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New draft guidance proposes a shift in how the FDA will evaluate certain device modifications

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On September 28, 2018, the U.S. Food and Drug Administration (FDA or the Agency) issued a draft guidance document, entitled "The Special 510(k) Program," which, when finalized, will supersede the currently in effect Special 510(k) policy outlined in "The New 510(k) Paradigm – Alternate Approaches to Demonstrating Substantial Equivalence" (March 20, 1998).[1] The modified policy described in this draft guidance is largely consistent with the core principles upon which the Special 510(k) pathway was created, but introduces a different, more expansive standard for assessing which devices are eligible for review under the program. The modified standard may enable device manufacturers to obtain a faster and less burdensome review for a broader scope of device modifications. The FDA has also launched a pilot program to evaluate the impact of the proposed updates to the framework, in which all Special 510(k) notices received on or after October 1, 2018 will automatically be included.

Background

The Special 510(k) program was originally established in 1998 to address situations where a manufacturer is required to file a new 510(k) notification for a relatively minor change to a previously cleared device.[2] The goal of the program was to streamline the review process for these minor changes by allowing manufacturers to leverage the controls established under the Quality System Regulation (QSR). Specifically, the FDA designated this pathway as appropriate for modifications to a manufacturer's own medical device that can be adequately verified/validated (at least primarily) through its internal design control and risk analysis processes. These internal validation measures are then reviewed in combination with the device's previously cleared 510(k) submission, allowing the company to also leverage the information that the FDA has already reviewed. The FDA committed to reviewing Special 510(k) submissions within 30 days of receipt, as compared to 90 days for Traditional 510(k) submissions, based on the less expansive nature of the application.

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[1] Available here.

[2] Per 21 C.F.R. § 807.81(a)(3), a premarket notification is required for significant changes or modifications to a legally marketed device, which are defined as ones which "could significantly affect the safety or effectiveness of the device" or are a "major change or modification in the intended use of the device."

The existing Special 510(k) program, however, is limited to changes that do not affect the previously cleared device's intended use or fundamental scientific technology. In practice, this means that any modification to a device's cleared indications for use (except very minor, non-substantive changes) is not eligible for review via a Special 510(k) notice. In addition, the current framework still leaves some ambiguity around what specific design or technological changes are eligible for review under a Special 510(k) notice. Consequently, it is not uncommon for a manufacturer to file a Special 510(k) notice, only to have the FDA convert the submission to a Traditional 510(k) notice. This can result in delays, especially if the manufacturer needs to obtain more comprehensive data to support the change, which is often the case.

The FDA's proposed changes to the Special 510(k) framework

The new draft guidance proposes updates to the Special 510(k) pathway to

- expand eligibility to cover certain changes to the indications for use; and
- clarify eligibility with respect to technological changes.

Under the revised framework, proposed changes that are made and submitted by the manufacturer authorized to market the existing device[3] would be eligible for the Special 510(k) pathway when

- performance data are unnecessary; or
- performance data are necessary, but well-established methods are available to evaluate the change and all data necessary to support substantial equivalence can be reviewed in a summary or risk analysis format.

The practical implications are similar to those under the existing standard, but the new draft guidance provides a clearer roadmap for assessing Special 510(k) pathway eligibility. In particular, it offers more granular guidance on the types of changes that are and are not eligible and clarifies the types of data the FDA considers appropriate for supporting a modification under this pathway. Specifically, the FDA indicates that "well-established methods" are those that have been established for evaluation of a device, device type, or scientific topic area and are validated according to scientific principles; these may include the manufacturer's own methods and acceptance criteria previously used to support clearance of the base device, methods found in an FDA-recognized voluntary consensus standard, or widely available and accepted methods published in the public domain, scientific literature, or found acceptable by the FDA through a device clearance/approval. The FDA also maintains that methods that rely on clinical studies or animal data to support substantial equivalence are not typically appropriate for the Special 510(k) pathway due to their variability and inability to be summarized.

