DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

JAN 2 7 2012

The Honorable Erik Paulsen
House of Representatives
Washington, D.C. 20515-2303

Dear Mr. Paulsen:

Thank you for your letter of November 3, 2011, cosigned by your colleagues in the Congressional Medical Technology Caucus and other members of Congress, expressing concerns about regulatory issues facing the medical device industry.

U.S.-based companies dominate the roughly $350 billion global medical device industry, and it is critical that we maintain American leadership in this field. The U.S. 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—a decade later, it is our country's fourth largest sector for venture capital investment.[2]

We agree with the statement in the October 2011 interim report of the President's Council on Jobs and Competitiveness[3] that a critical challenge for the drug and device approval processes is to *both* enable the timely development and availability of new therapies and technologies and protect patients from harm.[4] In fact, the Center for Devices and Radiological Health (CDRH) is undertaking a new, systematic approach to device regulation—one that will continue to focus on protecting public health by ensuring that devices are safe and effective, but will also focus on promoting public health by facilitating device innovation. The Council's report acknowledges this major initiative on the part of the Food and Drug Administration (FDA or the Agency) to streamline and improve the medical device approval process.[5]

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[1] PwC (formerly PriceWaterhouseCoopers), "Medical Technology Innovation Scorecard" (Jan. 2011) at p. 8, available at *http://www.pwc.com/us/en/health-industries/health-research-institute/innovation-scorecard.*

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

[3] President's Council on Jobs and Competitiveness, "Taking Action, Building Confidence: Five Common Sense Initiatives to Boost Jobs and Competitiveness," interim report (Oct. 2011), available at *http://files.jobs-council.com/jobscouncil/files/2011/10/JobsCouncil_InterimReport_Oct11.pdf.*

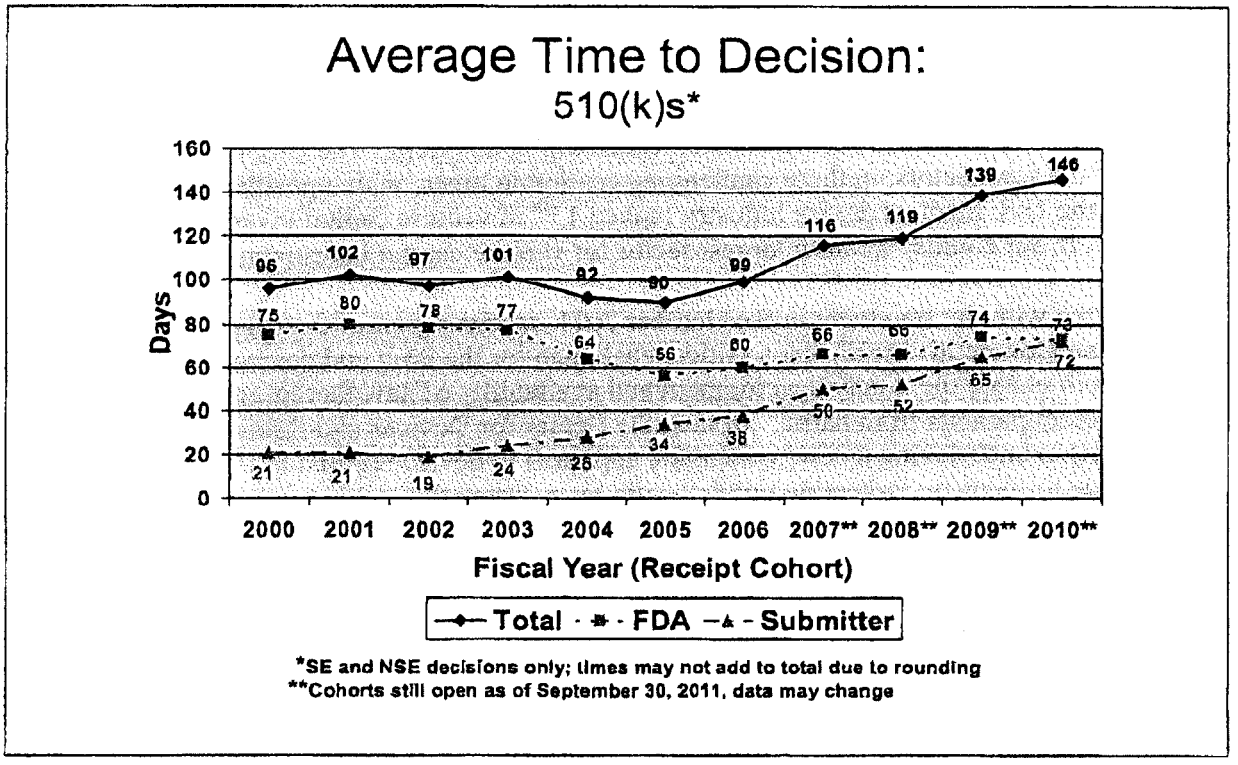
[4] Id. at p. 30.

