate.gov/press/Gpress/02_2006%20report.pdf. Accessed June 11, 2009.

¹² Coverage Analysis Group. Decision memo for vagus nerve stimulation for treatment of resistant depression (TRD). Baltimore, MD: Centers for Medicare and Medicaid Services, May 4, 2007. <http://www.cms.hhs.gov/mcd/viewdecisionmemo.asp?from2=viewdecisionmemo.asp&id=%201958>. Accessed June 9, 2009.

¹³ Center for Devices and Radiological Health. Guidance on the CDRH premarket notification review program (k86-3). Rockville, MD: Food and Drug Administration, June 30, 1986. <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm081383.htm>. Accessed June 9, 2009.

¹⁴ Center for Devices and Radiological Health. Office of device evaluation: annual report fiscal year 2006 and fiscal year 2007. Rockville, MD: Food and Drug Administration, June 19, 2008. <http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDRH/CDRHReports/ucm127516.pdf>. Accessed June 12, 2009.

¹⁵ Government Accountability Office. Medicare durable medical equipment: class III devices do not warrant a distinct annual payment update. Washington, DC: Government Printing Office, March 2006. Publication No. GAO-06-62. <http://www.gao.gov/new.items/d0662.pdf>. Accessed June 11, 2009.

¹⁶ 21 USC § 360c(i)(1).

¹⁷ 61 Fed Reg 15491-504 (April 8, 1996).

¹⁸ Mundy A. Political lobbying drove FDA process. *Wall Street Journal*. March 6, 2009:A1. <http://online.wsj.com/article/SB123629954783946701.html>. Accessed June 11, 2009.

¹⁹ Waxman HA, Stupak B, Pallone F. Letter to Dr. Joshua M. Sharfstein regarding clearance of the ReGen Collagen Scaffold. Washington, DC: Committee on Energy and Commerce, House of

Representatives, May 11, 2009.

http://energycommerce.house.gov/Press_111/20090511/fdaregen.pdf. Accessed June 12, 2009.

²⁰ Center for Devices and Radiological Health. FDA summary for the Orthopedic and Rehabilitative Devices Panel for the ReGen Collagen Scaffold. Rockville, MD: Food and Drug Administration, November 14, 2008. <http://www.fda.gov/ohrms/dockets/ac/08/briefing/2008-4400b1-01FDA%20Summary%20and%20Questions%20.pdf>. Accessed June 9, 2009.

²¹ Hines J, Lurie P. Testimony before FDA on Collagen Scaffold medical device. Washington DC: Public Citizen, November 14, 2008. <http://www.citizen.org/publications/release.cfm?ID=7620>. Accessed June 9, 2009.

²² ReGen Biologics to present at the Pacific Growth Equities Life Science Conference in San Francisco on June 6, 2005 [press release]. Hackensack, NJ: ReGen Biologics, May 25, 2005. <http://www.regenbio.com/usa/en/pressroom/594/>. Accessed June 9, 2009.

²³ Premarket notification; ReGen Collagen Scaffold (CS). Hackensack, NJ: ReGen Biologics, July 22, 2008. [http://www.fda.gov/ohrms/dockets/ac/08/briefing/2008-4400b1-01%20510\(k\)%20Intro%20082079.pdf](http://www.fda.gov/ohrms/dockets/ac/08/briefing/2008-4400b1-01%20510(k)%20Intro%20082079.pdf). Accessed June 9, 2009.

²⁴ Center for Devices and Radiological Health. Transcript of the Orthopedic and Rehabilitative Devices Panel of the Medical Devices Advisory Committee: part 1. Rockville, MD: Food and Drug Administration, November 14, 2008. <http://www.fda.gov/ohrms/dockets/ac/08/transcripts/2008-4400t01.pdf>. Accessed June 9, 2009.

²⁵ Sharfstein JM. Letter from Dr. Joshua Sharfstein to Senator Charles Grassley regarding clearance of the ReGen Collagen Scaffold. Rockville, MD: Food and Drug Administration, May 8, 2009.

http://www.thegraysheet.com/nr/FDC/SupportingDocs/gray/2009/051809_sharfstein_Letter_to_Senator_Grassley.pdf. Accessed June 9, 2009.

²⁶ 21 USC § 360c(i)(1)(A)(ii).

²⁷ O'Reardon JP, Solvason HB, Janicak PG, et al. Efficacy and safety of transcranial magnetic stimulation in the acute treatment of major depression: a multisite randomized controlled trial. *Biol Psychiatry*. 2007;62(11):1208-16.

²⁸ Lurie P, Park S. Testimony at meeting on repetitive transcranial magnetic stimulation, Duraseal and vagus nerve stimulation. Washington, DC: Public Citizen, January 26, 2007. <http://www.citizen.org/publications/release.cfm?ID=7499>. Accessed June 11, 2009.

²⁹ Center for Devices and Radiological Health. Transcript of the Neurological Devices Panel of the Medical Devices Advisory Committee. Rockville, MD: Food and Drug Administration, January 26, 2007. <http://www.fda.gov/ohrms/dockets/ac/07/transcripts/2007-4273t1.rtf>. Accessed June 9, 2009.

³⁰ 21 USC § 360c(i)(1)(D).

³¹ 21 USC § 360c(a)(3)(D)(ii).

³² Dichiaro J. Letter to Mark N. Melkerson responding to request for additional information for ReGen's Collagen Scaffold. Hackensack, NJ: ReGen Biologics, 2007.

<http://www.fda.gov/OHRMS/DOCKETS/ac/08/briefing/2008-4400b1-28-%20C.pdf>. Accessed June 9, 2009.

³³ Stine N, Lurie P, Wolfe S. Letter to FDA urging that the Vagus Nerve Stimulator not be approved for treatment of depression. Washington DC: Public Citizen, May 11, 2005.

<http://www.citizen.org/publications/release.cfm?ID=7385>. Accessed June 9, 2009.

³⁴ Lisanby SH, Husain MM, Rosenquist PB, et al. Daily left prefrontal repetitive transcranial magnetic stimulation in the acute treatment of major depression: clinical predictors of outcome in a multisite, randomized controlled clinical trial. *Neuropsychopharmacology*. 2009;34(2):522-34.

³⁵ Center for Devices and Radiological Health. FDA Summary for meeting of the Neurological Devices Panel for Neurostar TMS system. Rockville, MD: Food and Drug Administration, January 26, 2007.

http://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4273b1_01-FDAExecutiveSummary.pdf. Accessed June 9, 2009.

Mr. PALLONE. Thank you, Dr. Lurie. Now, as I said, we have 28 votes, so I am going to say at least an hour and 15 minutes, you know. We will probably be back around 12:00, between 12:00 and 12:30. I think you all said you could stay beyond that though. So we should be all right. Without further ado, the subcommittee is in recess.

[Recess.]

Mr. PALLONE. The subcommittee will reconvene. Let me apologize. We really thought we would be done by 12:00 or 12:30 at the latest, and obviously that is not the case. So I really appreciate the fact that the three of you stayed. I know that Dr. Lurie said he actually had to leave at 12:30 anyway, but I appreciate the fact that you stayed here all this time.

