DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
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STATEMENT

OF

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FOOD AND DRUG ADMINISTRATION
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BEFORE THE

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UNITED STATES SENATE

"MEDICAL DEVICES:
PROTECTING PATIENTS AND PROMOTING INNOVATION"

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INTRODUCTION

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

The Impact of Regulation on Device Innovation

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

U.S.-based companies dominate the roughly $350 billion global medical device industry. The U.S. medical device industry is one of the few sectors, in these challenging economic times, with a positive trade balance.[1] In 2000, the U.S. medical device industry ranked 13th in venture capital investment—now, a decade later, it's our country's fourth largest sector for venture capital investment.[2] In fact, more than 62 percent of the $631.4 million that venture capital

[1] PwC (formerly PriceWaterhouseCoopers), "Medical Technology Innovation Scorecard" (January 2011) at page 8, available at *http://pwchealth.com/cgi-local/hregister.cgi?link=reg/innovation-scorecard.pdf*.
[2] PriceWaterhouseCoopers/National Venture Capital Association, MoneyTree™ Report, Data: Thomson Reuters, Investments by Industry Q1 1995 – Q4 2010, available at *http://www.nvca.org*.

invested in the life sciences in the third quarter of 2011 went to medical device companies.[3] And, the medical device industry has produced a net gain in jobs since 2005, even while overall manufacturing employment has suffered.

As noted in a January 2011 report on medical technology innovation by PwC (formerly PriceWaterhouseCoopers), the U.S. regulatory system and U.S. regulatory standard have served American industry and patients well. As that report states, "U.S. success in medical technology during recent decades stems partially from global leadership of the U.S. Food and Drug Administration. FDA's standards and guidelines to ensure safety and efficacy have instilled confidence worldwide in the industry's products. Other countries' regulators often wait to see FDA's position before acting on medical technology applications and often model their own regulatory approach on FDA's."[4]

In terms of time to market, an industry-sponsored analysis[5] shows that low-risk 510(k) devices without clinical data (80 percent of all devices reviewed each year) came on the market first in the United States as often as, or more often than, in the European Union (EU). The EU typically approves higher-risk devices faster than the United States because in the EU, manufacturers must demonstrate safety and performance, while in the United States the standard for approval is safety and effectiveness.[6]

FDA has been meeting or exceeding goals agreed to by FDA and industry under the Medical Device User Fee Amendments (MDUFA) for approximately 95 percent of the

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

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

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

[6] See "Recast of the Medical Devices Directives: Public Consultation," available at *http://ec.europa.eu/consumers/sectors/medical-devices/files/recast_docs_2008/public_consultation_en.pdf*; European Commission, "Guidelines on Medical Devices: Clinical Evaluation: A Guide for Manufacturers and Notified Bodies" (Dec. 2009), at p. 4, available at *http://ec.europa.eu/health/medical-devices/files/meddev/2_7_1rev_3_en.pdf.*

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

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

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

Smart Regulation's Role in Facilitating Medical Device Innovation

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

Our goal has been to ensure that safety and effectiveness and innovation are complementary, mutually supporting aspects of our mission to promote the public health. As part of our process to improve CDRH's internal systems, we first reached out to stakeholders to hear their concerns and listen to their recommendations about our premarket programs. This is what we heard: industry felt that inadequate predictability, consistency, and transparency were

stifling innovation and driving jobs overseas; and consumer groups, third-party payers, and some health care professionals believed that one of our premarket pathways—the 510(k) program—did not provide adequate protection for American patients and did not generate sufficient information for practitioners and patients to make well-informed treatment and diagnostic decisions. In turn, CDRH employees expressed concerns that the 510(k) program had not adapted to the increasing complexity of devices, and that poor-quality 510(k) submissions, poor-quality clinical studies conducted in support of PMA applications, and an ever-growing workload were straining already overburdened premarket programs.