[5] Id. at p. 7.

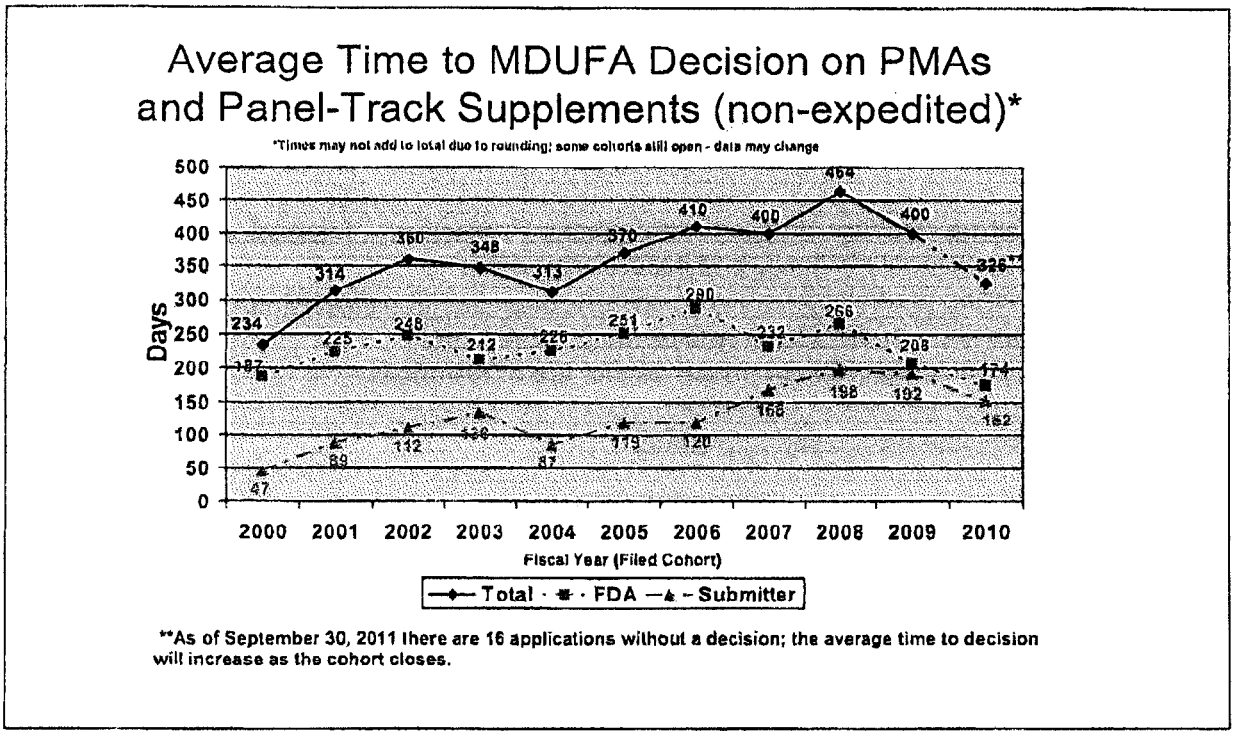
Improving CDRH's Premarket Review Programs

Your letter raises concerns about FDA performance in the medical device review process. 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 for premarket notification (510(k)s) and applications for premarket approval (PMAs)—the time that FDA has the application, *plus* the time the manufacturer spends answering any questions FDA may have—has increased.