The process, basically each of us, each member is allowed to ask you questions for five minutes. And then, as said, there may be written questions after particularly since what happened today, there will probably a lot of written questions. And you should get those within 10 days or so.

So I am going to start by recognizing myself for five minutes. You know what we are trying to do obviously is see if there is a need for legislation to correct the concerns that many of you have raised about the medical device approval process. And that is how you could be most helpful to us if you have suggestions. There is, of course, a bill that Mr. Dingell mentioned. Part of his—well it is actually his and Bart Stupak and my bill and others, but, you know, we separated out the food safety, but we still have the medical device and the drugs and the other provisions.

But that, in my mind, is more oriented towards inspections, lack of inspection, lack of resources. I don't believe that it directly addresses whether we should change the procedure in terms of, you know, approval. I don't think it relates to that. So that is kind of what I want to get answers from you on, and I guess my concern is that I don't think the issue is whether or not we should have a 510(k) process, although if any of you feel we shouldn't, you know, tell us.

But I don't think the issue is whether or not we should have it, but whether it is overly used and essentially abused, and whether or not this grandfathering, which was supposed to be essentially abolished, you know, or should be abolished and how long that should take or what the process should be to make sure that that is eliminated, if that is what you feel.

And I guess I will start with Dr. Maisel, but I will ask any of you the same question. It sounds to me like the 510(k) process is appropriate for a product that has the same effect as products that are currently safely and effectively on the market, almost like a generic, which maybe I shouldn't use. But I will use it because I kind of understand that.

But if a product has a new effect or is used in a new way, then it is important to go through the more rigorous premarket approval process so that the patient can know that this new technology will actually work and work safely.

So I guess what I am asking is is my analysis of that correct? And if that is true, is the problem that, you know, we have essentially extended this 510(k) process beyond products that are cur-

rently safely and effectively on the market and the products that are going to be very similar to those, and that somehow we have gotten beyond that? And I am just asking that very generally. And I will start with Dr. Maisel.

Dr. MAISEL. Well, I think you have it essentially correct. I think Congress actually did a pretty great job in forming a device law that correlates the risk of the device and the risk to the patient with the degree of rigor in which a product is reviewed. The problem with the 510(k), you do have it right. In order to be substantially equivalent, it needs to have the same intended use and the same technological characteristics, and if the technological characteristics are different, then it can't—those changes can't affect the safety and effectiveness.

What happens is that there is a lot of latitude that the FDA has in making those decisions. There is a lot of latitude in making a decision about whether a device has the same intended uses we have heard this morning already, and there is no real good definition of what differences in technological characteristics should warrant the more thorough evaluation.

There is a lot of reliance on bench testing, on testing in the laboratory of these products, which is fine except that there is no great correlation that that bench testing predicts clinical performance. And so there is this disconnect between the tests that are being done and how the product actually performs.

The other loophole that I think is a big loophole that we haven't really touched on is that companies can change their product and not file a 510(k) and not tell the FDA that they are marketing a different device. You do not have to file a 510(k) if a company changes a device and the company decides that there is no change in the safety and effectiveness of that device. Not the FDA. If the company decides that there is no change in safety and effectiveness and it is the same intended use, then they don't even have to tell the FDA that they have modified their device.

And there is a great example of this. The Edwards ET Logics valve was on the market for two and a half years. Many patients were implanted with it, and the FDA had no idea that it was even on the market. And finally they became aware it was on the market. They went to the company, and the company had followed FDA guidance that says if you change your device and there is no change in the safety and effectiveness, you don't need to tell us about it.

I mean that is a huge loophole that needs to be closed, and it is not that hard to close it. It requires legislation that says companies need to tell the FDA whenever they change a device and whenever they are marketing a modified 510(k) product, whether or not it affects safety and effectiveness.

Mr. PALLONE. Now, I am going to ask the other two to respond to, although I know the time is almost up. But you have been waiting here for six hours, so I am not going to worry about the time much. But you basically feel that we should have a 510(k) process? None of you—well, I will ask the others, but you are not advocating we should not have it but that it is just overutilized. It is much too subjective.

Dr. MAISEL. I think it is overused, and it would have been interesting to ask Congress back in 1976, their vision of what percentage of products would have gone through the PMA process. I can't imagine that they imagined only one percent of the devices would go through PMA process.

Mr. PALLONE. All right, but now what about this grandfathering? I mean I get so confused because it seems to me that you could have a device that was pre-'74 I guess, whenever we first passed the approval act, and that is grandfathered. Then you use the 510 to get approval for a device that is based on that grandfathered one, and then you can even use another device to grandfather, you know, to piggyback on the second one. So we have like, you know, generations—tell me if I am wrong—generations of devices that go back to this grandfather and never went through premarket approval.

I mean how would you have us deal with that?

Dr. MAISEL. I have to say that I would be interested in what Dr. Crosse has to say because she spent a lot of time obviously looking at the 510(k) program. I don't view that as a huge problem right now. I think the bigger problem is the FDA's assessment of the devices that are coming in front of them and the rigor with which they evaluate those devices, the level at which the bar is set for the evidence that the device is safe and effective. I don't lose sleep over the grandfather issue.

Mr. PALLONE. Okay. Well I will let the other two answer if you will, and then we will go to Lois, and we will see who else shows up. Go ahead, either one of you. Mr. Phillips?

Mr. PHILLIPS. I think there should be a 510(k) process because I will tell you I think that it has served consumers very well throughout the years. And I think that if you look at the totality of all decisions, we are talking about over a quarter million devices that have been cleared through the 510(k) process since 1976. And I think by and large, the devices that have become controversial are actually very few. So I think that there is overwhelming evidence that the program is actually a very valuable program.

Mr. Chairman, you asked a question about the grandfathering, and I appreciate Dr. Maisel's answer to that because I really don't think that it is a concern. All of those products that were grandfathered did go through an evaluation by experts both on independent advisory committees—and this is—in my testimony, I refer to 16 different expert advisory panels that reviewed all of these different types of devices. And they went through all of the different generic types. They looked at available information that was in the public domain at that time, which was published, peer-reviewed literature.

And they also factored in their own expertise, and they made their recommendations to the agency regarding what classifications those products should be placed in. And I think that actually that process had a tremendous amount of integrity.

As I said this morning, I think that part of the issues that we are all dealing with here or struggling with is the fact that in 1976 Congress envisioned that all of these class two products would be the subject of performance standards. And the agency was not successful in developing performance standards because the process

was too resource-intensive. That was the agency's explanation then, and I can tell you it is the explanation today.

Congress did allow the agency to switch from performance standards to what is called special controls, which are very flexible means of trying to mitigate risks associated with devices. And it can include actually clinical testing. So when I made the recommendation this morning that serious consideration be given to developing special controls for all devices in class three, what I was looking at was the situation that I think all of the panelists were dealing with, and that is these isolated incidents or clearances where there is criticism about not having proper clinical data or having proper testing.

I think there is a means under the existing statute to actually get all of those things in place for all of these problems at least as an opening measure before somebody thinks about opening the statute.

Mr. PALLONE. Okay, thank you. Dr. Crosse, and thank you for all you have done with the GAO report and all.