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

In August 2010, following extensive public input, we released two reports that identified issues regarding our premarket programs and proposed potential actions for us to take to address the underlying root causes. The number one problem we found was insufficient predictability in our premarket programs, which can create inefficiencies, increase costs for industry and FDA, and delay bringing safe and effective products to market. We identified several root causes of these issues. They include very high reviewer and manager turnover at CDRH (almost double that of FDA's drug and biologics centers); insufficient training for staff and industry; extremely high ratios of employees to front-line supervisors; insufficient oversight by managers; CDRH's rapidly growing workload, caused by the increasing complexity of devices and the number of overall submissions we review; unnecessary and/or inconsistent data requirements imposed on device sponsors; insufficient guidance for industry and FDA staff; and poor-quality submissions from industry.

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

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

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

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

Specific steps that we are taking include:

- Issuing guidance clarifying the criteria used to make benefit-risk determinations a part of device premarket decisions. This will provide greater predictability and consistency and apply a more patient-centric approach by considering patients' tolerance for risk in appropriate cases (draft guidance issued August 15, 2011);

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

efficiently, and that we appropriately apply the least-burdensome principle. For example, CDRH created the internal Center Science Council to actively monitor the quality and performance of the Center's scientific programs and ensure consistency and predictability in CDRH scientific decision-making (Center Science Council established March 31, 2011);

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

To best serve patients, both the medical device industry and FDA must have the flexibility to be innovative and entrepreneurial. First, CDRH must continue making critical improvements to our device program. Second, the medical device industry and CDRH must work together to ensure that the Center receives high-quality submissions, which contain the

information we need to make well-informed and timely decisions. Finally, CDRH must have adequate and stable resources to get the job done right and quickly. The latter is the subject of medical device user fee legislation reauthorization and Congressional appropriations.

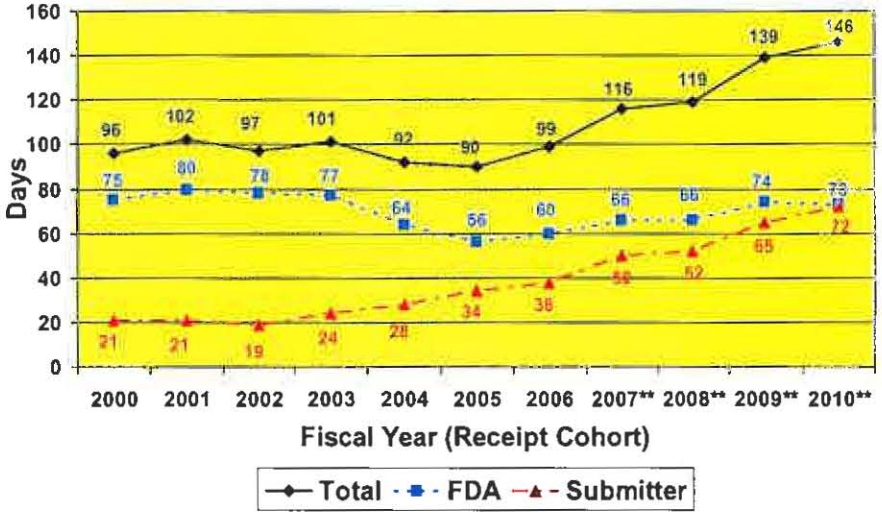
We believe that the actions we are taking now will have a positive impact within the coming year by providing greater predictability of data requirements through guidance, reducing unnecessary data requests through training and policy and process changes, implementing policies to appropriately balance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

Performance Issues in the Premarket Review Process

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

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

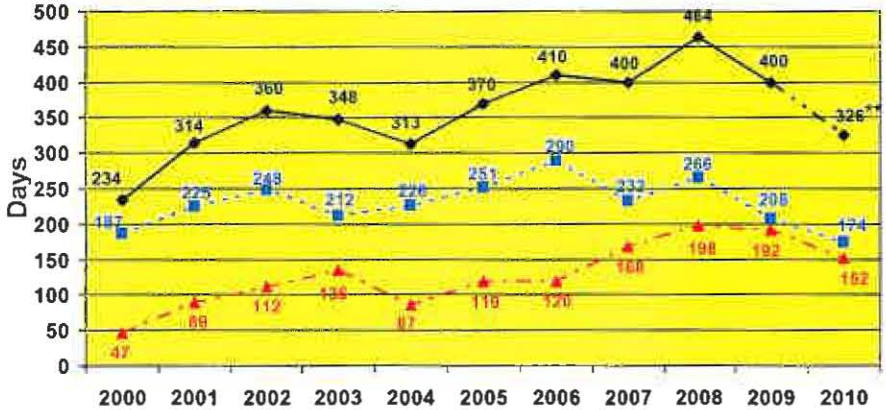
Average Time to Decision:
510(k)s*



*SE and NSE decisions only; times may not add to total due to rounding
**Cohorts still open as of September 30, 2011, data may change