Although FDA is meeting its 510(k) performance goals under the Medical Device User Fee Act (MDUFA), overall time to decision (i.e., FDA review time plus industry response time) for 510(k) submissions has been increasing since 2005, with industry time steadily increasing since 2002. This is due primarily to an increase in the number of review cycles and in the amount of time companies take to respond to requests for additional information.



Likewise, the total time for the review of PMAs has been increasing since 2004, with industry time increasing since at least 2000:



FDA recognizes its role in the increase in overall time to decision, and we are taking steps to address it. The two reports we released publicly in August 2010, with our analyses and recommendations, showed that we have not done as good a job managing our premarket review programs as we should have and that we need to take several critical actions to improve the predictability, consistency, and transparency of these programs.

For example, we have new reviewers who need better training. We need to improve management oversight and standard operating procedures (SOP). We need to provide greater clarity for our staff and for industry through guidance about key parts of our premarket review and clinical trial programs and how we make benefit-risk determinations. We need to provide greater clarity for industry through guidance and greater interactions about what we need from them to facilitate more efficient, predictable reviews. We need to make greater use of outside experts who understand cutting-edge technologies. And we need to find the means to handle the ever-increasing workload and reduce staff and manager turnover, which is almost double that of FDA's drugs and biologics centers.

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 United States 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:

- 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.

Specific steps that we are taking include:

- Issuing guidance clarifying the criteria used to make benefit-risk determinations a part of device premarket decisions to 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 SOP for when a reviewer can request additional information regarding a premarket submission and at what management level the decision must be made to provide greater predictability, consistency, and the appropriate application of the least-burdensome principle by reducing the number of inappropriate information requests (SOP issued November 2011);
- Creating SOP for managing review staff changes during the review of a premarket submission, in order to minimize the impact of staff reassignment during premarket review to ensure greater consistency in the Center for Devices and Radiological Health (CDRH) decision-making (SOP issued December 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 medical applications (draft guidance released July 19, 2011) and artificial pancreas systems (draft guidance released December 1, 2011);
- Revamping the guidance development process through a new tracking system and, to the extent resources permit, providing core staff to oversee the timely drafting and clearance of documents (December 2011);
- Improving communications between FDA and industry through enhancements to interactive review (some of these enhancements will be in place by the end of 2011 and are also the subject of user fee reauthorization discussions with industry);
- Issuing guidance describing the processes available to outside stakeholders to request additional review of decisions and actions by CDRH employees (draft guidance released December 27, 2011);
- Streamlining the clinical trial and 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 to create incentives to bring new technologies to the United States first (draft guidance issued November

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 devices);

- 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 (Council) to actively monitor the quality and performance of the Center's scientific programs and ensure consistency and predictability in CDRH scientific decision-making (Council established March 31, 2011);
- Creating a network of experts to help CDRH resolve complex scientific issues, which will ultimately result in more timely reviews. This network will be especially helpful as FDA confronts new technologies (SOP 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, and thereby leading to studies that are more likely to support the approval of their products (draft guidance released August 15, 2011);
- Issuing guidance describing current review practices for 510(k) submissions, to identify, explain, and clarify each of the critical decision points in the decision-making process FDA uses to determine substantial equivalence (draft guidance released December 27, 2011);
- Streamlining the *de novo* review process—the pathway by which novel, lower-risk devices without a predicate can come to market (draft guidance released September 30, 2011); and
- Piloting an internal Corrective and Preventive Actions (CAPA) system—a database in which office-level issues, such as inconsistency in application of policies or failure to follow policies or SOP, will be entered and assigned to a staff member for follow up and resolution, to formalize existing continuous improvement efforts and help to ensure that identified issues are tracked to resolution and appropriate corrective and preventive actions are taken (Office of Device Evaluation (ODE) pilot started December 2011).