In addition, the draft guidance reflects the Agency's continued emphasis on post-market design control requirements, per the QSR, as potential support for clearance of a modified device. For instance, QSR requirements such as design verification and validation and quality control procedures (e.g., matching design outputs/inputs, ensuring conformity with user needs, etc.) incorporate risk analysis and consideration of device function and safety. In this respect, the FDA's proposed approach is consistent with the FDA's heightened focus on the Total Product Life Cycle for medical devices, generally.

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[3] This initial criterion, already enforced under the current Special 510(k) policy, derives from the FDA's view that a manufacturer who modifies its own legally marketed device can conduct the risk analysis and necessary verification and validation activities to demonstrate that the design outputs of the modified device meet the design input requirements in a streamlined 510(k) submission.

The draft guidance explains that if a manufacturer determines under its design control procedures that no additional verification or validation testing is necessary to evaluate a change that otherwise requires 510(k) clearance, the Special 510(k) notice should include a scientific rationale supporting the conclusion that no test data is necessary. Alternatively, if performance data are required, as is often the case, the manufacturer should include in the Special 510(k) notice a justification for why the methods relied upon to assess the change qualify as well-established. Moreover, eligibility requires that the results of any verification/validation to support the given change be adequately reviewable by the FDA in a summary or risk analysis format. The draft guidance clarifies that usually, if the FDA's interpretation of the underlying data is required for a substantial equivalence determination, a summary format would result in loss of information, so a Special 510(k) notice is not appropriate.[4]

Appendix B of the draft guidance provides examples to help illustrate how the principles outlined above would be applied in practice. While these examples are sometimes esoteric, with much focus on the specifics of the fact pattern, the overarching lesson appears to be that well-established methods for evaluating a change will almost always come from (1) the previously cleared device submission, (2) an FDA-recognized consensus standard, or (3) FDA guidance materials. Moreover, manufacturers should be certain that the chosen method covers the totality of the change as it pertains to the device in question. For instance, the FDA's example of adding wireless control capabilities to an existing bilevel positive airway pressure (BiPAP) device notes that while there is a well-established method for validating electromagnetic compatibility (EMC), i.e., IEC 60601-1-2, that standard does not adequately address wireless technology EMC at present and, moreover, cannot be applied to BiPAP devices specifically. Specific examples are also provided of submissions that are inappropriate for the Special 510(k) pathway because the FDA could not reasonably conduct its review within the 30-day timeline (e.g., changes that involve several scientific disciplines, submissions that cover multiple devices with unrelated changes, submissions made following a recent quality system inspection that resulted in a violation for a design control that would impact the information under review in the Special 510(k) notice, etc.).

To evaluate the impact of the proposed updates, particularly with respect to improving FDA efficiency in reviewing 510(k) submissions, the Agency has launched a Special 510(k) pilot program.[5] The program will evaluate all Special 510(k) notices received on or after October 1, 2018 per the newly proposed eligibility criteria. Moving forward, sponsors should look closely at the new guidelines prior to submitting a Special 510(k) notice.

Summary

The new policy outlined in the FDA's draft guidance appears to offer a more straightforward manner for consistently assessing whether modifications, including both minor changes in indications and more expansive changes in technology, to legally marketed devices can be adequately reviewed through the streamlined Special 510(k) pathway. In addition, the FDA continues to emphasize the importance of having strong design control processes in place. To that end, this draft guidance may indicate that the FDA intends to scrutinize further design control procedures and implementation when conducting inspections. At the same time, the new guidance places some additional accountability on the Agency to provide justification to

[4] Along the same lines, the guidance identifies certain scenarios which categorically are considered to require review of complete test reports to establish substantial equivalence. These include, among others, changes to the indications for use that are supported by clinical, animal, or cadaver data and use of novel sterilization methods as described in the FDA's guidance, *Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile* (2000).
[5] See "Special 510(k) Program Pilot" here.

submitters when it decides to convert a filing from Special 510(k) notice to Traditional 510(k) notice.

Public comments on the guidance may be submitted to docket number FDA-2018-D-3304 through November 27, 2018. The FDA will host a webinar to discuss the Special 510(k) pilot program on November 8, 2018.

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