DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

STATEMENT

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BEFORE THE

SENATE SPECIAL COMMITTEE ON AGING

UNITED STATES SENATE

"A DELICATE BALANCE: FDA AND THE REFORM OF THE MEDICAL DEVICE APPROVAL PROCESS"

APRIL 13, 2011

Release Only Upon Delivery

INTRODUCTION

Mr. Chairman, Ranking Member Corker, and Members of the Committee, I am Dr. William Maisel, Deputy Center Director for Science and Chief Scientist of the Center for Devices and Radiological Health (CDRH) at the Food and Drug Administration (FDA or the Agency). Thank you for the opportunity to discuss the actions FDA is taking to enhance medical device safety, and our efforts to meet our public health goals of assuring the safety and effectiveness of medical devices while fostering innovation and important public health advances.

I joined CDRH last summer while the Center was in the midst of arguably the most comprehensive program review in its 35-year history. As part of this review, the Center has taken a hard look at how we conduct our business, how we utilize scientific information and make decisions, and how we can improve the health of American patients.

We have responded by taking strategic steps to strengthen our premarket evaluation and post-market surveillance of medical devices, while simultaneously promoting opportunities for medical device innovation. These steps will improve predictability, consistency, and transparency in our premarket and post-market programs and strengthen our scientific decision-making. However, we cannot do this alone.

Industry also shares a responsibility for the success of the review process and safety of medical devices. Data show that some companies submit poor quality applications, ask to meet with us but then ignore our feedback, or conduct poor quality clinical studies. This leads to unnecessary delays, wastes time and money for both industry and FDA, and exposes patients to unnecessary risks.

I am pleased to have this opportunity to provide an update on the important progress we have made in key programs at CDRH.

Background

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

The Medical Device Amendments of 1976 to the Federal Food, Drug, and Cosmetic Act (FD&C Act or the Act) gave FDA specific authority to regulate the safety and effectiveness of medical devices. When FDA makes a risk-based classification determination for a type of device, it assigns it to one of three regulatory classes.

Class I is the lowest risk category of devices and includes items such as adhesive bandages. These are devices for which the general controls of the Act—which include establishment registration and device listing, compliance with current Good Manufacturing Practice and labeling, record-keeping, and reporting requirements—are sufficient to provide reasonable assurance of safety and effectiveness.

Class II is a medium-risk category of devices and includes devices such as intravenous catheters and powered wheelchairs. These are devices for which general controls, by themselves, are insufficient to provide reasonable assurance of safety and effectiveness of the device, and for which there is sufficient information to establish special controls, such as special labeling requirements, mandatory performance standards and post-market surveillance, to provide such assurance.

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

Devices must comply with the statutory standards for PMA approval, 510(k) clearance, or 510(k) exemption, all of which include considerations of safety and effectiveness. Most devices are cleared through the premarket notification [510(k)] process. FDA typically evaluates more than 4,000 510(k) applications and approximately 40 original PMA applications per year.

Improvements to the 510(k) Program

The 510(k) program is intended to support FDA's public health mission by meeting two important goals: making available to consumers devices that meet the statutory standards pertaining to safety and effectiveness, and fostering innovation in the medical device industry. In recent years, concerns have been raised both within and outside of FDA about whether the current 510(k) program optimally achieves these goals. In light of these concerns, and in keeping with the good government practice of periodically assessing the effectiveness of existing programs, FDA launched in September 2009 a two-pronged, comprehensive assessment of the 510(k) process to determine whether changes should be made to the program so that it can better achieve its goals. The first part of this assessment was the formation of two staff working groups—one to review the 510(k) program and make recommendations to strengthen it; the other to review how the Agency incorporates new science into its decision-making process and recommend how it can do so more predictably. As a second part of this assessment, FDA requested an independent evaluation by the Institute of Medicine (IOM). Established by the National Academy of Sciences, the IOM provides independent, objective, evidence-based advice to policymakers, health professionals, the private sector, and the public. The results of the IOM program evaluation are expected to be publicized this summer.