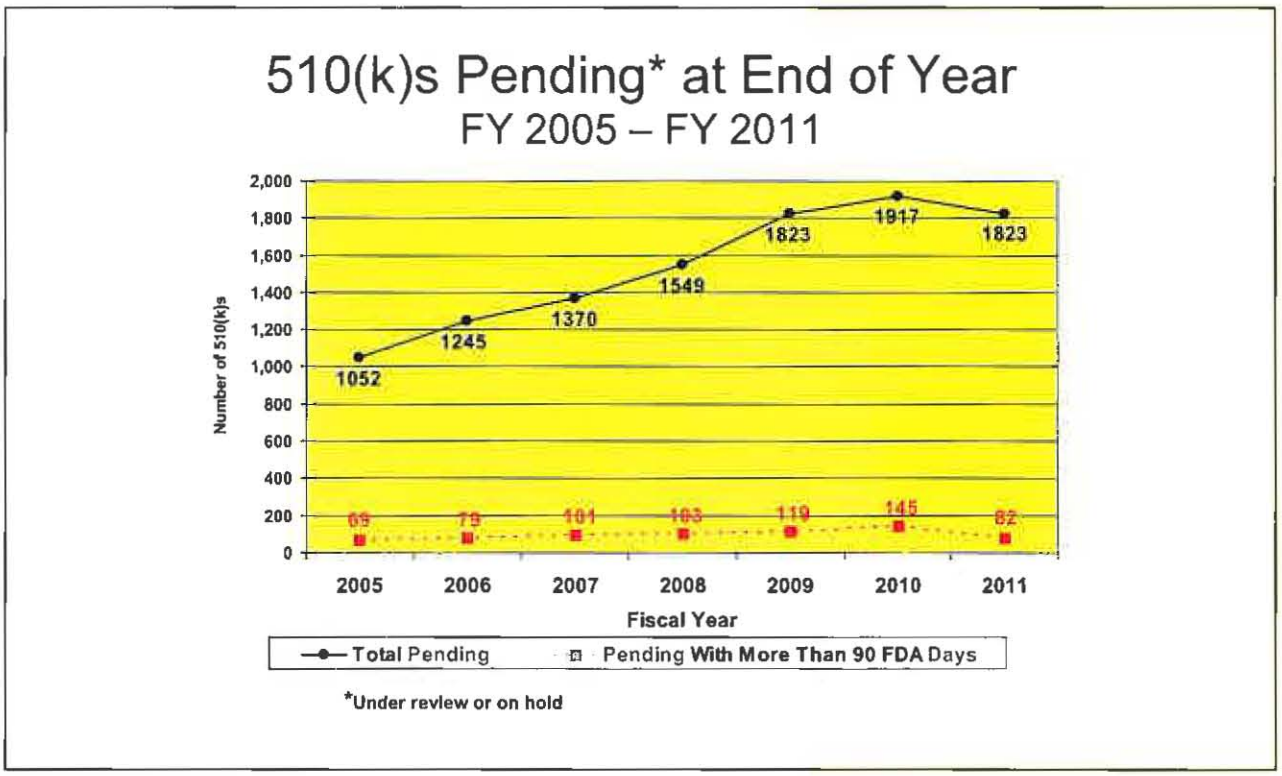
Average Time to MDUFA Decision on PMAs and Panel-Track Supplements (non-expedited)*

*Times may not add to total due to rounding; some cohorts still open - data may change

