Continuing Evolution of the US FDA 510(k) Process

US FDA is considering introducing some bold changes to the 510(k) review process. A new report describes these considerations, including the possible creation of a new Class IIb device subset.

Comment period

On 5 August 2010, the United States (US) Food and Drug Administration (FDA) published a notice in the *Federal Register*[1] requesting public comment on two preliminary reports[2, 3] issued by FDA's Center for Devices and Radiological Health (CDRH). The reports recommend specific steps that CDRH could take to foster medical device innovation, enhance regulatory predictability and improve patient safety. It should be noted that the recommendations are preliminary and that CDRH is soliciting comments on the reports. The comment period ends on 4 October 2010, but awareness of the contents of the reports is useful because some recommendations, if adopted, will lead to significant changes.

Once FDA has assessed public input and other necessary reviews have been completed, the agency will announce the changes that have been selected for implementation and the associated timelines. FDA also states that some proposed changes may be referred to the Institute of Medicine (IOM) for further review. The commissioning of the IOM to conduct an independent review of the 510(k) programme was discussed in a previous article.[4] It should also be noted that even though FDA has not yet made any decisions regarding the changes to be implemented, the 510(k) report contains useful information that can be taken into consideration during the development of 510(k) submissions.

The first report was developed by the 510(k) Working Group, established in September 2009, which provides preliminary recommendations to strengthen the 510(k) premarket review process. The second report is from the Task Force on the Utilization of Science in Regulatory Decision Making. Only the 510(k) Working Group Report is discussed below. Other aspects of recent FDA initiatives for improving the 510(k) review process and suggestions for meeting 510(k) submission challenges were discussed in the previous article mentioned above.

510(k) report

Volume I is a 120-page report including an Executive Summary that provides an overview of findings and recommendations together with sections on background and goals, working group methods, history of the 510(k) programme, findings and recommendations, and conclusions. In addition, four appendices contain a summary of staff feedback, summary of the 18 February 2010 Public Meeting, summary of written public comments, and a reviewer survey.

For those who do not have time to review the entire report initially, review of selected portions of the report will provide an overall understanding of the recommendations. For example, the Table of Contents lists the seven major findings and recommendations, the Executive Summary provides additional narrative infor-

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mation, and Section 5, Findings and Recommendations, provides very detailed information including case studies and examples illustrating the issues under discussion.

In addition, the report contains very interesting background information on the history of the 510(k) programme and Working Group methods and organisation. For example, the 510(k) Working Group, which included representatives from across CDRH, was organised into 10 subgroups. Each subgroup was assigned a specific area of concentration, such as bundling, device modifications, de novo classifications, indications for use and so on. Awareness of the primary topics considered by these subgroups helps explain the origins of the recommendations that have been made.

The report contains seven major findings and recommendations. A discussion of all seven is beyond the scope of this article; thus, readers are strongly advised to review all seven because each finding and recommendation contains several related issues with one or more recommendations addressing each issue. In some cases, the issue-related recommendations represent important differences from current practice and would require submitting significant additional information to FDA, if adopted. The following three findings and recommendations are provided as examples.

■ **5.1.1. Finding:** There is insufficient clarity with respect to pivotal terms in the definition of "substantial equivalence." **Recommendation:** CDRH should clarify the meaning of "substantial equivalence" through guidance and training for reviewers, managers and industry.

■ **5.1.3. Finding:** Although there exists an alternative regulatory pathway for devices that lack a clear predicate but whose risks do not warrant Class III controls (i.e., the process for Evaluation of Automatic Class III Designation, also known as the de novo classification process), this pathway, as currently implemented, is inefficient and has not been utilized optimally across the Center. **Recommendation:** CDRH should reform its implementation of the de novo classification process to provide a practical, risk-based option that affords an appropriate level of review and regulatory control for eligible devices.

■ **5.2.1. Finding:** It is challenging for CDRH to obtain, in an efficient and predictable manner, the information it needs to make well-supported premarket decisions and assure that each new or modified 510(k) device is substantially equivalent to a valid predicate. **Recommendation:** CDRH should take steps through guidance and regulation to facilitate the efficient submission of high-quality 510(k) device information. It can achieve this, in part, by better clarifying and more effectively communicating its evidentiary expectations through the creation, via guidance, of a new "Class IIb" device subset.