Ms. CROSSE. Certainly. You know we looked at this issue quite extensively, and I would have to agree that the 510(k) process in general seems to be working well and as intended. When we looked at the percentage of device applications—not applications, I am sorry. Under the 510(k) process, device submissions that came in, you know, 86 percent of them were judged as having both the same intended use and the same technology, and only 14 percent as having a different technology that needed to be evaluated for whether it posed any risk to the safety of the device.

So the vast majority there are coming in as the same intended use and the same technological characteristics. I think the question is exactly what Dr. Maisel said, is the evidence of that that FDA is accepting adequate. Where we have had some problems in looking at FDA's reviews of devices, both under PMAs and under the 510(k)s is the kind of information that FDA is accepting as sufficient to make their determinations.

And that is really something that we are not qualified in any individual case to question, to say no, really we have a different opinion about this technology. So we are not coming out and pointing to specific devices, but I think overall you do have a question about whether or not there is a greater need for clinical data in some instances and whether FDA is accepting that small companies can't be expected to have the same level of clinical information as a large company would be expected to produce or that you can't have the same kind of studies being conducted and that this is enough.

You know so we have seen some evidence of that, but it is a small number of cases where we have seen that occurring. And so, you know, it is not a question of legislative authority. It is a question of the application of that in the scientific review.

Mr. PALLONE. Okay, thank you. Our vice chair, gentleman from California, Ms. Capps.

Ms. CAPPS. Thank you. Excuse me. I am going to try to avoid the questions that you have asked. Since it is just the two of us, we will try to see how much we can cover quickly. Thank you very much on my behalf as well for your patience with today's proceedings.

I have two different topics to bring up. I will address the first one to Mr. Phillips, but I actually would love to get some comment from anyone who wants to on this topic, both of these topics.

One, the 510(k) process is only one component of the regulatory controls composed on medical devices intended to ensure safety and efficacy. In fact, the U.S. medical device regulations have been models for regulatory processes developed in some other countries as well. Mr. Phillips, can you describe or does anyone want to describe other regulatory controls besides the 510(k) and their roles in protecting patients and health care professionals?

And let me just ask the question, the second one on this topic. I know there are concerns about these different elements of the approval and regulatory process. Does anyone want to comment on how congressional efforts to give the FDA more funding and resources could help this 510(k) and other processes as well to improve and be more effective?

Mr. PHILLIPS. Yes, ma'am. If you look at the controls that are available to the agency to ensure safety and effectiveness, they actually have a wide variety of different controls. Premarket notification is actually what is referred to as one of the general controls for medical devices. That is under the 1976 amendments.

Other general controls include provisions against adulteration and misbranding. There are labeling requirements. There is registration listing, which basically identifies establishments so that they can do, the agency can do inspections. So GNP inspections would be part of the general controls.

The same thing with some postmarket surveillance activities, for example, records and reports like medical device reporting. Those are referred to as the general controls, and they apply to all medical devices regardless of the class because they apply to class one, two, and three.

It is interesting because premarket notification is a general control that applies to all products. But under the FDA Modernization Act of 1997, most class one devices were exempted from 510(k) review. In fact, the agency had the authority to reserve certain devices if they met what was called the reserved criteria. And there is probably 10 percent of the class one medical devices that still come in under 510(k).

It is almost as if that action by Congress changed premarket notification or 510(k) from more than just a general control to a special control that would apply primarily to class two medical devices. I mean in reality that is what has really happened.

It is also interesting because if you look at what the agency has under special controls as tools that can ensure safety and effectiveness, as I said in my morning testimony, they have a tremendous amount of controls that are available to them to apply to devices as they believe necessary from not just premarket notification but, you know, patient registries in a postmarket period.

There can be clinical data that is required. There can be specialized labeling. There can be agency guidelines that are put into place. So there is a wide variety of different tools that can be applied.

For the class two devices, it is difficult to describe how well those controls can ensure safety and effectiveness because by and large,

class two devices today are not subject to special controls. And that was sort of the problem that I pointed to this morning because I think that would be one of the first things that I would think of is that there could be more special controls, guidance documents, that looks at the risks that are associated with class two devices and figuring out what are the proper mitigation measures that address those risks. And again I think that the agency has really a wide variety of things that are available to them should they elect to apply those for the regulation of devices.

As far as, you know, what efforts or funding could Congress ensure that the agency has? I am not an advocate for just simply increasing FDA's budget by any specific amount or any specific percentage. I have heard of people saying well, the agency should have their budget doubled. I think that the agency should receive the funding that could allow them to take care of the priority issues that need to be taken care of.

And clearly I think the two that come to my mind is inspections because clearly there is no question. The agency has to have more of a presence in facilities, whether it is class one, two, or three, than what they do today. That is one.

I think in the postmarket area, I think again that is an area where there needs to be resources applied at the agency, not just necessarily in personnel with the analysts that can look at MDR reports or adverse events that are coming into the agency, but also to improve the infrastructure that they have in order to be able to process the reports that come in. I think as Marcia Crosse indicated in her testimony, it is a tremendous amount of data that is coming into the agency. And I really don't think they are equipped to deal with that information as efficiently as what they really should. So I think that that is a big issue.

In the premarket area, you know, we have already said that for the class threes, the agency has already moved out to take the very first steps to ensure that they get the class three devices subject to premarket approval. The steps that they have taken so far are the easy steps. The more difficult steps are assuming that the PMAs come in for all of these different products. The agency is going to have to be able to process those applications, and they are not going to be able to process them at existing staffing levels. So with that, I will close my answer.

Ms. CAPPS. Okay, Mr. Chairman, do I have your permission to continue as though it was almost like a second round, or would you rather me stop? I have another question.

Mr. PALLONE. No, I think you continue and then Mr. Burgess is here. And we will let him continue. Are you able to stay a few more minutes, Dr. Maisel?

Dr. MAISEL. Yes, I am.

Mr. PALLONE. Okay, go ahead.

Ms. CAPPS. Thank you very much. Since it has been this long, I feel like maybe we want to have a little more robust conversation than we might have otherwise. In other words, I am interpreting what you are saying, and I want to see if anyone else wants to add to it, the 510(k) model, while a good one, isn't offering—there might be some others like inspection and postmarkets that, if there were more resources, could also add to the robustness of the regulations

and the evaluation in achieving the goals. Would you like to comment?

Ms. CROSSE. Well, yes, I would say in fact that the process requires the postmarket steps, and in fact, it is constructed to depend upon the postmarket steps. And that has been where the greatest problems have been with FDA's resources and ability to attend to the kinds of adverse event reports that come in that let them know about problems that couldn't necessarily be known in advance until they are out in widespread use.

Ms. CAPPS. And you could make the correlation—I am not asking you to define it—between the amount of resources that, if you are limited you are going to put them into the 510(k). But if you had more, you would put more because inspections require more resources obviously.

Ms. CROSSE. Well, it is that, and it is structured under the user fees that there is funding for the premarket steps. The user fees are paying for the premarket steps—

Ms. CAPPS. But not the postmarket.

Ms. CROSSE [continuing]. But had not been, until very recently, available to pay for some of these postmarket steps. There is now additional funding for the inspections, and I would concur that that has been a great area of weakness and that they are now beginning to address.