Importantly, FDA sought public input during both the development and review of the two internal reports. We engaged in extensive public outreach in developing and receiving

feedback on the preliminary proposals developed by the working groups, including two public meetings, three town hall meetings, three public dockets and many smaller meetings with different stakeholder groups. Final reports containing 55 recommendations were issued in August, 2010. In keeping with our commitment to transparency and stakeholder collaboration, FDA again sought public comment on the reports and recommendations before moving to its next step.

In January 2011, after reviewing public comment, the Agency announced actions it would take to strengthen the 510(k) process. FDA intends to initiate 25 actions implementing 47 of the 55 recommendations, including development of new guidance and enhancement of staff training. The Agency is also providing the IOM an opportunity to provide feedback on seven particularly complex recommendations before making a final decision on their implementation. For the recommendations being implemented, there will be additional opportunities for public input, where appropriate. For example, we held a public meeting last week to seek additional feedback on the recommendation to create an online repository of medical device labeling to include photographs that would provide easier access to important health information for patients and health care professionals, without breaching manufacturers' product trade secret information.

Implementation of our 510(k) action plan will improve product safety. For example, the recommendation to issue guidance on clinical study design will strengthen the design and performance of premarket clinical trials used to assess medical device safety and effectiveness. As part of the action plan, CDRH is also implementing a standard practice

of issuing "Notice to Industry" letters to allow the Agency to more quickly inform stakeholders of new safety concerns, or to clarify evolving regulatory expectations in response to new scientific information. Finally, FDA is strengthening collection and analysis of post-market information by modernizing its information technology (IT) infrastructure, and by developing better data sources, methods, and tools for analyzing meaningful post-marketing information.

The 510(k) and Science workgroup reports, recommendations, and useful related links are all available on FDA's website at *http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHReports/ucm239448.htm*.

Innovation Initiative

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

- Establishing a priority review program for pioneering technologies;

- Establishing a voluntary, third-party certification program for U.S. medical device test centers designed to promote rapid improvements to new technologies during a product's development and clinical testing stages;
- Creating a publicly available core curriculum for medical device development and testing to train the next generation of innovators;
- Better leveraging of device experience and data collected outside the United States; and
- Engaging in formal horizon scanning—the systematic monitoring of medical literature and scientific funding—to identify and predict important advances in technology, in order to prepare for and respond to transformative innovative technologies and scientific breakthroughs.

Medical Device User Fee Act Performance

While the Agency continues its efforts to improve the 510(k) program and encourage product development, FDA's device review performance has been consistently strong. As FDA's FY2010 Medical Device User Fee Act Performance Report to Congress indicates, 95 percent of the over 4,000 medical device applications subject to user fees that FDA reviews every year (FDA reviews over 9,000 submissions annually) are reviewed within the goals that were agreed to by the medical device industry under the Medical Device User Fee Amendments of 2007 (MDUFA). Under the 510(k) program—the pathway used for 90 percent of the devices we examine each year—90 percent of our

reviews were completed in 90 days or less, and 98 percent of reviews were completed in 150 days or less, as we committed to do under MDUFA.

There are a limited number of areas in which we are not meeting the goals agreed to with the industry, although our performance in those areas is generally improving. This is the result of several factors, including increasing workload, turnover of key staff, growing device complexity, and poor-quality submissions. The number of applications for premarket approval and panel-track supplements (for "breakthrough" devices) has increased by 48 percent over the past two years. In addition, medical devices are becoming more technologically complex, as reflected by the growing number and variety of technical experts that FDA must consult during the review process. Finally, a significant number of submissions received by the Agency are incomplete or fail to address basic elements, such as the device's description or proposed indications for use. Based on a recent analysis we performed, more than half of the 510(k) submissions received by FDA have quality problems. Although FDA is meeting its performance goals for 510(k)s, these submission quality problems delay the completion of the marketing clearance process and unnecessarily divert resources from more productive activities in the review process. The current legislative authority for MDUFA, reauthorized in 2007 by the FDA Amendments Act (FDAAA), will expire in September 2012. Accordingly, FDA has been holding public meetings and conducting discussions with both regulated industry and stakeholder groups in developing recommendations for reauthorization of this critical program.

