

Concerns For 510(k) Sponsors After FDA Proposes Major Shift

By **Kristin Davenport, Christina Kuhn and Amy Leiser** (September 18, 2023, 10:08 AM EDT)

For several years, the U.S. Food and Drug Administration's Center for Devices and Radiological Health has been vocal about its views regarding the limitations of the 510(k) pathway and the need for modernization to keep up with advances in technology. In 2018, the CDRH proposed an approach that would sunset older predicates and promote the use of more modern predicates.[1]

It therefore comes as no surprise that the CDRH just released three new draft guidances aimed at modernizing the 510(k) program.[2]

One of these draft guidances pertains to "Best Practices for Selecting a Predicate Device to Support a Premarket Notification [510(k)] Submission." [3] If finalized, this draft guidance would drastically shift the process for identifying predicate devices for a substantial equivalence comparison.

The draft guidance introduces four new so-called best practices for selecting a predicate device used to support a 510(k) premarket notification. When there are multiple "valid predicates," i.e., legally marketed devices to which a 510(k) submitter could demonstrate substantial equivalence for the new device based on intended use and technological characteristics, 510(k) sponsors should use the best practices to select between those valid predicates.

The draft guidance also creates a new process by which 510(k) sponsors should evaluate which valid predicates meet these best practices, describe and justify their predicate selection process pursuant to the best practices in a 510(k) submission, and summarize these principles in the publicly posted 510(k) summary.

The agency's goal is to promote innovation and improve safety by "driving innovators toward reliance on more modern predicate devices or objective performance criteria." [4] The FDA believes that consideration of these best practices "will encourage the evolution of safer and more effective medical devices in the 510(k) program over time." [5]

While there may be public health benefits from modernizing the 510(k) process, the draft guidance raises meaningful questions about the potential legal and regulatory implications of the FDA's proposed new approach. It also raises a number of potential practical challenges.



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The draft guidance, if finalized, would have significant impact on all companies that will be submitting 510(k)s for new devices or for modifications to previously cleared devices. Such companies should consider submitting comments to the FDA on the draft guidance.

Best Practices and Recommendations for 510(k) Sponsors

According to the best practices, a valid predicate device should:

- Have been cleared using "well-established methods," such as methods from a consensus standard or FDA guidance;
- Continue to meet or exceed safety or performance expectations, taking into account post-market reports of design-related malfunctions or adverse events;
- Not have any "unmitigated use-related or design-related safety issues," including consideration of FDA safety communications; and
- Not be subject to "an associated design-related recall."

The draft guidance recommends that 510(k) submitters include in their submissions a description of how they applied these best practices in selecting a valid predicate device.

The examples suggest that 510(k) submitters should include a table identifying all valid predicates and describing how each valid predicate does or does not reflect each of the four best practices, along with a rationale for selecting among the predicates.

In cases where no valid best practices predicate is available, the CDRH recommends that the 510(k) submitter describe "how any known concerns with the valid predicate device have been mitigated with the subject device (e.g., design features, performance testing)."[6]

Potential Legal and Regulatory Implications of Proposed Predicate Selection Process

The draft guidance, if implemented, could present a significant departure from the current standard in the law for when a device can no longer be used as a predicate.

Under the law, a device cannot serve as a predicate if it has been removed from the market at the FDA's initiative or has been determined to be misbranded or adulterated by judicial order.[7] Otherwise, a 510(k) sponsor is free to choose any predicate and, under current practice, does not have to justify the selection of a predicate to which substantial equivalence is claimed.

Although the CDRH carefully describes the best practices as "recommendations" that "are not intended to propose any changes to applicable statutory and regulatory standards,"[8] it is unclear whether, in practice, these recommendations would effectively become requirements. For example, if a 510(k) submitter ignores the recommendations in the draft guidance to provide information about the predicate selection process, will the CDRH require that information in order to complete its review of the 510(k) submission?

While the draft guidance acknowledges that there may not always be a valid predicate that meets the best practices, if a 510(k) includes a predicate that was not selected in accordance with best practices

and the CDRH believes there is a best practices predicate, will the CDRH review the 510(k) submission?

Beyond fundamentally altering the process for predicate selection, the draft guidance also could potentially affect substantial equivalence determinations.

Under the law, a device is substantially equivalent to the predicate if it (1) has the same intended use, and (2) either has the same technological characteristics or, if it has different technological characteristics, is shown to be as safe and effective as the predicate and does not raise different questions of safety or effectiveness.[9]

The draft guidance, if implemented, could require certain 510(k) submitters to demonstrate superiority, as opposed to substantial equivalence, to the predicate device. Under the draft guidance, if no predicate selected in accordance with best practices is available, the 510(k) submitter should describe how "any known concerns with the valid predicate device have been mitigated with the subject device." [10] In effect, this means that the 510(k) submitter has to show that the new device is safer and/or more effective than the predicate because it mitigates risks that may be present for the predicate.