Readers will be particularly interested in Finding 5.2.1. The 510(k) Working Group recommends that CDRH develop

guidance defining a subset of Class II devices, called Class IIb devices, for which clinical information, manufacturing information or, potentially, additional evaluation in the postmarket setting typically would be necessary to support a substantial equivalence determination. FDA states that delineating between Class IIa and Class IIb would not reconfigure the current three-tiered device classification system established by statute; it would represent only an administrative distinction. Unfortunately, the creation of Class IIa and Class IIb in the United States is not based upon harmonising classification designations with those in Europe under the Medical Devices Directive (93/42/EEC). That is, devices that are classified as Class IIa or Class IIb in Europe will not necessarily be in the same classes in the United States in spite of the use of the same classification terminology. Readers interested in having a clearer idea of this recommendation should review section 5.2.1 of the 510(k) Working Group report.

FDA 510(k) webinar

On 31 August 2010, FDA held a two-hour webinar to discuss the details of both reports and allow FDA to respond to questions and concerns raised by the medical device community. The CDRH representatives participating in the webinar were Dr. Jeffrey Shuren (Director), Dr. Alberto Gutierrez (Office of In Vitro Diagnostics), Ms. Christy Foreman (Office of Device Evaluation), and Dr. Jonathan Sackner-Bernstein (Associate Center Director, Post Market Operations).

Participants wishing to submit questions did so and selected questions were read aloud by the moderator, receiving responses from one or more of the CDRH representatives. Some of the questions and FDA responses were quite interesting and helped to further understand the recommendations made in the two FDA reports. For example, participants expressed significant interest in the introduction of a Class IIb category. An archived audio recording of the webinar can be found on the CDRH website.[5]

Chosen pathway

It is notable that FDA and industry representatives continue to enthusiastically support the 510(k) process, which is based upon a premise that seems at odds with the very nature of medical devices. That is, 510(k) clearance decisions are based on a comparison between newer devices and older ones, whereby the newer ones need to meet the safety and effectiveness level of the older ones. Manufacturers must sometimes even minimise the improvements in their devices to ensure that they will be considered equivalent to older predicate devices. This is a pity since it is clear that the 510(k) process is not the only feasible regulatory pathway.

A system that does not penalise medical devices for having evolved is the European medical device CE marking process. To meet CE mark requirements, devices must meet a set of essential requirements. This very often involves technical and clinical data comparisons between the new device and other similar devices on the market; however, there is no need for the restrictive comparisons that characterise the 510(k) process. Thus, the CE marking process does not penalise manufacturers for having designed and developed medical devices that have evolved and that can be shown to be safer and perform better than similar older devices.

The fact that FDA is expending so much energy and resources on trying to resolve seemingly insurmountable problems with the 510(k) process is even more interesting when one considers that FDA is a founding member of the Global Harmonization Task Force, whose regulatory model is based on medical devices meeting a set of essential principles, an approach largely based on the European CE marking process. FDA has shown interest in this model by initiating in 2004 the Summary Technical Document (STED) pilot programme to assess the feasibility of the STED format and content for certain PMA applications and 510(k) submissions. It is unclear whether or not a sufficient number of manufacturers have participated in the pilot programme, which requires not only submission of documentation in the harmonised format, but also the predicate device comparison data that are normally required for 510(k)s.

It may be time for serious consideration of an alternative US pathway to better reflect the dynamic medical device sector. The current resistance to change may be more deleterious in the long run than embracing a new US regulatory system that really fosters innovation.

References

1. Docket No. FDA-2010-N-0348, "Center for Devices and Radiological Health 510(k) Working Group Preliminary Report and Recommendations, and Task Force on the Utilization of Science in Regulatory Decision Making Preliminary Report and Recommendations; Availability for Comment." http://edocket.access.gpo.gov/2010/2010-19339.htm
2. CDRH Preliminary Internal Evaluations – Volume I, 510(k) Working Group, Preliminary Report and Recommendations, August 2010. www.fda.gov/downloads/AboutFDA/CentersOffices/CDRH/CDRHReports/UCM220784.pdf
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4. M. E. Donawa, "The Evolving US 510(k) Review Process," *European Medical Device Technology*, May 2010. www.emdt.co.uk/article/evolving-us-510k-review-process
5. Webinar: FDA Discussion on the Draft 510(k) and Use of Science in Regulatory Decision Making Reports. A link to the webinar can be found on the CDRH Preliminary Internal Evaluations site: www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHReports/ucm220272.htm

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