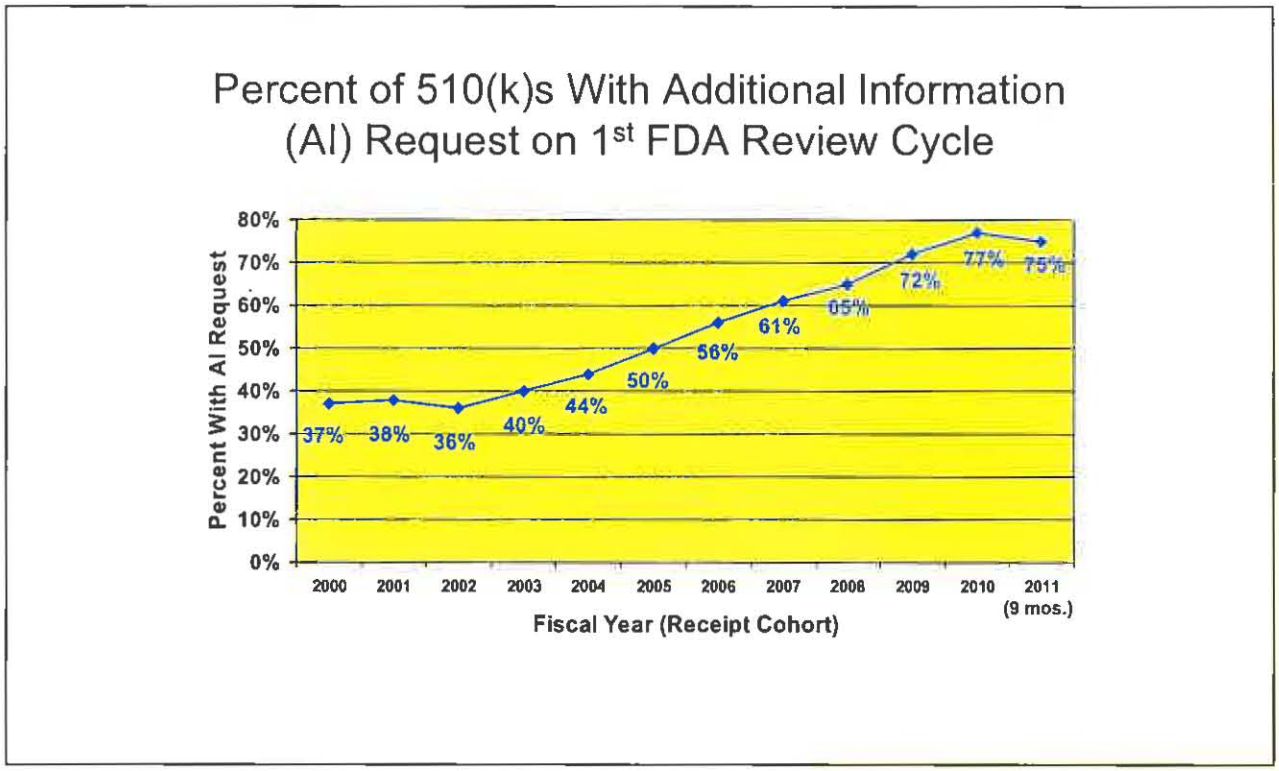


**As of September 30, 2011 there are 16 applications without a decision; the average time to decision will increase as the cohort closes.

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



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



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

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

Moving Forward: Reauthorization of MDUFA

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

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

As the MDUFA reauthorization process moves forward, it is important to understand and keep in mind the significant differences between FDA's medical device premarket review programs—the 510(k) and PMA programs—and the Agency's program for review of drugs under the Prescription Drug User Fee Act (PDUFA). PDUFA fees account for about two-thirds of the drug review program's budget—nearly $568 million in FY2010—while user fees under MDUFA fund only about 20 percent of the device review program.

The structures of the user fee programs also differ in very significant ways. The fee for FY 2012 associated with review of a New Drug Application (NDA) requiring clinical data is $1,841,500[7]—much greater than the $220,500 fee[8] charged for review in FY 2012 of a PMA for

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

high-risk medical devices (a business with gross receipts under $30 million qualifies for the "small business" PMA fee of about $55,000—75 percent less than the full fee). For lower-risk devices cleared under the 510(k) review program, the fees are even lower: $4,049 per 510(k) application review ($2,024 for small businesses).