They are also beginning to address some of their IT infrastructure problems that have limited their ability to analyze some of the information that they have even when they have received it. And so I think that they are beginning to take steps, but I see particular weaknesses on the postmarket side.

Ms. CAPPS. Okay, any—

Dr. MAISEL. May I respond to that?

Ms. CAPPS. Yes, please.

Dr. MAISEL. So I agree that certainly increased resources will undoubtedly help the FDA. I think it would be impossible to dispute that. And I agree that the postmarket area and areas like inspections will help. I think we would be naive to think that throwing money at the issue is going to solve the problem.

Ms. CAPPS. I agree.

Dr. MAISEL. And I am not saying you are implying that, but we could give the FDA unlimited resources. But if we don't change their approach to evaluating products, if we don't change the science-based evaluations, then we are still going to be faced with problems.

Ms. CAPPS. I see. I will turn to another topic then with permission. You know it is interesting. Usually when we think of FDA, we think of safety. But effectiveness is just—we always say safety and effectiveness. And today we focused primarily on safety, but whether a device works or not is, I would submit, equally important. I am sure you agree. The history of Food and Drug and Cosmetic Act includes many instances where Congress has had to tighten regulations because the products being marketed weren't living up to their goals and were, in fact, ineffective.

Despite this history, we hear from some that we need to keep the barriers low even for potentially lifesaving devices to enter the

market. To do otherwise, these critics argue, could stifle innovation and keep patients from treatments that may heal them.

But what concerns me is that if there is not enough study of the effectiveness of devices before they are marketed, patients and their doctors are forced to make decisions about whether or not to use the device that really may have never adequately been demonstrated to work.

Mr. Maisel, maybe I will start with you this time. In this case, I will just use an example because I was a coauthor. I have been a school nurse, and so I know about external defibrillators. This panel has endorsed Ms. Sutton's bill, the Josh Miller—and he was a student—Hearts Act in a bipartisan fashion because this bill would put lifesaving devices in every school. It is a big step. Don't always think of schools as being a place where they are needed, but there is evidence that they have been.

I do agree with that policy, but I also am very concerned particularly with not fully developed people that these devices work. Dr. Maisel, can you tell us about that particular situation with your experience?

Dr. MAISEL. I think you have picked out a very important medical device, external defibrillators, which have been proven in well-conducted clinical studies to save lives.

Ms. CAPPS. Yes.

Dr. MAISEL. Sudden cardiac deaths claim about 330,000 lives each year in this country. It kills more people than AIDS and breast cancer combined. I mean it is a huge deal, and we are fortunate to have a good therapy. Now, interestingly the automatic external defibrillator is one of the class three 510(k) devices mentioned in the GAO report.

And if you doubt that there is an issue with the 510(k) program, this is the poster child for the problem because since 1996, there have been 52 recalls affecting automatic external defibrillators. There has been over 300,000 AEDs that have been recalled. One in five AEDs out in distribution in this country have been recalled.

Ms. CAPPS. Yet they were put out.

Dr. MAISEL. They are put out, and the challenge of—I think it is unrealistic and impossible to think that every iteration of an external defibrillator is going to be clinically evaluated. I don't think it should be, and I don't think it can be. But we need to figure out a better way to evaluate these devices—

Ms. CAPPS. You have an idea?

Dr. MAISEL [continuing]. Instead of approving them each time based on the fact that it is as good as the one that just came—

Ms. CAPPS. Right.

Dr. MAISEL [continuing]. Down the line. I think another thing, another important point you made was the safety and effectiveness point.

Ms. CAPPS. Right.

Dr. MAISEL. It is impossible to assess safety without knowing the effectiveness. If I told you a medical device kills two percent of the people who get it and ask you is that safe or not, you can't answer the question. Compared to what? You need to know, you know, maybe the disease is 100 percent fatal without the device and everyone lives who gets it. So two percent sounds great. Maybe no

one dies without the device and two percent die with it, and then it is terrible. You need to know effectiveness if you are going to evaluate safety.

Ms. CAPPS. I will ask all three of you. Do you think we have adequate resources or methodology to do that? Maybe that is too harsh a question. What should we be doing in this area that we are not doing now?

Ms. CROSSE. I am not certain that it is an issue of either resources or methodology. I mean it seems to me it is an application of current existing approaches or an ability perhaps in that particular instance for the agency to say, you know, you can only have so many iterations before you have to provide some other sort of information, which might be a different regulatory approach. But it is not clear that there is evidence to establish that. It is not something we have really directly looked at.

Ms. CAPPS. Is it that there is not evidence to establish it or we have not asked those kind of questions?

Ms. CROSSE. I think probably either.

Ms. CAPPS. Is it in that area that we should push?

Ms. CROSSE. We haven't got anything that I would be able to give you an answer about how one might go about or what would be necessary.

Ms. CAPPS. Well, let me just focus on the recalls of the AED. Those came, I imagine, because people had untoward effects or didn't work when they were—

Dr. MAISEL. So the FDA and our country has a medical device reporting system, and so adverse events that manufacturers become aware of that cause harm to patients are required to be reported to the FDA.

Ms. CAPPS. Right.

Dr. MAISEL. And companies become aware of these things, and so since 1996, there have been approximately 370 deaths associated with failure of AEDs. And so in response to device failures that get reported, companies become aware of them and recall their product because they have defects, whether they are related to the circuitry in the device, battery function. These are complicated devices, and things happen to them.

Ms. CAPPS. Are they recalled at the insistence of FDA?

Dr. MAISEL. Virtually every recall of most devices are "voluntary" recalls by the manufacturer, meaning that the manufacturer becomes aware of a problem and then chooses to issue a voluntary recall, sometimes with the coercion or urging by the FDA. And there are rare occasions where the FDA will issue a recall if the company doesn't. But most of them are voluntary.

Ms. CAPPS. Is there anything within the Food and Drug Administration that has jurisdiction in this area, where, if there is a recall, that there is an action that is taken by the FDA?

Ms. CROSSE. Well, FDA has the authority both to order a recall or certainly to evaluate the information, urge the company, alert them to the problems that they are seeing and the adverse event data if the company is not aware of it already. Usually the company would become aware of—

Ms. CAPPS. Right.

Ms. CROSSE [continuing]. Something first, but, you know, one could argue this is an example of the system working as it is designed that when adverse events are identified, recalls occur. I think the question then becomes what does FDA do with that information? If they see a pattern, what then feeds back into their evaluations of subsequent devices when those applications come in? And I can't answer that question for AEDs.

Dr. MAISEL. I would also say if I were designing the FDA in a postmarket surveillance system, I would want the FDA to be the one finding some of the problems. It is extremely rare that they are actually the ones that identify the postmarket problem despite the fact that they are asking for data.

Almost always it is the clinical community that comes up with the problem or the manufacturer gets reports and identifies it and reports it to the FDA. It is very rare that the FDA combs their database and their reports and comes up with an a-ha moment where they have identified something.

Ms. CAPPS. Well, Mr. Chairman, this is not a point I want to belabor, but it seems to me a point of perhaps interest of further discussion at another time. It appears to me that when something comes to light, when the public knows it, then something happens. But I am also mindful that you can't always count on that to happen necessarily. But I will leave it at that, and thank you very much.