Post-market Surveillance Activities

FDA recognizes the importance of post-market surveillance (PMS) and utilizes a multi-faceted approach to monitor the performance of medical devices after marketing clearance or approval to ensure their continued safety and effectiveness. FDA uses several PMS tools to accomplish effective monitoring of device performance. For example, the Agency requires medical device manufacturers to follow certain PMS requirements for marketed devices, including adverse event reporting for all devices, and tracking systems and post-market surveillance studies or post-approval studies for select devices. This approach provides for nationwide surveillance through adverse event reporting, complemented by targeted efforts, such as post-approval studies. However, medical devices present unique post-market challenges because of their diversity and rapid product evolution. Importantly, key infrastructure improvements, such as increased electronic adverse event reporting, the establishment of the Unique Device Identification (UDI) system, and the incorporation of UDI into health-related electronic records, will have a profound and positive impact of the nation's ability to adequately monitor medical devices in the post-market period.

Mandated Post-market Studies

FDA currently has two authorities with which to require manufacturers to conduct postmarket studies: post-approval study (PAS) authority under section 515 of the Act, and PMS authority under section 522 of the Act. PAS authority allows FDA to ask a device manufacturer to conduct a study (or studies) of a PMA device, as a condition of its

approval, to address product performance in the post-market period (e.g., long-term safety). Consistent with the Agency's transparency initiative, overall study status, including study results for completed studies, are posted on FDA's website.

Authority under section 522 allows FDA to require post-market surveillance studies for certain Class II or Class III devices, for example to address significant public health issues that arise in the post-market period. Section 522 studies may be required for certain categories of devices, including implants and devices expected to have significant use in pediatric populations.

Over the past two years, the program has significantly expanded, and there are currently 38 section 522 studies in process. There are a total of 337 PAS requirements. FDA carefully monitors manufacturer compliance with their post-market responsibilities. As of April 6, 2011, 290 studies (86 percent) are in compliance [this includes 150 completed (44 percent) and 140 ongoing (42 percent)]; 47 studies (14 percent) are out of compliance. Reasons for studies being out of compliance include failure to progress according to the agreed upon timeline (46) and failure to agree on a protocol within six months of PMA approval. In addition, we have developed a PAS Inspection Program to audit select PASs for possible violations of applicable regulations. Failure to comply with a required PAS or a section 522 Order can result in regulatory action including, but not limited to, a warning letter, seizure, injunction, and/or civil money penalties.

Adverse Event Reporting

FDA uses two principle systems to capture device-related adverse event and product problem reports: the Medical Device Reporting regulation (MDR) and the Medical Product Safety Network (MedSun).

MDR is the mechanism by which FDA receives over 300,000 significant medical device adverse events from manufacturers, importers, and user facilities annually. FDA carefully evaluates the reports received to identify safety concerns of public health importance. FDA recognizes the limitations inherent in passive reporting systems such as MDR, including underreporting of adverse events and the submission of incomplete or difficult-to-understand reports. Many reports lack sufficient information to accurately identify the product in question. FDA works with reporters to partially offset this limitation. In addition, the UDI system under development, described below, will help overcome this shortcoming.

Recognizing the shortcomings of passive reporting systems, FDA launched MedSun in 2002. MedSun is an "active" adverse event reporting program that allows FDA to work collaboratively with the clinical community to identify, understand, and solve problems with the use of medical devices. Over 350 health care facilities, primarily hospitals, participate in the MedSun Network. The Agency has continued to develop its MedSun regional representative program, comprised of trained MedSun representatives, including physicians and nurses having expertise in risk management, patient safety, quality improvement, biomedical/clinical engineering, materials management, and surgical services, who facilitate on-site data gathering, and will focus on efforts to automate

detection and reporting, and improve outreach to user facilities in the MedSun system to stimulate user facility reporting.

Data Mining

To complement individual review of adverse event reports, FDA has implemented data mining capabilities which, based on automated statistical algorithms, can detect potential safety signals among the hundreds of thousands of reports received annually. Early experience in piloting these capabilities with select device groups has proved promising. Efforts are currently underway to evaluate the use of data mining for all device malfunction reports which comprise over 60 percent of all adverse event reports.

Device Recalls

A medical device recall is a method of removing or correcting products that are in violation of laws administered by the Agency, and can serve as a mechanism to advise patients and healthcare providers about dangerous devices that are defective or otherwise improperly marketed.

