

### **Improving FDA's 510(k) Review Process**

**February 24, 2010**

On February 18, the U.S. Food and Drug Administration (FDA or the Agency) held a public meeting titled “Strengthening the Center for Devices and Radiological Health’s 510(k) Review Process” to discuss changes to the 510(k) process. While divergent views were expressed at the meeting by FDA, industry, and other stakeholders, FDA officials stated their intent to move forward to propose changes to the 510(k) review process in May 2010. Device manufacturers, therefore, should be actively involved in the discussion to ensure that the existing 510(k) process is improved to ensure efficient and timely introduction of safe and effective devices in the United States, without compromising innovation. Comments must be submitted to the FDA docket (FDA Docket Number FDA-2010-N-0054 at <http://www.regulations.gov>) by the March 19, 2010 deadline.

#### **Introduction**

Over the last several years, concerns have been raised about whether the 510(k) clearance process optimally achieves its intended goals of making safe and effective devices available to consumers and promoting innovation in the medical device industry. Following congressional inquiry and the January 2009 report by the U.S. Government Accountability Office, FDA commissioned the Institute of Medicine (IOM) to conduct an independent review of the 510(k) program and, if necessary, to recommend administrative, regulatory, and/or statutory changes. In his February 16, 2010 letter to FDA Commissioner Margaret A. Hamburg, Sen. Chuck Grassley (R-Iowa) asked FDA for a status report on its efforts to update guidelines for medical device makers seeking device clearance through the 510(k) process by March 2, 2010.

Given that the IOM study is not expected to conclude until March 2011, the Center for Devices and Radiological Health (CDRH) has also convened an internal 510(k) Working Group to recommend possible actions that CDRH could take in the short term, and to identify longer term options FDA could consider to strengthen the program. As part of this effort, CDRH held a public meeting with stakeholders on February 18 to obtain input on a number of challenges associated with the 510(k) process, and requested comments on topics in a January 27, 2010 Federal Register Notice (75 Fed. Reg. 4,402). The meeting focused on issues relating to the following four areas:

- Predicate devices
- New technologies and scientific evidence
- Practices CDRH has adopted in response to a high volume of 510(k) submissions

- Postmarket surveillance and new information about marketed devices

## **Issues Discussed at the February 18 Public Meeting**

At the meeting, Jeff Shuren, M.D., J.D., Director of CDRH, as well as other participants, stressed the need for data indicating what exactly is *not* working in the current 510(k) process prior to implementing any changes, so that the proposed solutions can be directly linked to identified problems and the resolution of the problems can be measured quantitatively. The participants also stressed the need to differentiate between any perceived problems with the 510(k) process itself, such as, the need to make changes in the legislation and regulations, and the implementation problems, or how well the existing laws and regulations are interpreted and implemented.

In general, industry participants at the meeting seemed to agree that the 510(k) process is working overall. But critics expressed their concerns that innovative devices cleared by the 510(k) process are not as safe or effective as other medical devices on the market. Further, while industry participants were supportive of the 510(k) process, they cited several ongoing implementation issues, including uncertainty/lack of predictability of the review process, review delays, lack of transparency at FDA, inconsistency in review outcomes over time and among FDA branches and reviewers, and insufficient specific guidance from the Agency. Some of the more significant issues discussed at the meeting are summarized below.

### *Issues Related to Predicate Devices*

- **“Multiple and Split Predicates”**

FDA has expressed concerns that when a submitter uses more than one predicate to support substantial equivalence, the “new” device may be very different from any other device on the market, and creates difficulty in assessing substantial equivalence. For example, this might occur when one predicate is used for the indication for use, and a second predicate is used for demonstrating substantial equivalence for the technology. FDA’s comments indicate a preference for establishing substantial equivalence to a single predicate, which may be a policy being implemented informally by the Agency, but industry participants cautioned that this could substantially limit innovation.

- **“Outdated Predicates”**

Generally, a 510(k)-cleared device may be used as a predicate, regardless of whether or not the device is still in use, remains relevant to current standards of care, or has been replaced by new technology. FDA is also looking for comments on whether there should be stricter criteria for what predicate devices are eligible for use in new 510(k) submissions and for specific examples of the beneficial or problematic use of “outdated” predicate devices.