Mr. PALLONE. Thank you. Thanks so much. Mr. Burgess.

Mr. BURGESS. Thank you, Mr. Chairman. I thank the witnesses for bearing with us. I hope you were able to watch the drama on television in the House floor all day, spellbinding. I am sure you were on the edge of your seats through all of those reconsiderations.

Dr. Crosse, on the 510(k) process we have been discussing, that is only one component of regulatory controls imposed on medical devices intended to secure their safety and efficacy. What other controls are there, and what, if any, are the GAO's recommendations for the Food and Drug Administration to incorporate those if they haven't already done so.

Ms. CROSSE. Well, I think that the other key controls from our point of view are those postmarket controls, the ability of the agency to ask for further study, for additional data, for monitoring of the devices by the companies, and also the adverse event systems that FDA has. We have not pointed to legislative remedies being needed in this area. The kinds of problems that we have seen are ones that FDA currently has authority, but in some instances not resources to actually conduct, you know, the kinds of postmarket oversight as necessary.

They have begun to take some good steps in that area. They have a Med Sun system that they have created where they have some additional surveillance, more active surveillance system ongoing. They haven't had the resources to be able to review all the reports that are coming in that are being generated by that system. So that kind of control, we think, would be important for them to be able to exercise to have a better understanding and, as was just stated, to be able to identify some of the problems that may be cropping up more quickly to be able to take actions more readily

and to ensure that they are on top of whether companies are following through on the commitments that they have requested at the time that something is cleared or approved for marketing. So those kinds of controls.

Mr. BURGESS. Does that fit with, you know, your description? In a perfect world, the FDA would be the one that finds problems and alerts the health care committee to the problem. But the reporting system is such that after just a few adverse events, the FDA at least should develop some institutional curiosity as to investigate these.

Dr. MAISEL. Right, I mean I don't think the FDA should be the only one, and I think that Congress recognized that when they set up this system. We need people on the front lines reporting the adverse events and the device malfunctions. And for the most part, manufacturers actually do a really great job of taking their product and the reports of malfunctions and figuring out what goes wrong and fixing the devices and resubmitting 510(k) applications. That is what we want them to do.

But it would be nice for the FDA to be able to take the 200,000 device adverse event reports that they get and be able to sort through those and find a pattern of malfunction or devices that are going wrong with this large database they have. And there will be investments in information technology, and they are moving in that direction.

Mr. BURGESS. Well, I was just going to ask you. What is it that prevents that from happening today? Is it the IT architecture that is available?

Dr. MAISEL. I think that is a major component. The other component is that the quality of the data they get is suspect. An adverse event report could say patient had device implanted and died, and that could be the entire report. So a lot of times, they are spending time calling clinicians or trying to figure out what really happened. They might not even know the serial number of the device or the company that made the device. It is very difficult for them to connect the dots, and it is going to require significant investment.

Mr. BURGESS. Well, now you had a patient who had an implantable cardiac device and had an adverse event. Did you report that? How did you go about notifying the FDA that there was a problem, or was that problem already recognized so this was just one of many?

Dr. MAISEL. It was both. I mean the device had already been recalled. The patient had been informed that his device was recalled. We had had a discussion about the management options, and the lowest risk option for him was to leave the device in place. And unfortunately he had an adverse event. I reported it to the FDA via the Med Watch system, but for an outlier of all the adverse event reports reported to the FDA about over 95 percent come from manufacturers. It is very rare that health care providers report adverse events. There is a little incentive for them to do it other than it is the right thing to do in the goodness of their heart. They don't get paid for it. It takes a considerable amount of time.

Mr. BURGESS. Would a provider limit future liability that they might incur if they went through the adverse reporting system, much like NASA has for the air traffic control system? There is a

get out of jail free card if you report an adverse event in the nation's skyways. Do we have such a thing for adverse events?

Dr. MAISEL. No, and I am not really sure that that would have any impact on the reporting. I don't think physicians are—my sense is events aren't being reported because they are concerned about liability. They have, like you, a busy day, and there is 10 minutes of their day that they don't have to give away. They can go do something else, and no one is going to come after them. And they don't have to do it so it is not required.

Mr. BURGESS. Just one other observation on the AEDs because this has been important, and, yes, this committee has been involved. And I have been involved with my state legislators back home in Texas to get these devices at water parks and high school football games and what have you. And I will never forget a town hall meeting I had in South Lake, Texas one time when a man went into v-tac and v-fib sort of in the waiting area. And they fortunately had an AED, but it was locked up in the basement downstairs. So it really didn't do anyone any good. And I can tell this story because the paramedics arrived quickly, and the AED, in fact, saved his life.

But after I got back up here to the capital, I began to look around. Where are our AEDs? I was informed that we had appropriated money and we had purchased the AEDs, and they were indeed locked up in a cabinet somewhere because we hadn't gotten permission from the architect of the Capitol to place the cabinets and we hadn't agreed on the type of cabinetry that should be placed in the historic buildings around the Capitol.

So, you know, you can do all the right things and still be left with—at some point, the decision tree falls apart, and you don't get the information or the device into the hands of the people who need it.

Dr. Maisel, based on your experience chairing the Food and Drug Administration's postmarket heart device advisory panel, on the panel, how long does it take you to review a device when it comes to your attention, when there is a report made?

Dr. MAISEL. The sponsor of the device in the FDA prepare a pretty remarkable panel pack that often runs into hundreds of pages that includes both the administrative record, our review of the bench testing and engineering, the clinical studies. And then we get it several weeks in advance, and, you know, it takes hours, you know, probably 10 hours or more to review. And then we usually have an eight-hour meeting to discuss the results.

Mr. BURGESS. So it is somewhat cumbersome and time consuming?

Dr. MAISEL. I guess it depends on your perspective.

Mr. BURGESS. Now, April this year, there were some Food and Drug Administration employees that sent a letter to the President saying that the device process was essentially broken. Now, is that a statement that you could find agreement with, or do you think that is an overreaction?

Dr. MAISEL. I don't know that I want to comment on what these individuals said because I don't know what their allegations were based on. I will say I think we are here today because we all feel that there are things that can be done better. I can say in working

with literally hundreds of individuals at the FDA, I have yet to come across someone who I did not feel was trying to do the right thing for the American public.

It is not like there are people walking around at the agency who are trying to circumvent the rules. I think they are trying to do the best they can with the resources that they are given.

Mr. BURGESS. So the motives are pure, but what about, then, the process itself? And what about the 510(k) process? And we have heard testimony that it may not even involve clinical testing in humans. It may be just simply bench testing, or it may be testing in laboratory animals.

Dr. MAISEL. I think, you know, I think Congress has done an amazing job of giving FDA a roadmap, a recipe book of what they are supposed to do for certain types of devices. But there is leeway in that roadmap. There is judgment that the FDA needs to apply to a given device in a given situation. And I think one of the problems is that judgment is applied inconsistently.

And I think, for obvious reasons, we are focusing a lot on the 510(k), but I don't think we should completely ignore the PMA process. Yes, it represents only one percent of devices, but some of those individual devices go out to several million people. I mean there are tens of millions of people who get PMA devices. Four out of five PMA devices are approved via the PMA supplement pathway, not via the original PMA pathway. And the PMA supplement pathway, 80 percent of the PMAs approved is a much, much lower bar.