It is our hope that taking actions to increase submission quality and avoid inappropriate requests for additional information, along with the receipt of adequate resources through budget authority and MDUFA reauthorization, will prevent avoidable delays and reduce total time to decision, which will, in turn, get safe and effective devices to market faster.

More details regarding our actions to improve the medical device premarket review process may be found on FDA's web site at

http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHReports/ucm276272.htm and *http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHReports/ucm276286.htm*.

Measuring Premarket Review Times

Your letter suggests that FDA should recognize and correct the disparity between "FDA time" versus "real time" when tracking device approvals. Pursuant to the performance goals agreed to by FDA and industry in 2007, MDUFA metrics reflect FDA time only; they do not reflect the time taken by device sponsors to respond to requests for additional information. As a part of MDUFA reauthorization discussions with industry, we are considering performance goals and tracking that would pertain to total (overall) time.

Utilizing the Least-Burdensome Approach in Device Regulation

We agree that a least-burdensome approach to medical device regulation should be followed. The 1997 Food and Drug Administration Modernization Act (FDAMA) added two provisions, known as "the least burdensome provisions," to the Federal Food, Drug, and Cosmetic Act (FD&C Act or the Act). CDRH implemented these provisions with a 2002 guidance document entitled, *The Least Burdensome Provisions of the FDA Modernization Act of 1997: Concept and Principles; Final Guidance for FDA and Industry*, issued on October 4, 2002 (available at *http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm085994.htm*).

That guidance document interprets least-burdensome to mean "a successful means of addressing a premarket issue that involves the most appropriate investment of time, effort, and resources on the part of industry and the FDA." The guidance further specifies that the least-burdensome provisions do not affect the statutory premarket review standards for devices. CDRH believes the least-burdensome principle articulated in the 2002 guidance—that premarket and other regulatory requirements should be closely tailored to the regulatory need—is a basic principle of good government and at the core of effective regulation.

On August 11, 2011, CDRH Director Jeffrey Shuren, M.D., sent an all-hands e-mail to staff entitled "Least Burdensome Principle is Critical to Advancing CDRH's Mission to Protect Public Health." His message to staff summarized the origin of the provision in the law, discussed FDA's implementation of it through guidance, emphasized its importance to protecting public health and fostering innovation, and reaffirmed CDRH's commitment to its implementation.

In addition, in November 2011, the Center issued standard SOP on the appropriate level of management approval to request additional information from a device sponsor in response to a premarket submission, in part to ensure the appropriate application of the least-burdensome principle.

Harmonization with International Device Testing Standards

We consider the potential benefits of harmonization with international testing standards on an ongoing basis. Harmonization (or convergence) of regulatory programs, including data requirements to support premarket applications and submissions, as well as the sharing of information and best practices between countries, can reduce regulatory burdens on industry, create efficiencies for CDRH, and increase patient access to important devices internationally. We strongly believe that there should be continued harmonization (and convergence) efforts and sharing of best practices between countries.

Many domestic and international consensus standards address aspects of safety and/or effectiveness relevant to medical devices. Many of these standards have been developed with the participation of CDRH staff. CDRH believes that conformance with recognized consensus standards can support a reasonable assurance of safety and/or effectiveness for many applicable aspects of medical devices. Therefore, information submitted on conformance with such standards should have a direct bearing on safety and effectiveness determinations made during the review of IDE, PAM, or Humanitarian Exemption (HDE) applications, or Product Development Protocols (PDP). For Premarket Notifications (510(k)s), information on conformance with recognized consensus standards may help establish the substantial equivalence of a new device to a legally marketed predicate device. This information may be used to show that the new device is as safe and effective as the predicate in the areas covered by the standards. If any premarket submission contains a declaration of conformity to the recognized consensus standards, this declaration should, in many cases, eliminate the need to review the actual test data for those aspects of the device addressed by the standards.