This approach is also reflected in the companion draft guidance, "Recommendations for the Use of Clinical Data in Premarket Notification [510(k)] Submissions," [11] which suggests that 510(k) submitters may need to submit clinical data to demonstrate substantial equivalence when a newly identified or increased risk for the predicate device has arisen since its introduction to the marketplace.

Practical Implementation Challenges and Open Questions

The draft guidance leaves open a number of questions about how the CDRH plans to implement the proposed approach.

One major concern is that the best practices predicate may not be the closest match from a substantial equivalence standpoint, i.e., it may have different indications or technological characteristics. For example, if the 510(k) submitter makes a modification to its own device, but that device is subject to a design-related recall, under the best practices, the 510(k) submitter would need to choose a different predicate that is less similar to the new device and therefore may require more data to demonstrate substantial equivalence.

It is also unclear how 510(k) submitters should weigh the four best practices criteria. For example, if the application of best practices leads to two potential predicate candidates, one with an unmitigated use-related or design-related safety issue and the other with an open design-related recall, how should the submitter choose the predicate?

The draft guidance also does not address when and how the CDRH would communicate concerns that the 510(k) submitter has not implemented the guidance recommendations, such as 510(k) submissions that do not include information about the predicate selection process or the CDRH disagreements with the 510(k) submitter's predicate selection. Would that issue be raised during the acceptance review for the 510(k) or in an additional information request? If the latter, how would the 510(k) submitter address that issue at the 510(k) review stage, assuming that the substantial equivalence data submitted in the 510(k) relate to the chosen predicate and may include side-by-side testing?

Another potential concern relates to the CDRH's expectation that the 510(k) submitter review the CDRH's databases, such as the MAUDE database or the recall database, to determine whether a

predicate device has an unmitigated safety issue or is subject to a design related recall.

Not only could this review be very onerous if there are multiple valid predicates or the predicates have a large volume of medical device reports, but the submitter's ability to draw any conclusions about whether an MDR or recall is design-related or may affect safety and/or effectiveness may be limited by the high-level nature of the information in these databases. The draft guidance also leaves open the question of how a disagreement between the CDRH and the submitter with regard to any conclusions drawn would be handled.

It may also be challenging for 510(k) submitters to manage the predicate selection process, given that the post-market safety information for predicates can be continually evolving.

Selection of a predicate often occurs early in the development process, particularly if comparative performance or clinical testing will be needed to support the 510(k) submission. However, the post-market safety information available for predicate devices that informs whether they meet the best practices could evolve during that time period, or even during the FDA's review of a submitted 510(k).

Are 510(k) sponsors expected to continually monitor the post-market safety information (e.g., MDR submissions) for all valid predicates throughout the development and premarket review process? What happens if a selected predicate device that met the best practices at the time of selection subsequently is subject to a design-related recall or FDA safety communication?

Finally, the predicate manufacturer may be adversely affected by negative CDRH-reviewed statements in the 510(k) summary for the new device, such as that the predicate device had an unmitigated design-related safety issue which was mitigated or eliminated in the new device. The draft guidance does not contemplate that the predicate manufacturer could weigh in on these statements, yet they could have a significant competitive or product liability impact and may potentially affect the predicate manufacturer's post-market obligations.

Comments on the draft guidance may be submitted to the electronic docket at Regulations.gov until Dec. 6.

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[1] Press Release, Scott Gottlieb and Jeffrey E. Shuren, Transformative New Steps to Modernize FDA's 510(k) Program to Advance Review of the Safety and Effectiveness of Medical Devices (Nov. 26, 2018). Although CDRH previously considered retiring older predicate devices, see FDA, Modernizing the Food and Drug Administration's 510(k) Program: Request for Comments (Jan. 2019), it moved away from that proposed approach after considering public comments.

[2] On September 7, 2023, FDA also issued two other draft guidance documents related to its 510(k) program: Evidentiary Expectations for 510(k) Implant Devices and Recommendations for the Use of Clinical Data in Premarket Notification [510(k)] Submissions. Comments on all three draft guidance

documents may be submitted until December 6, 2023.

[3] <https://www.fda.gov/media/171838/download>.

[4] FDA, Best Practices for Selecting a Predicate Device to Support a Premarket Notification [510(k)] Submission: Draft Guidance for Industry and Food and Drug Administration Staff 3 (Sept. 2023).

[5] *Id.* at 4.

[6] *Id.* at 6.

[7] FDCA § 513(i)(2).

[8] FDA, Best Practices for Selecting a Predicate Device to Support a Premarket Notification [510(k)] Submission: Draft Guidance for Industry and Food and Drug Administration Staff 4 (2023).

[9] FDCA § 513(i)(1)(A)(ii)(I).

[10] FDA, Best Practices for Selecting a Predicate Device to Support a Premarket Notification [510(k)] Submission: Draft Guidance for Industry and Food and Drug Administration Staff 6 (2023).

[11] <https://www.fda.gov/media/171837/download>.