A lot of those PMA supplements are 180-day PMA supplements, which is a class that Congress set up, and that doesn't necessarily require clinical data. The Sprint Fidelis lead that my patient had is a perfect example. That was approved via a PMA supplement, zero clinical data before this life-sustaining device goes into people.

Mr. BURGESS. Well, given that, and just speaking of the 510(k) world for a moment, what changes to that process would you suggest? And are those changes within the purview of the FDA and within the tools that they have right now? Or is that going to require additional input from Congress?

Dr. MAISEL. I do believe that the FDA has most of the tools that they need. Whether they will use them and be applied is a different story, and so that is sometimes where Congress can obviously help and direct them to apply. I think that there needs to be better clarification of which type of 501(k) devices should have clinical data associated with them. I don't think it should be a case-by-case basis. I am a reviewer sitting at the FDA, and I am going to look at this device and make my best judgment.

There need to be standards. There need to be guidance, I think from Congress, to the FDA about what you expect, what we expect to see for certain types of products. And it should be based on the risk of the product, and it should be based on the risk to patients. I think you could weigh in the effectiveness as well, as we spoke about. I mean for a product that is a life-sustaining product that is a really important product, I am willing to accept a different safety standard. I am willing to have less data if it is a really important product. And for products that are a me-too product, and

we have other products that are just as helpful, I think the standards are different.

But I think Congress can help by clarifying the standards for the FDA or at the very least, FDA needs to be more transparent about how they are going to apply their standards.

Mr. BURGESS. You may be overestimating the ability of Congress, but you can ask. I appreciate the acknowledgement. Let me ask you a question that is really not fair and it calls for rank speculation and you may regret—

Dr. MAISEL. I am good at that so—

Mr. BURGESS. Yeah, me too. You may regret that you stayed here all day, but we are faced now—this is an important issue that we are dealing with. And we need to get it right, and the fact that we have been here all day focusing on it indicates that there is a problem that we need to get right.

Now, we are also in the process of looking at very complex biologic molecules, and I realize they are not devices. These are medications. The issue of follow-on biologics is coming up to our committee, and we are helping the FDA decide the best way to approach the assessment of so-called follow-on product.

And it seems to me there are so many similarities here. I mean, although one is a device and one is a complex biologic molecule, we are talking about using a certification procedure that is somewhat abbreviated or at least has the flexibility to be somewhat shortened from what the normal procedure would be. In this case, in the biologics case, going through a new drug application. And in the device case, going through the full PMA rather than a 510(k) process.

Is that an unfair analogy to draw between the issue of follow-on biologics and the issue that we are dealing with here today with the 510(k) process?

Dr. MAISEL. Well, I think you have described it well. I mean they do have components of both drugs and devices. I think the lesson would be we don't know a lot about them. There is a lot we still need to learn about biologics. And we need to have a total product life cycle. We can't just have a premarket evaluation and put them on the market and start having patients get them and then forget about them.

At the same time, we don't want them to go into patients and just study them after they are into hundreds or thousands of patients. So I think that whatever program is established needs to carefully balance the benefit to patients or at least the potential benefit to patients so that we can get these important products out to them quickly, but at the same time study them. Require postmarket studies so that we can make sure that the products are doing what they are supposed to do and that patients are safe.

Mr. BURGESS. And the concept of the life cycle is one that is really extremely important because many of these devices are implanted in someone whose forward life expectancy may be two, three, or four decades. And is the device capable of holding up in conditions inside the human body over that time and particularly the artificial joint replacements that we have seen.

And even getting into dental procedures. There can be analogous situations there. I really do appreciate you sharing that with us today. Mr. Chairman, I am going to ask that since Dr. Lurie, I

guess, had to leave, and I had a set of questions that I wanted to pose to him. But can I do that in writing?

Mr. PALLONE. Absolutely, and I said to the panel that since a lot of the members didn't come back you should expect that you will get some written questions. Usually we ask the members to get them in within the next 10 days.

Mr. BURGESS. You can have them before I leave.

Mr. PALLONE. Well, we will, you know, open the record obviously for the written questions in light of—well, we always do anyway but particularly today because of the long day.

Mr. BURGESS. Let me just ask Mr. Phillips one final question because he has been so patient to sit here all day. Now, we have heard testimony, it seems like hours ago now, that only 10 to 15 percent of 501(k) submissions contain any clinical data, and you obviously have had some experience working at the FDA. Do you think that within the 501(k) approval process that there should be some clinical data available or some clinical trials performed?

Mr. PHILLIPS. I think without question the answer is yes because what we have seen is clearly over time evolution and technology changes. We talked about, Dr. Lurie talked about issues of intended use, and without question, when you start dealing with changes in intended use and changes in technology, invariably, there is going to be situations where you are going to have to have human experience.

Mr. BURGESS. And so you really answered the second part of that question. It should be human. It cannot be just bench testing or animal testing.

Mr. PHILLIPS. You know it is interesting because I, you know, through my career, I have hung out with a lot of engineers. And to a very large extent, you find that you can get a lot of precise information regarding engineering analysis. We talked about, for example, the breakage of a lead. There is a lot that you can do to characterize the strength and integrity of a lead.

I think that, you know, for premarket evaluation, there has to be a balance that is struck. And I think that we talk about the total product life cycle, and I think from an FDA regulatory perspective, they have to have the controls in place to provide adequate assurance, reasonable assurance of safety and effectiveness in the short term. But I think there needs to be postmarket controls so that you can monitor in a very vigilant way performance once products get to market.

I think that there are many situations where it is perfectly reasonable to allow a product to go to market based upon preclinical engineering analysis and data. But in order to do that, you have to have high confidence that you have mechanisms in place that are going to be able to pick up problems once products are out and available in a much larger population.

You know clinical trials with medical devices, a large clinical trial is 200 to 300 patients for a medical device. And clearly there is a limit as to how much you can even detect in a relatively small patient population. And keep in mind the duration of trials, a long trial is a two-year trial for a medical device. And many of these products, as you just indicated, are going to be placed into individuals for very lengthy periods of time, perhaps the rest of their life.

So I think that there has to be a focus on trying to figure out what the proper premarket, postmarket balance is so that we don't develop a system which really becomes a deterrent to industry, innovating and developing new technologies but gives the American public the confidence that once products are made available, that there are mechanisms in place to pick up any kind of events that represent, you know, something of significance that they need to know about or other clinicians need to know about.

Mr. BURGESS. Well, Dr. Lurie also referenced a compound that was used for articular surfaces and the fact that this was a weight-bearing structure made a difference as well. So something like that where there is a long length of time for intended use in someone's body. And there is a special situation that this is a weight-bearing structure. It seems to me, and I think obviously I am no expert, but it seems to me that this is one of those situations that would not lend itself to a facilitated or abbreviated process but one where you would want to have the availability of all the data possible and then the longitudinal studies since again we are talking about something that exists over—is intended to be used over a long period of time, longitudinal studies become very important as well. Would you not agree with that?

Mr. PHILLIPS. Well, I would agree with that in concept, but let me also disclose that the example that Dr. Lurie was addressing in his remarks this morning, I am an actual consultant for that company. So I want to make sure that everybody is aware that there is that relationship.