Role of Industry in Recalls

Generally, a recall is triggered when a manufacturer recognizes that a product failure requiring a recall exists. A product failure can include problems such as design flaws, errors in labeling or defects introduced during the manufacturing process. In most cases, firms that market defective or otherwise violative devices recall them voluntarily, often following discussion with FDA of the Agency's concerns about their products.

Role of FDA in Recalls

FDA has authority to compel recalls of medical devices that pose significant risks of injury or death to patients. While this authority is a critical public health protection, the Agency has only had to use this authority sparingly, such as when a manufacturer fails to voluntarily recall a device that is a serious health risk. Once the device recall process is initiated by the firm, FDA classifies, coordinates, and monitors the recall.

The success of FDA's device recall efforts requires prompt notice to patients and health care professionals and efficient recall classification. CDRH is leading a range of transformative projects to build its strength in these areas.

In fall 2010, CDRH began its Recall Process Improvement project to enhance the efficiency and clarity of the medical device recall process. In March 2011, staff developed strategies to improve notification and classification of recalls. These strategies include educating industry on recall documentation and reporting, improving efficiency of communication between Agency components, and standardizing the recall classification processes. Further, the Agency has improved its internal tracking of device recalls.

FDA continues its effort to assist manufacturers and is planning an online educational tool focusing on recalling firms' reporting obligations. Educating industry on the information required to be submitted following initiation of a recall will result in more

timely and complete recall documentation. Finally, as requested by industry, FDA is preparing a guidance document that clarifies the difference between modifying a device to enhance safety to respond to adverse events, and a modification to correct a violation. CDRH anticipates issuing the guidance document by August 31, 2011.

Registries

FDA takes a proactive role in fostering registry development. FDA has worked with multiple stakeholders to begin, or further the development of, many national registries, and is currently involved in over 20 registry efforts. These include, among others, an anaplastic large cell lymphoma (ALCL) registry to collect information regarding cases of breast implant-associated ALCL; the Improving Pediatric and Adult Congenital Treatments registry on transcatheter procedures and devices used to treat congenital heart disease; and the National Implantable Cardioverter Defibrillator registry, which has expanded to identify adverse events associated with defibrillator leads. In addition, registries are often used in the conduct of mandated post-market studies. Currently, there are over 60 PAS studies that involve registries.

FDA is leading an effort to develop and implement a national strategy for the best public health use of health-related electronic data that incorporates UDIs and leverages existing procedure and device registries. A workshop addressing the issues and challenges involved with incorporating UDIs into health-related electronic records is planned for this year.

FDA has also recently led efforts to link national registry data with Center for Medicare and Medicaid Services claims data to study the safety of drug-eluting coronary stents, endoscopic vein harvesting for coronary artery bypass grafting, and transmyocardial revascularization for intractable angina. Further linkage capabilities will be explored this year under the Sentinel Initiative.

Medical Device Epidemiology Network (MDEpiNet)

The MDEpiNet Initiative was launched in 2010 to create collaborations with academic centers that have epidemiologic, statistical, and clinically relevant expertise. This established network will join with FDA experts to address evidence gaps and develop innovative approaches for conducting robust studies to improve FDA's understanding of the safety and effectiveness of medical devices throughout their life cycles. This public-private partnership will involve other stakeholders, such as other public health agencies, data holders, and consumer representatives, and will leverage their collective expertise to significantly improve the credibility, relevance, and efficiency of clinical research regarding medical devices. Evidence synthesis will be an important component of MDEpiNet. As medical devices move through their total product life cycles, there is a need to continually update their benefit/risk profiles in the context of new scientific evidence. Advances in epidemiologic and statistical methods and information technology now permit access to, and synthesis of, evidence available from varied data types and data sources including clinical trials, PASs, registries, health-related claims data, and published literature.

Unique Device Identification (UDI)

Section 226 of FDAAA of 2007 directs FDA to promulgate regulations establishing a UDI system for medical devices. FDA is developing a proposed regulation to issue in 2011. The system established by the rule, once finalized, will require the label of every medical device to bear a UDI, except where the rule provides for alternative placement of the UDI or provides an exception for a particular device or type of device. The UDI Database, which will be built and maintained by FDA, will contain identifying information about the device. It will not contain any patient information.