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

Smart Regulation's Role in Assuring Patient Safety

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

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

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

patients well by preventing devices from entering the U.S. market that were later shown to be unsafe or ineffective.[9]

Some have suggested that the United States adopt the medical device regulatory system of the EU. Yet, outside the United States, pressure is growing toward *greater* premarket scrutiny of medical devices. A recent report concluded that "[f]or innovative high-risk devices the future EU Device Directive should move away from requiring clinical safety and 'performance' data only to also require pre-market data that demonstrate 'clinical efficacy,'" and "[t]he device industry should be made aware of the growing importance of generating clinical evidence and the specific expertise this requires."[10]

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

Because of these factors, it is impossible to track medical device approvals, adverse events, or recalls in the EU, since there are few to no publicly accessible, centralized systems for collecting and monitoring information about medical device approvals or safety problems. The use of Notified Bodies has been criticized as encouraging "forum shopping" by sponsors to

[9] See, *e.g.*, D. Cohen and M. Billingsley, "Europeans Are Left to Their Own Devices," British Medical Journal, 342:d2748 (2011), available at *http://www.bmj.com/content/342/bmj.d2748*.
[10] Belgian Health Care Knowledge Centre, "The Pre-market Clinical Evaluation of Innovative High-risk Medical Devices," KCE Reports 158 (2011) at p. vii, available at *http://www.kce.fgov.be/index_en.aspx?SGREF=202677*.
[11] See "Recast of the Medical Devices Directives: Public Consultation," available at *http://ec.europa.eu/consumers/sectors/medical-devices/files/recast_docs_2008/public_consultation_en.pdf*; European Commission, "Guidelines on Medical Devices: Clinical Evaluation: A Guide for Manufacturers and Notified Bodies" (Dec. 2009), at p. 4, available at *http://ec.europa.eu/health/medical-devices/files/meddev/2_7_1rev_3_en.pdf*.

identify those Notified Bodies with the most lax operating standards, and the varying levels of expertise among Notified Bodies has been critiqued.

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

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

FDA continues exploring ways to get medical products to patients with serious and life-threatening diseases or conditions faster, but lowering U.S. approval standards isn't in the best interest of American patients, our health care system, or U.S. companies whose success relies on the American public's confidence in their products. According to the IOM, "FDA should be clear that its role in facilitating innovation in medical devices is to develop regulatory thresholds

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

[13] "The Truth About Medical Devices," British Medical Journal, vol. 342, at pp. 1115-1130 (May 21, 2011), available at *http://www.bmj.com/content/342/7807/Feature.full.pdf* (Deborah Cohen, "Out of Joint: The Story of the ASR," *British Medical Journal* 2011; 342:d2905; Deborah Cohen and Matthew Billingsley, "Medical Devices: European Patients Are Left to Their Own Devices," *British Medical Journal* 2011; 342:d2748); see also Fiona Godlee, "Editorial: The Trouble With Medical Devices," *British Medical Journal* 2011; 342:d3123, available at *http://www.bmj.com/content/342/bmj.d3123.full*; Carl Heneghan et al., "Medical-Device Recalls in the UK and the Device-Regulation Process: Retrospective Review of Safety Notices and Alerts," *BMJOpen* (May 2011), available at *http://bmjopen.bmj.com/content/early/2011/05/12/bmjopen-2011-000155.full.pdf*.

that are rigorous enough to satisfy the agency's primary objective of ensuring that marketed devices will be safe and effective throughout their life cycles but realistic enough to permit timely entry of new devices into the market."[14]

We are pleased that a U.S. medical device industry trade association, AdvaMed, has stated that it supports maintaining our current rigorous standards of safety and effectiveness for marketing medical devices: "The medical technology industry has long recognized that a strong and well-functioning FDA is vital to maintaining America's preeminence in medical technology innovation, and we support the current regulatory framework in the U.S."[15]

CONCLUSION

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

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

[14] Institute of Medicine, "Medical Devices and the Public's Health: The FDA 510(k) Clearance Process at 35 Years" (2011), at p. 197, available at *http://books.nap.edu/openbook.php?record_id=13150*.
[15] Advanced Medical Technology Association (AdvaMed), "AdvaMed Statement on the House Energy and Commerce Subcommittee Hearing on FDA Device Regulation" (July 20, 2011).

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