But, you know, it is interesting because I think that you need to look at the body of evidence that was provided on that particular device as well. It was a 510(k) clearance, but there was a tremendous amount of data, in fact a lot more data in that submission than what is in the vast majority of 501(k) applications.

There can be a lot of discussion as to the quality of the data, what that data established, but I think for all practical purposes, the intended use of that device was well corroborated with the data that was included in this submission.

I understand that Dr. Hamburg and Dr. Sharpstein are looking into that issue right now, and interested to find out what their assessment is.

Mr. BURGESS. Well, Mr. Chairman, I will just come back to where I started this morning. It begs the question where is the FDA. So I hope we will have a follow-up hearing at some point, and I know the calendar is condensed and compressed. And we are all pressed for time, but it is hard to have this type of hearing on this type of evaluation and evaluating rather the process the FDA uses without having the FDA here to weigh in on it.

And, Dr. Maisel, let me just say too I am so grateful you are here. And we have heard so much from the science board on the FDA that yeah, we need to fund. They do need more money, but the procedures and the policies are things that need to be looked at as well.

And then, of course, in the brave new world of the FDA regulating tobacco, and I don't know how you ever decide that it is—you can decide that it is effective, but I don't know how you ever decide that it is safe. And they have a mission that is—we have

given them a mission that is virtually impossible for them to perform.

But really appreciate all the witnesses being here today and staying with us so long. I will yield back to the chairman.

Mr. PALONE. Thank you, Dr. Burgess. Again thanks, you know, for your patience, but I am glad that you came back and we were able to ask the questions that we did ask today. We will have some more written questions, but thanks again. Have a good and safe trip home. And without further ado, the subcommittee hearing is adjourned.

[Whereupon, at 7:35 p.m., the Subcommittee was adjourned.]

[Material submitted for inclusion in the record follows:]

Statement of the Honorable Anna G. Eshoo
House Committee on Energy and Commerce, Subcommittee on Health
Hearing on “Medical Devices: Are Current Regulations Doing Enough for Patients?”
June 18, 2009

Thank you, Mr. Chairman, for holding this hearing today.

Medical devices have brought amazing breakthroughs into the field of healthcare. Heart valves, defibrillators, and pacemakers have saved countless lives and transformed the way millions of patients live their lives. America is the leader in medical innovation and American medical devices are used to treat people around the world.

I look forward to hearing from our witnesses today, especially from Ms. Crosse from the GAO. While medical devices can offer hope to people who thought they had insurmountable conditions, it's the responsibility of the FDA to regulate these products for safety. It's my understanding that several devices on the market before the passage of the *Medical Device Amendments* were “grandfathered in” and may not have had the same oversight and regulation as new products. I'm eager to hear if there have been problems with these devices and how widespread these problems have been.

I'm surprised to see that the FDA is not a participant on our witness panel. Since we are discussing the FDA and, likely, how it can improve, I think the Agency should be testifying today. I would like to note that this is the *second* hearing in one week where we've examined key issues relative to the FDA and their responsibilities, but they have not been invited to participate.



United States Government Accountability Office
Washington, DC 20548

July 23, 2009

The Honorable Henry A. Waxman
Chairman
Committee on Energy and Commerce
House of Representatives

Subject: Responses to Question for the Record - GAO Testimony Entitled *Medical Devices: Shortcomings in FDA's Premarket Review, Postmarket Surveillance, and Inspections of Device Manufacturing Establishments*

Dear Chairman Waxman,

This letter responds to your July 14, 2009 request that we address for the record questions related to the Subcommittee's June 18, 2009 hearing about medical devices and whether current regulations are doing enough for patients. Our response to the question, which is in the enclosure, is based on our previous work and knowledge of the subjects raised by the question.

If you have any questions about the letter or need additional information, please contact me on (202) 512-7114 or at crossem@gao.gov or contact Patricia Yamane on (206) 287-4772.

Sincerely yours,

Marcia Crosse
Director, Health Care

Enclosure

Enclosure I

Enclosure I

**Response to Post-Hearing Question for the Record
Medical Devices: Shortcomings in FDA's Premarket Review, Postmarket
Surveillance, and Inspections of Device Manufacturing Establishments**

**Subcommittee on Health
Committee on Energy and Commerce
House of Representatives
June 18, 2009**

**Question for Marcia Crosse
Director, Health Care
U.S. Government Accountability Office**

Question for the Record Submitted by the Honorable Joseph R. Pitts

- 1. I appreciate the work that GAO has done to find ways in which Congress can improve the FDA's review and approval process for medical devices, but I think it is also important to point out the good work that FDA does through the 510(k) process to get products to patients quickly. According to GAO's report, more than 13,000 reviews were done on Class I and II devices from 2003 to 2007, ensuring that patients can quickly access improved products in these less risky device categories (which range from bandages to medical imaging equipment). I feel that while there is room for improvement for some devices, we must keep in mind the importance of ensuring patients can access technology improvements in a timely manner for those less risky products. Isn't it true that the 510(k) process remains a good and timely way to ensure products make it quickly and safely to market?**

Our recent work indicates that FDA's 510(k) process is an important part of FDA's premarket review of medical devices. The 510(k) process is generally faster and less expensive than FDA's more stringent premarket review process, the premarket approval (PMA) process. We found that during the period October 1, 2002 through September 30, 2007, nearly 12,000 class I and class II device submissions were cleared through FDA's 510(k) process. These devices represent about 30 percent of all devices listed with FDA by device manufacturers during this time period, and about 94 percent of the devices that were cleared or approved through FDA's premarket review. In addition, we found that of the class II devices cleared through the 510(k) process during this time, FDA determined that all had the same intended use and 86 percent had the same technological characteristics as devices that were already on the market. We did not, however, evaluate the scientific validity of FDA's determinations or of FDA's classification of device types, so we cannot comment on whether the 510(k) process adequately ensures public safety.

PHILLIPS CONSULTING GROUP, LLC

**P. O. Box 39
McHenry, Maryland 21541
Telephone – 202-420-9042**

July 27, 2009

The Honorable Henry A. Waxman
Chairman
Committee on Energy and Commerce
House of Representative
United States Congress
2125 Rayburn House Office Building
Washington, D.C. 20515-6115

Dear Chairman Waxman:

Thank you for the opportunity to appear before the Subcommittee on Health on June 18, 2009 and participate at the hearing entitled "Medical Devices: Are Current Regulations Doing Enough for Patients?" It was an honor and a privilege to be called upon to provide my perspective on FDA regulation of medical devices; an area that I have devoted my entire professional career to advancing.

This letter is a response to your letter dated July 14, 2009 in which you forwarded questions directed to me from the Honorable Joseph R. Pitts, representative of the great state of Pennsylvania. As instructed, my response is addressed to Congressman Pitts and follows the text of the questions that he raised. My response is attached to this letter.

If you or any members of your committee require any further assistance and you believe that my knowledge and experience could be helpful, please do not hesitate to call on me.

