



Client Alert



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FDA Releases Draft Guidance on Changes to Existing Devices and When to Submit a New 510(k)

The Food and Drug Administration's (FDA) Center for Devices and Radiological Health (CDRH) issued a draft guidance to clarify when changes to an existing device will require the submission of a new 510(k) premarket notification.¹ The issuance of the draft guidance fulfills one of the 25 action items outlined in CDRH's January 2011 *510(k) and Science Report Recommendations*, part of the agency's ongoing review of the device premarket review process. When finalized, this guidance document will supersede the agency's 1997 guidance, *Deciding When to Submit a 510(k) for a Change to an Existing Device*. While the draft guidance is not legally binding, it represents the FDA's current thinking on the subject.

The purpose of the draft guidance is to aid manufacturers in distinguishing changes that require submission of a new 510(k) from changes that may simply be documented in accordance with device Quality System Regulations (QSRs).² Among other changes, the revised guidance omits the flowcharts and clarifying definitions found in the 1997 guidance document. Instead, the draft guidance presents a series of questions, representing various types of device modifications, and provides numerous example responses. The revised format is likely a deliberate effort by the agency to force manufacturers to consider the full text of the guidance in deciding whether to submit a new 510(k), instead of relying on the simplified flowchart. The guidance focuses on manufacturing, labeling, technology or performance specifications, and materials changes.

The FDA regulations require the submission of a new 510(k) whenever a device will be "significantly changed or modified in design, components, method of manufacture, or intended use."³ The regulation further states that the following situations constitute "significant changes" that require premarket notification:

1. 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.
2. A major change or modification in the intended use of the device.⁴

¹ *Guidance for Industry and FDA Staff, 510(k) Device Modifications: Deciding When to Submit a 510(k) for a Change to an Existing Device (Draft Guidance)* is available at <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM265349.pdf>.

² See 21 C.F.R. Part 820.

³ See 21 C.F.R. § 807.81(a)(3).

⁴ *Id.*

As with the 1997 guidance, this revised draft guidance is intended to clarify the meaning of “significant changes.” The draft guidance emphasizes the distinction between a change that *does* and a change that *could* affect a device’s safety or effectiveness, noting that 510(k) submissions are also required for the latter, which encompasses a greater number of potential changes. The potential effect of the new guidance is significant, as the circumstances that will not require a new 510(k) appear to be limited. The FDA notes that, “device changes intended as improvements to a device’s safety or effectiveness could significantly affect” the product’s safety or effectiveness and, therefore, require a new 510(k). Before providing specific examples, the draft guidance outlines the following seven underlying “basic principles” to guide manufacturers in deciding whether to submit a premarket notification:

1. 510(k) notifications are required before initially marketing a new device (i.e., one that is not a modified version of the manufacturer’s already-cleared device).
2. Changes to 510(k)-exempt devices do not require premarket notification if the particular change falls within specified limits, as stated in the applicable regulations.
3. In determining whether a modification is significant, manufacturers should compare the modified device to the *most recently FDA-cleared version* of the device, not to a more recent version of the device that was modified by changes not requiring submission of a 510(k).
4. For each individual change to the device, manufacturers should consider the questions presented in the draft guidance (i.e., each scenario summarized in the table below) to determine whether a new 510(k) is required.
5. Even if individual changes do not require a new 510(k), premarket notification could be required if, collectively, the changes could significantly affect the device’s safety or effectiveness.
6. Manufacturers must comply with the QSRs to document, validate or, where appropriate, verify specification changes prior to implementation, unless the device is exempt from QSRs.
7. Manufacturers should establish standard operating procedures for evaluating whether changes trigger the 510(k) requirement. If only one of multiple proposed changes triggers the premarket notification requirement, all proposed changes should be described in the notification (including changes implemented without notification since the device’s last 510(k) clearance). If a manufacturer determines that the device modification could not significantly affect safety or effectiveness and decides not to submit a new 510(k), the conclusion should be scientifically justified, and the rationale should be documented in accordance with the QSRs.

The draft guidance attempts to classify device modifications into three categories:

1. Changes likely to require a new 510(k).
2. Changes generally unlikely to require a 510(k).
3. Changes in a gray area where manufacturers should consult the appropriate review division to determine whether a 510(k) should be submitted.

The agency notes that the draft guidance does not address issues unique to specific devices or combination products. In particular, the FDA plans to release device-specific guidance to address nanotechnology. In the interim, the draft guidance urges manufacturers to consult with the agency regarding nanotechnology-related changes to devices. Manufacturers should continue to consult existing device-specific guidance, as appropriate.

