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Medical Device Update: FDA Issues Final Guidance on 510(k) Determinations, Use of "Split" Predicates Strongly Discouraged

On July 28, the Food and Drug Administration (FDA) issued a final guidance titled "The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]."[1] Device manufacturers should be aware of key changes to FDA's policies that may affect their 510(k) submissions, including new limitations on the use of multiple predicates, the unacceptability of split predicates, an increase in the content and detail required for 510(k) summaries, and FDA's intent to "verify the accuracy and completeness" of 510(k) summaries. In describing the critical decision points of the 510(k) review process, the final guidance emphasizes how safety and effectiveness are considered during the review. The inclusion of this discussion is likely in response to criticism of the 510(k) process in recent years.

The newly issued guidance finalizes the draft version, which issued on December 27, 2011 and supersedes the Center for Devices and Radiological Health Premarket Notification Program, 510(k) Memorandum 86-3 (June 30, 1986). The final guidance does not include sections on the Special and Abbreviated 510(k) programs, which were included in the draft version; these will be included in a separate guidance document.

Provided below is a summary of the final guidance.

Use of Multiple Predicates/"Split" Predicates

In the new guidance, FDA encourages manufacturers to identify a single predicate device to demonstrate substantial equivalence, but it does not prohibit using multiple predicates. However, FDA states that "split predicates," which identify one predicate for the intended use and another predicate for the technological characteristics, are "inconsistent with the 510(k) regulatory standard." Section 513(i) of the Federal Food, Drug, and Cosmetic Act defines "substantial equivalence" as a device with the same intended use as the predicate device **and** the same technological characteristics or different technological characteristics that do not raise different questions of safety and effectiveness than the predicate device. **Although the guidance does not state explicitly that split predicates will not be accepted, the clear implication is that using split predicates will not lead to a finding of substantial equivalence.** When multiple predicates are used, the guidance recommends that there be a "primary predicate," with indications for use and technological characteristics that are most similar to the device that is the subject of the 510(k).

The guidance provides examples of when multiple predicates are appropriate, including, for example, when combining features from two or more predicate devices with the same intended use into a single new device, when seeking to market a device with more than one intended use, or when seeking more than one indication for use under the same intended use. The guidance also states that manufacturers may use a "reference device" to support scientific methodology or standard reference values (e.g., to characterize the coating on an orthopedic implant).

Intended Use

FDA clarifies the meaning of the terms "intended use" and "indications for use," noting that "intended use" means the general purpose of the device or its function and that it includes the indications for use. "Indications for use" describes the disease or condition the device will diagnose, treat, prevent, cure, or mitigate, including a description of the target patient population. To be determined substantially equivalent, the device's indications for use must fall within the intended use of the predicate device. The guidance describes that a change in indications for use will result in a new intended use when the change in indications for use raises different questions of safety and effectiveness (e.g., a change from a diagnostic indication to a screening indication or vice versa, a change in

1. View the guidance at http://www.fda.gov/downloads/MedicalDevices/.../UCM284443.pdf.

the patient population, or a change in the anatomical structure of use).

Technological Characteristics

In any 510(k) review, FDA evaluates whether there are technological differences between the new and predicate devices. If differences exist, FDA then determines whether those differences raise different questions of safety and effectiveness. The guidance states that key characteristics that FDA will consider include device design, materials, and energy sources. To assist manufacturers in assessing whether there are different questions of safety and effectiveness, the guidance includes several examples. These include changes in energy from mechanical to electrical and changes in the mode of application of a device.

Performance Data

The guidance states that, although descriptive information alone may be sufficient to demonstrate substantial equivalence in some cases, performance data are typically needed. This may be nonclinical bench performance testing and/or clinical testing. The guidance provides examples of when clinical data may be required. These include when there is a new or modified indication for use, when there are technological differences that raise different questions of safety and effectiveness, and when nonclinical test methods are not validated, are limited, or are inappropriate to demonstrate substantial equivalence.

510(k) Summary

Although 510(k) summaries are a required element of a 510(k) submission and their content is prescribed by FDA regulation, there is significant variability in the content of such summaries. For example, for 510(k)s filed by a manufacturer for improvements or changes to its cleared device, it is often difficult to determine from the summary how a particular device was modified. Further, a summary does not always reveal whether clinical testing was conducted to support substantial equivalence. To provide greater transparency and better ensure that the 510(k) summary reflects the information provided in a submission, the final guidance provides detailed information on the content of the 510(k) summary. For example, a sample summary is provided as an appendix and includes a listing of technological differences from the predicate and a summary of the nonclinical and clinical testing performed.

Contacts

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