Sincerely,



Philip J. Phillips
President
Phillips Consulting Group, LLC

Attachment

cc: The Honorable Frank Pallone
Chairman, Subcommittee on Health


PHILLIPS CONSULTING GROUP, LLC

P. O. Box 39
McHenry, Maryland 21541
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Memorandum

Date: July 27, 2009

To: The Honorable Joseph R. Pitts

From: Philip J. Phillips 

Re: Follow-up Questions
Subcommittee on Health
June 18, 2009 Hearing entitled “Medical Devices: Are Current Regulations Doing
Enough for Patients?”

I have prepared responses to the two questions that you directed to me following the above reference hearing. As instructed by Chairman Waxman, my responses follow a restatement of your questions.

- 1. I appreciate the work that GAO has done to find ways in which Congress can improve the FDA's review and approval process for medical devices, but I think that is also important to point out the good work that FDA does through the 510(k) process to get products to patients quickly. According to GAO's report, more than 13,000 reviews were done on class I and II devices from 2003 to 2007, ensuring that patients can quickly access improved products in these less risk device categories (which range from bandages to medical imaging equipment). I feel that while there is room for improvement for some devices, we must keep in mind the importance of ensuring patients can access technology improvements in a timely manner for these less risky products. Isn't it true that the 510(k) process remains a good and timely way to ensure product's make it quickly and safely to market?*

I believe that the 510(k) process is an effective tool that ensures the American public that manufacturers attempting to market new devices are subject to the proper degree of FDA regulation commensurate with the product's risk and the agency's ability to assure that the product is safe and effective.

Having said this, the 510(k) process is one of the most misunderstood and mischaracterized regulatory programs in existence today. Despite popular opinion, risk is not the universal factor that distinguishes Class II devices from Class III devices. In reality, Class II and Class III devices may present equivalent risk. What distinguishes Class II and Class III designations is whether FDA believes that each new device within a generic device type must be demonstrated to be safe and effective or whether there are established and recognized scientific means that can ensure that the device will be safe and effective.

Take your example; medical imaging equipment. Currently, medical imaging equipment is regulated in class II or class III depending on its technology and intended use. The vast majority of this equipment is regulated in class II because the risks of radiation exposure, as well as misdiagnosis from poor image quality, are well understood and the means to mitigate these risks are established. The basis for FDA regulating these devices in class II rests on the agency's confidence that conformance with performance standards and against well established methods will ensure patients that they will not face unreasonable radiation exposure and that the image quality produced will allow accurate interpretation. Digital mammography imaging equipment, however, is currently regulated in Class III subject to PMA requirements. The basis for Class III regulation relates to FDA's determination through the 510(k) process that this technology and its intended use was not "substantially equivalent" to existing medical imaging technology. Interestingly enough, with time and experience FDA recently proposed a "reclassification" of digital mammography imaging equipment from class III to class II. Has the risk of digital mammography changed over time? No. What presumably has changed is the confidence that the agency has in assuring that new digital mammography systems will be safe and effective through adherence to requirements less than a device-by-device demonstration of safety and effectiveness that is required by PMA.

To the best of my knowledge, there has never been a study correlating 510(k) clearance and time to market entry. In fact, not all devices that receive 510(k) clearance actually go to market. There are simply too many factors other than fulfilling FDA requirements that determine whether a new device actually makes it to market, let alone doing so in a timely manner. Your question reflects the universally recognized view that FDA is the gatekeeper. While this is true, not all devices get beyond the gate. Nevertheless, regulation in class II with the possibility of a timely clearance does a tremendous amount to ensure that the manufacturer is not deprived of at least the opportunity to pursue market introduction. This is too often an underappreciated consequence of being eligible for a 510(k) review. Being determined to be class III, on the other hand, signals a risky, resource intensive path to the same gate and beyond. Unfortunately, relatively few manufacturers are capable of assuming the risk and burden associated with Class III regulation. Even successful companies find themselves not being able to compete in the marketplace because of the postmarket burden associated with their Class III status. Given the importance of proper classification for new medical technology, it is critical that the 510(k) process results in the correct decision and that the outcome of the process is not constantly second guessed.

2. *The January 2009 GAO report studied the entire 510(k) process yet made recommendations related only to the approval process for Class III devices (i.e., pacemakers and heart replacement valves). We know that Class III devices involve much more risk in the use of the product, such as they are expected to be used to maintain life or which special controls may be expected to maintain safe*

use of the product. When looking at a risk-based model, which includes ensuring that more scrutiny and resources are devoted to ensuring the safety of those products that pose the most risk to patients, it appears that GAO focused their recommendations appropriately to ensure safety for patients. Do you agree that Class III devices are those which should remain the focus of reform, to ensure appropriate assurances are made for the safety of those devices which pose the most risk to patients?

To answer your question with a simple “yes” perpetuates a fundamental misunderstanding with FDA device regulation, namely that a device’s regulatory classification reflects the device’s inherent risk. As I stated in response to question Number 1, a Class II device may present the same or greater risk than a Class III device. Regardless of regulatory class, every risk that can be reasonably mitigated should be, and those risks that cannot be mitigated must be viewed in the context of the device’s probable benefit. To a very large degree, this is accomplished through FDA’s existing regulatory framework for medical device regulation.

Other than the GAO’s observations regarding the “preamendment” class III devices that remain subject to 510(k) requirements, I am not aware of evidence that suggests that FDA regulation of class III devices requires reform. Barring the class III devices that were the focus of the GAO’s report, FDA regulation of class III devices represents the most strict and comprehensive regulation in the world.

In regard to the “preamendment” class III devices that were the focus of the GAO report, FDA has initiated the steps necessary to fill this gap in regulation. At this stage, all that the agency needs is the commitment and resources to follow through on its actions. Congress can certainly provide support to FDA to this end.

The criticisms that intermittently surface with the 510(k) program go deeper than what was investigated by the GAO. We must all realize that it is the 510(k) program that sorts out which new devices are regulated in class II and which ones are placed in Class III subject to rigorous PMA requirements. Therefore, if we agree that class III devices deserve the greatest amount of FDA attention, we must also acknowledge that it is the 510(k) process that will determine which devices receive the extra attention.

There has been little criticism of FDA because of the devices that are determined to be class III through the 510(k) process. With the exception of the recipients of these decisions, there seems to be acceptance that these decisions are appropriate. The intermittent criticism of the program seems to always focus on a small proportion of the overall agency decisions that allow new devices to go to market in class II. It is my opinion that these criticisms can be resolved with a better understanding of the 510(k) program and a slight modification in how FDA approaches decision-making. In any event, criticism over a small number of

Agency decisions should not result in wholesale changes to what is otherwise a highly successful regulatory program.

Although not required by either of your questions, I have a suggestion that may address the intermittent criticisms. As I stated in my oral and written testimony, I favor FDA promulgating Class II special controls for all Class II devices. To date, the only Class II devices that have special controls are the ones that have been the subject of post-1990 rule-making which made it “convenient” for FDA to take this type of action. Convenience should not be the determinant of whether optimum regulation is achieved. Just as the preamendments Class III devices require PMA, Class II devices require special controls. Prioritizing the hundreds of Class II device types and beginning the process of promulgating special controls to assure safety and effectiveness will fulfill the intent of the law, increase regulatory consistency, and lead to a more credible and transparent 510(k) process. All that is required to begin this process is direction and resources.

