Design Changes and 510(k) Submissions

The US has a variety of pre-market submission types designed to help ensure a medical device is safe and effective. One of the most common is the pre-market notification authorized by section 510(k) of the Food, Drug, and Cosmetics Act. In common language, it is simply a 510(k) submission.

A manufacturer submits a 510(k) prior to marketing a device in the US for which a Premarket Approval (PMA) is not required. However, there are some exemptions and exceptions.

A 510(k) demonstrates to FDA that the device is at least as safe and effective, substantially equivalent, to a legally marketed device that does not require a PMA. The legally marketed device used for comparison is usually called a predicate device or just a predicate. If FDA concurs, it will issue an order, in the form of a letter, finding the device substantially equivalent and allowing marketing in the US. This order "clears" the device for commercial distribution.

Design Changes

As long as the device doesn't change, it remains substantially equivalent. However, the device could change through a design change in §820.30(i) or a production change in §820.70(b). The FDA's Quality System Inspection Technique, QSIT, considers them redundant. A device change under either section could trigger a new 510(k).

In discussing design changes the QSR preamble says, "Note that when a change is made to a specification, method, or procedure, each manufacturer should evaluate the change in accordance with an established procedure to determine if the submission of a premarket notification (510(k)) under … 21 CFR §807.81(a)(3) is required. Records of this evaluation and its results should be maintained."

In other words, the preamble recommends a procedure to evaluate each change against the criteria in 21 CFR §807.81(a)(3). The result is a determination on the need to submit a new 510(k).

Substantial Equivalence

A 510(k) requires demonstration of substantial equivalence to another legally U.S. marketed device. Substantial equivalence means that the new device is at least as safe and effective as the predicate.

A Device Advice page[1] on the FDA–CDRH website provides a description of substantially equivalent, SE. The logic diagram in Figure 1 illustrates the decision path. A claim of substantial equivalence does not mean the new and predicate devices must be identical. Substantial equivalence considers the intended use, design, energy used or delivered, materials, chemical composition, manufacturing process, performance, safety, effectiveness, labeling, biocompatibility, standards, and other characteristics, as applicable.

[1] http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/default.htm

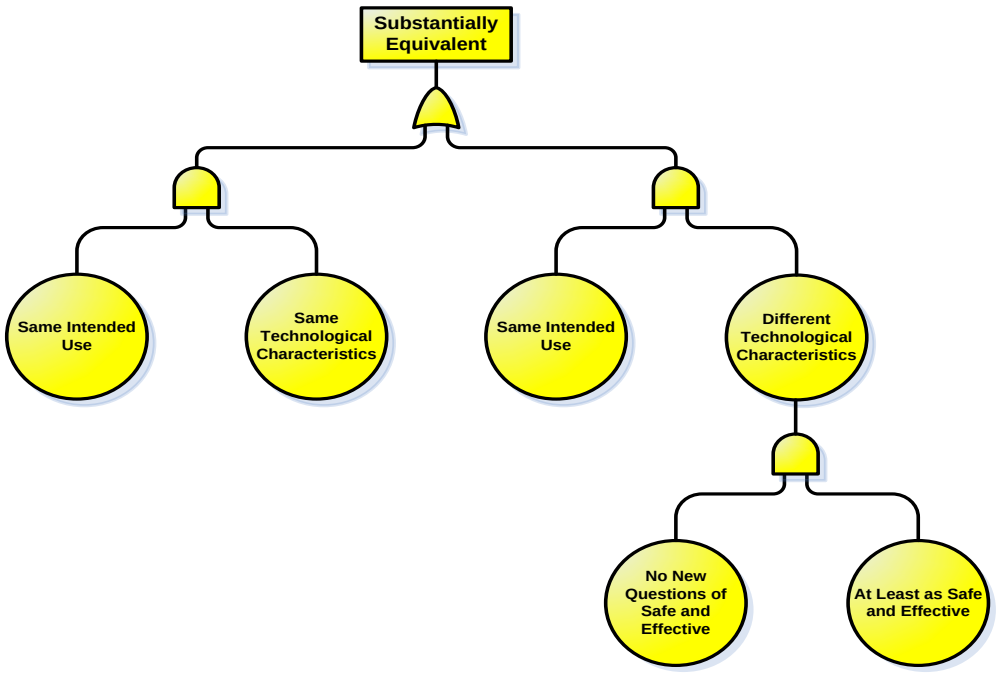

Figure 1 Substantially Equivalent

21 CFR §807.81(a)(3)

The regulation requires a premarket submission to FDA under various circumstances. The one of interest here says:

> (3) The device is one that the person currently has in commercial distribution or is reintroducing into commercial distribution, but that is about to be significantly changed or modified in design, components, method of manufacture, or intended use. The following constitute significant changes or modifications that require a premarket notification:
>
> > (i) A change or modification in the device that could significantly affect the safety or effectiveness of the device, *e.g.*, a significant change or modification in design, material, chemical composition, energy source, or manufacturing process.
> >
> > (ii) A major change or modification in the intended use of the device.