- **“Predicate Creep”**

FDA is concerned that incremental device changes that seem innocuous individually in one 510(k) submission, may accumulate over time to create a device that is significantly different from the original device (in other words, “predicate creep”). Similarly, FDA is concerned with “non-inferiority creep” when a series of clinical non-inferiority studies is conducted over time. For example, device B is non-inferior to A, device C is non-inferior to B, and device D is non-inferior to C), but the difference in effectiveness between device A and D may approach clinical significance.

Some meeting participants, particularly those representing end users of medical devices, expressed concerns over updated and upgraded devices that have no backward compatibility to other components of a system because of “predicate creep,” resulting in the need for hospitals to replace the whole system at great expense. Although this may be an illustration of potential consequences of the sequential introduction of modifications to devices, the role of the pre-marketing review process by FDA in addressing this issue is not clear.

### *Issues Related to New Technologies and Scientific Evidence*

- **De Novo Process**

In general, industry participants agreed that there were problems with the scope and timeliness of the existing de novo process for down-classification of low risk devices that have received a Not Substantially Equivalent determination due to lack of a predicate. FDA has cited challenges regarding determining whether a device without a predicate is a low risk device, and whether adequate evidence exists to demonstrate its safety and effectiveness.

- **“Different Technological Characteristics” and “Different Questions of Safety and Effectiveness”**

FDA cited general challenges in determining the type and amount of information needed for clearing a new device under the 510(k) process. The industry participants specifically cited lack of clarity on how the Agency determines when clinical studies in humans are needed. FDA is seeking comments on how the Agency should identify and characterize the risks associated with a new technology that do not raise “different questions of safety and effectiveness” and whether there are types of new technology that should not be considered appropriate to be cleared for marketing through the 510(k) process. FDA is also asking whether it should define “different questions of safety and effectiveness.”

### *Issues Related to Practices CDRH Has Adopted in Response to a High Volume of 510(k) Submissions*

In response to a large number of 510(k) submissions, CDRH has adopted a number of practices to allow for less resource-intensive reviews, including the third-party review program, the Special 510(k) under the 510(k) Paradigm, bundling of devices in 510(k) submissions, and reliance on 510(k) submitters’ assertions of conformance to recognized standards (as in the Abbreviated 510(k) program).

The Agency acknowledged that due to resource constraints, CDRH often must rely on a single reviewer to assess each 510(k) submission. Bundled submissions (multiple models, for example, similarly designed dental implants) or bundled devices (for example, bedside monitors with multiple parameters) in particular are more time-consuming to review, especially when multiple CDRH divisions are involved in the review process. FDA has also expressed concerns with the often poor quality of third-party reviews. FDA is seeking comments on the advantages and disadvantages of each of these practices, as related to the quality and timeliness of 510(k) reviews.

### *Issues Related to Postmarket Surveillance and New Information about Marketed Devices*

Agency participants noted limited FDA authority on postmarketing studies. The types of information that FDA receives are limited to adverse event reports, recalls, and inspectional findings. FDA is seeking comments on whether it should exercise more authority in this area, including imposing postmarket surveillance studies as a condition of 510(k) clearance, allowing for the rescission of 510(k) clearance

decisions under a broad range of circumstances, using available postmarket information in review of similar devices, reviewing and clearing the final printed labeling prior to marketing, and requiring reporting of any changes in ownership of a 510(k).

## Summary

FDA and meeting participants endorsed the need to increase transparency and achieve consistency. FDA expressed its belief that developing clear definitions and guidance and supplying additional authorities may be required. Industry would like to have the predictability and efficiency of the review process and de novo classification process increased, without implementing changes that will negatively impact innovation.

Dr. Shuren put forth an aggressive timeline when he stated that the FDA would be issuing recommendations for strengthening the 510(k) review by May 31, 2010. Because of the compressed timeline and the limited opportunity for contributing suggestions for improvements, interested parties should submit detailed and supported comments before the new deadline of March 19, 2010. CDRH's goal is to begin implementation of changes by September 30, 2010.

If you have any questions or would like more information on the 510(k) clearance process for medical devices or for assistance with preparation or review of the comments to the FDA, please contact either of the following Morgan Lewis attorneys:

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