The following table summarizes various types of modifications and notes additional considerations for manufacturers in determining whether a 510(k) notification is required.⁵ As previously noted, one of the “basic principles” advises manufacturers to consider whether any of the following situations apply to *each proposed change*. For example, proposed changes to a device’s length, thickness and material should be considered three individual changes.

Situation	New 510(k) Required?	Additional Considerations
Manufacturing Process Changes		
Manufacturing process information was reviewed as part of the original 510(k) submission	Likely yes	If the manufacturing processes factored into the original clearance decision, there is a higher likelihood that changes to the process could significantly affect safety or effectiveness (e.g., contact lenses, wound dressings, infusion pumps).
Change in packaging or expiration dating	Generally no	A 510(k) may be necessary where methods or protocols not described in the original 510(k) are used to support new package integrity or shelf-life claims.
Change in sterilization	Depends on whether the change could significantly affect the device’s safety or effectiveness	<p>510(k) is required if sterility assurance level (SAL) is less than 10^{-6}.</p> <p>If SAL remains better than 10^{-6}, a new 510(k) is not required.</p> <p>For example, a 510(k) is required if changing from moist heat sterilization to e-beam radiation, or if the changes result in the device being provided non-sterile when it was previously provided sterile (or vice-versa).</p>

⁵ We provide some, but not all, of the examples identified by the FDA.

Situation	New 510(k) Required?	Additional Considerations
Labeling Changes		
<p>Change affects the indications for use</p> <p>“indications for use” refers to the description of the disease or condition the device will diagnose, treat, prevent, cure, or mitigate, including a description of the patient for which the device is intended</p>	<p>Yes, for most changes</p>	<p>A change removing certain indications or limiting use within the currently cleared indication <i>due strictly to marketing reasons</i> would not require a new 510(k).</p> <p>For example, a device is cleared for three uses, and the company decides to market for only two of the indications due to market demand. This will not likely be viewed as a “major change” requiring a new 510(k). In contrast, a company decision to market for two of the indications because of complaints or corrective action about the third use might be a major change, necessitating a new 510(k).</p> <p>A new 510(k) is usually required for:</p> <ul style="list-style-type: none"> • changes allowing reuse of devices previously labeled “single use only;” • changes from prescription (Rx) to over-the-counter (OTC) uses; • a change from Rx use in a clinical setting to Rx use at home (home use devices); or • changes from general to a specific patient population (e.g., an undefined patient age group to a pediatric population).
<p>Change adds a contraindication</p>	<p>Yes, but labeled “change being effected”</p> <p>The company can market with modified labeling, unless the FDA says otherwise.</p>	<p>In the interest of public health, manufacturers may add a contraindication prior to receiving clearance, as long as the 510(k) is submitted concurrently and labeled “change being effected” (CBE).</p> <p>The draft guidance notes that the agency will exercise enforcement discretion if the device is marketed with the change prior to receiving clearance and the new 510(k) is submitted to the FDA concurrently.</p>
<p>Change deletes a contraindication</p>	<p>Yes</p>	<p>This type of change expands the indications for use and requires a new 510(k).</p>

Situation	New 510(k) Required?	Additional Considerations
Change in instructions for use	Yes	<p>Such changes are likely to significantly affect safety or effectiveness (and possibly changes in indications for use).</p> <p>For example, a new 510(k) is required for:</p> <ul style="list-style-type: none"> • a modification to include additional or new instructions on how to interpret data from a diagnostic device; or • a modification to include additional or new instructions about incision procedures for a cutting instrument or laser.
Change in warnings or precautions	Discuss with the FDA	<p>A new 510(k) is generally not required to add warnings or precautions, but manufacturers are encouraged to discuss it with the FDA.</p> <p>Note: A new 510(k) is likely required to <i>delete</i> warnings or precautions because of the significant effect on safety or effectiveness.</p>
Some other labeling change	Generally no	<p>For example, a new 510(k) is not required for:</p> <ul style="list-style-type: none"> • language clarifications that do not change the meaning; • aesthetic or organizational changes to the way information is displayed; • logo changes; or • name changes.
Technology, Engineering and Performance Changes⁶		
Change alters the fundamental scientific technology of the device	Yes, because of the significant potential effect on safety or effectiveness	Note: This encompasses changes in both the design principle of the device (i.e., the underlying scientific principle by which the device operates) and the method by which that principle is applied.
Change in energy type (i.e., the type of power input to or output from the device)	Likely yes	For example, a change from external power source to battery, or change from microwave energy to radiofrequency energy, requires a new 510(k).