The regulation provides an opportunity for a device manufacturer to develop the necessary criteria. A common approach is a Yes/No checklist based on the regulation to establish the evaluation criteria. Apply it to each design change or production change, record the response, document the reason for the response, and maintain it as a quality record.

Unfortunately, there is a potential problem with this approach; the regulation includes some undefined and ambiguous terms such as “significant” or “major”. To help address this issue, FDA-CDRH issued a guidance document to help make the determination.

The 1997 Guidance
The guidance is number K97-1, *Deciding When to Submit a 510(k) for a Change to an Existing Device.*

The guidance explains, "The key issue here is that the phrase 'could significantly affect the safety or effectiveness of the device' and the use of the adjectives 'major' and 'significant' sometimes lead to subjective interpretations. Because of this, manufacturers have frequently expressed the need for more specific guidance in applying the regulatory standard in their decision making."

The guidance further explains, "This document proposes a flowchart model that can be used by manufacturers in their decision-making to analyze how changes in devices may affect safety or effectiveness. In the model, we attempt to address changes to devices at a level detailed enough so that application of the broad principles contained in the regulations would minimize disagreements between manufacturers and the Agency. The goal of the model is to provide guidance in answering a manufacturer's questions on whether a 510(k) should be submitted for a particular type of change and to minimize the number of instances where the answer would be uncertain. Taken as a whole, this guidance, and the model it describes, provides the agency's best definition of when a change to a device could significantly affect safety or effectiveness."

The guidance has a Main Flowchart that leads to more specific device areas: labeling, technology, performance, and material. In addition, there are two special cases. In one, the device change is due to a recall or corrective action. In the other, the device is an *in vitro* diagnostic device.

Each flowchart has a series of Yes/No questions that define the path through the flowchart. The result is either "Documentation" or "New 510(k)". The text explains the actions to take in each case.

Each of the Yes/No questions has an explanatory text. This provides information on what to consider in formulating the response and deciding if the answer to the question is Yes or No.

The guidance recognizes that a device may have many changes over time and that individually, each change may not require a new 510(k). This guidance recommends evaluation of each change individually as well as a collective evaluation of all changes since the most recent 510(k) clearance. The idea is that individually, no one change triggers a new 510(k), but collectively the device may no longer be substantially equivalent to the cleared device.

Once the changed device receives 510(k) clearance, it becomes the basis of comparison for the next sequence of changes.

The Withdrawn Draft Guidance
FDA-CDRH had planned to update the 1997 guidance and issued a draft to which industry objected. Eventually, a new law required FDA to withdraw it, revert to the 1997 guidance, and meet some other conditions before issuing a new draft guidance.

The New Draft Guidance Documents

On August 8, 2016, FDA-CDRH published two draft guidance documents. UCM514771 is *Deciding When to Submit a 510(k) for a Change to an Existing Device*. UCM514737 is *Deciding When to Submit a 510(k) for a Software Change to an Existing Device*. The two drafts are usually termed the base guidance and the software guidance.

The base guidance uses flowcharts to describe the path through the decision making process. The main flowchart starts with whether the intent of the change is to significantly improve the safety or effectiveness of the device, for example, in response to a known risk, adverse event, *etc*. If yes, then the change "could significantly affect safety or effectiveness" and likely result in a new 510(k).

The main flowchart leads to other flowcharts related to changes in labeling, technology, engineering, performance, or materials. The flowcharts to use depend, in part, on whether the device is an IVD. In addition, a separate section includes considerations on risk management. While not covered by a flowchart, the section looks at risks (harm to patient or user) both before and after risk reduction. While not a requirement, the section uses ISO 14971:2007 to help illustrate the points.

The software guidance uses one flowchart to analyze the change to determine the need for a new 510(k). The draft guidance applies only to software in the device and does not cover production or QMS software, see 21 CFR §820.70(i). It also has a section on the application of risk management, and refers to ISO 14971:2007.