US FDA Draft Revised Guidance on When to Submit a New 510(k)

After more than 14 years, US FDA has updated guidance on when to submit a 510(k) after making a change to an existing cleared device. This article discusses important similarities and differences between the new draft and current guidance.

US FDA regulations specify in 21 CFR 807.81(a)(3) when a 510(k) must be submitted, but the agency acknowledges that the language used in the regulation sometimes leads to varying interpretations of when a 510(k) is required for a device modification. This realisation led to publication of the 1997 guidance document, which is still currently in effect, titled "Deciding When to Submit a 510(k) for a Change to an Existing 510(k)" (www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080235.htm).

However, much has happened since the 1997 guidance was issued, including a major revision of the Quality System Regulation (21 CFR 820). In addition, in January 2011 CDRH published the "Plan of Action for Implementation of 510(k) and Science Recommendations," with the aim of enhancing predictability, consistency and transparency of the premarket review process (www.fda.gov/downloads/AboutFDA/CentersOffices/CDRH/CDRHReports/UCM239450.pdf). One of the items identified in the Plan of Action included publication of an update to the 1997 Device Modifications Guidance (www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm265274.htm).

US FDA is requesting comments on the new draft guidance, some aspects of which are much stricter than the 1997 guidance without obvious benefits. Thus, it is hoped that readers will obtain a copy of the draft guidance as soon as possible, review it carefully and submit comments where they believe that modifications are required. The Federal Register Notice announcing the availability of the guidance document (www.gpo.gov/fdsys/pkg/FR-2011-07-27/html/2011-18923.htm) provides details on how to submit electronic or paper comments, which need to be submitted to the agency by 25 October 2011.

Regulatory constraints

US FDA regulations require that a 510(k) must be submitted when a device is in commercial distribution or will be reintroduced into commercial distribution but is about to be significantly changed or modified in design, components, method of manufacture or intended use. Readers should refer to 21 CFR 807.81(a)(3) to review the text of the regulation.

An important distinction is made in the draft guidance between a change that "could significantly affect" either the safety or the effectiveness of a device and one that does significantly affect the safety or effectiveness of a device. The guidance goes on to state that whether a change does affect safety and effectiveness is typically demonstrated by the results of testing submitted in a 510(k) notification. The guidance then states that, in most cases, testing cannot conclusively show that a change could not affect safety or effectiveness.

Why is this an important point? Because some manufacturers believe that if they can show that safety and effectiveness are not affected by a change, there is no need to submit a new 510(k). Unfortunately, the regulations require the submission of a 510(k) if a change could significantly affect safety or effectiveness. That is, the regulations require US FDA to check the conclusions reached by the manufacturer.

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Important overall changes

One of the most noticeable changes in the draft guidance document is the absence of flow charts, which were a major feature of the 1997 version of the guidance. The current 1997 document has a main flow chart consisting of questions on the type of change being considered, such as a change following a recall or corrective action, new labelling and so forth. Depending on the type of change being considered, the user is directed to one of three separate flow charts covering changes to labelling, technology or performance, and materials. A fourth flow chart is to be used if the change concerns materials used in IVD devices. Current guidance mainly consists of explanations of individual issues that should be considered for each of the numbered questions in the flow charts. Some readers may believe that the flow charts were helpful; however, their absence should lead to a greater concentration on the text of the guidance.

The new draft guidance is organised into a discussion of four types of changes:

- manufacturing changes in Section V
- labelling changes in Section VI
- technology, engineering and performance changes in Section VII
- materials changes in Section VIII

Each section on a particular type of change contains a series of questions regarding the change being considered. Each question is followed by detailed advice on how to assess the particular change or issues related to the type of change. Manufacturers should answer each question for each individual change to their devices until a decision is made either to submit a 510(k) or to document the change together with the basis for concluding that it does not require a 510(k). For example, the guidance advises that if a manufacturer changes the length of a device, the thickness of the device and the material of the device, each of these three changes should be considered individually.

The new draft guidance contains some of the same questions, advice and examples on how to interpret the guidance as the current document; however, the draft guidance has been expanded, covers areas not previously addressed and includes new examples.

Manufacturing process changes

Section V, Manufacturing Process Changes, is a new section in the draft; however, some of the information that it contains was included in 1997 guidance. Of the three questions included in the section, one is new: Was manufacturing process information part of the original 510(k) submission? However, the other two—Is there a change in packaging or expiration dating? Has there been a change in sterilisation?—are included in the section on technology, engineering and performance changes of the 1997 document.

Regarding the need to evaluate manufacturing process changes, the draft guidance indicates that where manufacturing processes were examined during the original clearance process, there is a higher likelihood that manufacturing process changes could

significantly affect safety or effectiveness. In this case, changes to manufacturing processes that could affect device specifications are likely to require submission of a new 510(k).

Guidance on other types of changes

The questions and discussions under Section VI, Labelling Changes, are similar to those in the 1997 document on labelling changes, except that a new question has been added: Is it a change in instructions for use? In addition, the example "changes from prescription use in a clinical setting to prescription use in a home setting (home use devices)" is an example of a change that usually requires a new 510(k). This differs from the 1997 guidance, which states that a 510(k) is needed for changes from prescription to over-the-counter devices; however, an exception is made if home-use instructions are provided with devices that require a prescription, but whose use in the home is accepted medical practice in the United States. The 1997 guidance further states that many prescription devices are used in the home with increasing frequency and the agency believes that 510(k)s are not necessary to add home-use labelling.

Section VII, Technology, Engineering, and Performance Changes, should be carefully reviewed by readers because the advice on these types of changes has been expanded in important ways. For example, new guidance or questions address changes related to:

- device ergonomics or the patient/user interface
- dimensional specifications
- how the device receives, transmits or displays electrical signals or data
- the addition of an aspect of autonomous or semi-autonomous control to the existing device.

The last question under this section—Does the change affect how the device is likely to be used in practice?—is new and contains six additional questions. These are intended to help determine whether changes to device technology, engineering or performance are significant changes requiring a new 510(k), which will enable US FDA to evaluate whether "appropriate information" in the labelling about a use not currently identified in the labelling is necessary.

Some of the issues discussed in Section VIII, Materials Changes, of the draft guidance, are the same as those in the 1997 guidance; however, reference to the Biomaterials Compendium has been removed and the number of questions has been significantly condensed. In addition, there is no longer a section discussing materials changes for IVD products.

The guidance provided in Section IX of the new draft document—Is clinical data necessary to determine substantial equivalence?—is similar to that provided in the 1997 document with one important difference. The current guidance states that in the case of IVD devices, clinical samples may be collected and analysed to demonstrate that the device continues to conform to performance specifications as contained in a voluntary standard or as described in a previous 510(k). The guidance states that a new 510(k) is normally not necessary in this situation. By contrast, draft guidance indicates only that IVD devices have different testing requirements and that the Office of In Vitro Diagnostics should be contacted if questions exist regarding the need for a new 510(k).

US FDA's current thinking

The draft guidance may be only a draft issued to obtain comments, but it more accurately reflects US FDA's current thinking than the 1997 document. Companies may wish to consider the draft as well as the current guidance regarding the need to submit a new 510(k) after making a device change. Doing so may help avoid problems that could occur if manufacturers decide that a 510(k) is not needed based only on 1997 guidance, which may no longer reflect US FDA's current views on a particular type of change. Unfortunately, because of the more conservative interpretation of the regulations in the draft guidance, if many of its provisions are eventually adopted, it is likely that manufacturers will need to submit many more 510(k)s in the years ahead. That is, if the 510(k) programme survives.

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