Establishment of a UDI system is of critical importance in fulfilling the promise of a robust and multi-faceted PMS effort. Health-related electronic data from large data sources, such as health insurers and integrated health systems, contain a wealth of public health information that could be harnessed to contribute to understanding device safety and effectiveness. Currently, however, these data cannot be used to identify specific device exposures in patients. A vast amount of potentially useful data regarding patient safety and outcomes remains untapped. Incorporation of this key data element will greatly facilitate many important public health-related activities including:

- reducing medical errors;
- reporting and assessing device-related adverse events and product problems;
- facilitating recalls;
- assessing the benefit/risk profile of medical devices in large segments of the U.S. population;
- post-market surveillance;

- tracking and tracing;
- anti-counterfeiting/diversion;
- import review;
- disaster/terror preparation; and
- anticipating and tracking product shortages.

Recognizing the transformative nature of UDI, FDA is developing the IT infrastructure necessary to support the effort, including the creation of a searchable UDI database that will serve as the authoritative source for all UDIs and UDI-related information. FDA is planning to award a contract for UDI database development in 2011. FDA is also planning to incorporate UDIs into adverse event reporting and to link UDIs to manufacturer registration and product listing to facilitate adverse event analysis and identification of important safety signals. Furthermore, pilot efforts are underway to incorporate UDIs into other registries that are early in their development. FDA is also hosting a workshop this year to identify opportunities and challenges involved with incorporating UDIs into health-related electronic records.

Sentinel Initiative

FDA's Sentinel Initiative is aimed at fostering the development and use of a national infrastructure of electronic health care data systems for medical product safety surveillance. Sentinel will transform FDA's ability to track the safety of all FDA-regulated products, complementing existing systems such as those previously discussed. The incorporation of UDI into these data sources will greatly advance the device

component of the Sentinel Initiative and improve our understanding of the risk/benefit profile of medical devices. For active surveillance to be truly robust, longitudinal patient records are needed. As mentioned previously, registry data can be linked to longer-term data, such as claims data, to create longitudinal patient care profiles while adhering to existing standards for ensuring patient privacy. Within Sentinel, efforts are currently underway to explore best methods for linkages, as well as development of common data models across claims data sources and validation studies of claims-based outcomes. Sentinel is well-suited to such inquiries and development of optimal active surveillance efforts.

Government Accountability Office (GAO) Evaluations

In January 2009, GAO identified medical products safety in its High-Risk Series, in part, because of FDA's growing responsibilities, increasing product complexity, and the marked globalization of the medical products industry. FDA recognizes the challenges that GAO identified and is taking affirmative steps to implement measures designed to address GAO's identified concerns. For example, CDRH has taken important steps to strengthen post-market monitoring of device performance.

GAO has also cited FDA's failure to fully implement the requirement in the Safe Medical Devices Act of 1990 to either reclassify the remaining Class III pre-amendments device types (devices that were on the market on or before May 28, 1976) that are allowed to enter the market through the premarket notification process, or require PMAs for these devices. Since that report was issued, FDA has been addressing this concern using a risk-

based approach. Of the original 140 Class III 510(k) pre-amendment devices identified, only 26 remain subject to 510(k). CDRH is actively evaluating all 26 of these products, according to the process required by regulation, and expects to down-classify or require PMA's for the remaining products by the end of 2012.

CONCLUSION

FDA evaluates thousands of medical devices annually and the vast majority of these devices perform well and improve patient health. Through our recently completed comprehensive programmatic review, FDA is taking actions to further strengthen our scientific decision-making to increase the predictability, consistency, and transparency of our processes and policies, and to revolutionize the way we conduct postmarket surveillance. Through smarter device regulation, our efforts are already starting to pay off. In the last year, for example, we identified and addressed safety concerns affecting drug infusion pumps, automated external defibrillators, and medical imaging technologies that emit radiation, such as CT scanners. FDA's medical device center will continue to support the United States' position as the leader in safety, medical device technology, and innovation, and make good on our commitment to promoting and improving the health of the American public.

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