Conformance with recognized consensus standards, however, may not always be a sufficient basis for regulatory decisions. For example, a specific device may raise a safety or effectiveness issue not addressed by any recognized consensus standard, or a specific FDA regulation may require additional information beyond what conformity to the recognized consensus standards provides. Under such circumstances, conformity with recognized standards will not satisfy all requirements for marketing, or investigating, the product in the United States.

CDRH is invested in the development of medical device standards and participates significantly in the development process. The Center's Office of Science and Engineering Laboratories (OSEL), Standards Management Staff (SMS), is responsible for facilitating the recognition of national and international medical device consensus standards. SMS manages the Standards Program, a regulatory support activity consisting of cross-office teams within CDRH and FDA. This involves working closely with the Standards Developing Organizations (SDOs), advertising standards liaison representative positions, facilitating a CDRH recommendation to serve on a particular standards activity, and maintaining an appropriate standards database, providing access to established standards for all CDRH staff, field inspectors, and industry.

SMS continually updates currently recognized standards and coordinates the recognition of new voluntary consensus standards for medical devices and radiation-emitting electronic products. SMS ensures that appropriate medical device standards are published in the *Federal Register* at least twice annually, and maintains a database of recognized consensus standards, which is available on FDA's web site at *http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Standards/default.htm.*

For almost two decades, FDA has participated in the Global Harmonization Task Force (GHTF) along with the other founding member countries—the European Union, Canada, Australia, and Japan. Through GHTF, we have produced many high-level policy documents. These documents have provided the greatest value to countries that are in the process of establishing a device regulatory system, while providing relatively limited value to the member countries, because they are too high-level and do not address the complexities of implementation. Implementation of these policies and other harmonization activities will require regulators to share with their counterparts the operational aspects of their regulatory programs as well as privileged and confidential information. GHTF does not allow for these types of interactions between regulators. Moreover, due to the limited membership of GHTF, new harmonization efforts have been undertaken by other countries, thereby increasing the likelihood of countries adopting disparate approaches to device regulation.

To address these limitations, CDRH has been working with the other GHTF member countries to create a new forum for international medical device regulators, with broader membership, to focus on implementing harmonization (and convergence) activities while continuing to develop new, and update existing, policy documents in collaboration with industry and other stakeholders.

The first meeting to create the new forum took place in Washington, D.C., in February 2011. A second meeting took place in Ottawa, Canada, in October 2011. We expect to hold the first meeting of the new forum in 2012; industry and other stakeholders will be invited to attend that meeting and will continue to play an active role.

Addressing Advisory Panel Conflicts of Interest

Your letter suggests that FDA address the unintended consequences of the conflict-of-interest rules for advisory panels.

We share your concern that FDA advisory committees should provide the Agency with unbiased advice. Recruiting and screening potential advisory committee members for conflicts of interest poses a challenge for the Agency, but we recognize that these activities are necessary to ensure the impartiality of the advice we receive. At the same time, we are always interested in improving our efficiency.

Any changes to the conflict-of-interest laws would require legislative action. We are aware that several members of Congress have suggested legislative changes. Although the Administration has not taken any positions on these proposals, we look forward to discussing these different approaches going forward. We are also continuing to review our internal processes to determine if there are areas where we can make improvement.

Implementing a Premarket Submission Tracking System Accessible to Industry

As part of MDUFA negotiations, industry has suggested that an option would be to develop a dashboard for companies for each submission, similar to what the U.S. Patent and Trademark Office offers patent submitters, to track their applications through the process. FDA does not currently have a system which would allow companies to view a dashboard of their submissions. Implementation of such a system would require creating a secure remote access system, which would allow each submitter to log into. This type of system would be very costly and difficult to develop. FDA has expressed a willingness to provide more detailed information on progress made toward accomplishment of MDUFA commitments. The Agency currently presents data quarterly on MDUFA performance goals; providing additional information is something we can consider and will continue to discuss with industry.

Thank you, again, for contacting us concerning this matter. If you have further questions, please let us know. The same letter has been sent to your cosigners.

Sincerely,

Michelle Mital

for Jeanne Ireland
Assistant Commissioner
for Legislation