⁶ Manufacturers should first review the aforementioned labeling questions, because technology changes may affect device labeling.



Situation	New 510(k) Required?	Additional Considerations
Change has the potential to significantly alter the performance characteristics or specifications of the device	Yes, with comparative testing provided, because of direct performance impact and potential safety or effectiveness issues	For example, changes in device sensitivity
Change in ergonomics or the patient/user interface	Depends on whether the change can expand how the device will be used or affect how it will perform	<p>A new 510(k) is likely not required if the change is only to increase comfort in using the device. However, certain changes may have unintended effects on safety or effectiveness and could require a new 510(k).</p> <p>For example, relocation of a device motor to make the device handpiece less bulky could result in increased risk of patient burns, even if only intended to increase user comfort. This type of change would require a new 510(k).</p>
Change in dimensional specifications	Depends on the device type and component being modified, and whether the dimensional changes could significantly affect safety and effectiveness	Typically, a new 510(k) is required if a dimensional change falls outside the cleared dimensional tolerance range; however, a 510(k) is not required if modifications fall within previously cleared size ranges.
Change in software or firmware	Depends on whether the change may significantly affect the device's safety or effectiveness	<p>A new 510(k) is likely required if a software change:</p> <ul style="list-style-type: none"> • could expand the capability of the device or affect performance; or • could affect a clinical algorithm. <p>Some low-risk changes may be made following the QSR (including design controls) and documenting the appropriate validation testing.</p>



Situation	New 510(k) Required?	Additional Considerations
Modification impacts how the device receives, transmits, or displays electrical signals or data	Yes, for most changes, because of the potential significant impact on safety or effectiveness	For example, altering the device display from a monitor to a hand-held device, or changes from wired to wireless data communication.
Modification intended to add an aspect of autonomous or semi-autonomous control to the existing device	Yes	If the modification takes away control of the device or decision-making from the user, the change likely introduces new risks of safety or effectiveness, requiring a new 510(k).
Change being implemented to address a specific risk or failure mode for the device	Likely yes	<p>Changes implemented to address known or newly-identified safety risks or failure modes are, by definition, likely to significantly affect safety or effectiveness.</p> <p>For example, implementation of new alarms or new alarm setpoints, modifications to the user interface to display new information that may be used to manage device settings, or design modifications intended to eliminate known failure modes.</p>
Modification is likely to alter or expand the use of the device in practice	Yes, because of the potential to significantly affect safety or effectiveness	<p>This includes modifications to allow for the device's use in a different or modified type of procedure, or to treat or diagnose a different disease or condition apart from that previously cleared.</p> <p>Note: A new 510(k) should be submitted particularly in cases where the modification could create a reasonable likelihood of off-label use that could cause harm.</p>



Situation	New 510(k) Required?	Additional Considerations
Modification allows for the use of the device in a new, expanded, or more specific patient population	Yes, because of the potential to significantly affect safety or effectiveness	<p>For example, modifications to a ventilator to allow for treatment of pediatric patients, whereas the device previously was cleared for use only by patients with a tidal volume in the adult range, would require submission of a new 510(k).</p> <p>Note: Particularly in cases where the modification could create a reasonable likelihood of off-label use that could cause harm, a new 510(k) should be submitted to enable FDA to evaluate whether appropriate information in the labeling about a use not currently identified in the labeling is warranted.</p>
Modification significantly changes or alters an established medical procedure associated with the device	Yes, because the new use may raise new safety risks or lead to less effective use of the device	For example, components of a surgical kit are combined with a surgical handpiece to allow a medical procedure to be performed with one device. This change modifies the procedure, and could significantly affect the safety or effectiveness of the device.
Modification is intended to allow for the use of the device in a new environment	Likely yes, because of potential new risks	For example, a stationary electrocardiogram (EEG) device cleared for use in hospitals is modified to allow for use in pre-hospital settings, such as ambulance transport.
Change is intended to allow the device to be used by a lay person outside of a clinical setting	Yes, because of potential safety or effectiveness concerns	This includes a change in the device indication from prescription to over-the-counter or for home use.
Modification allows for the device to provide new information or data to the user for patient assessment or diagnostic purposes	Likely yes	<p>For example, a device that previously derived four parameters from an EEG waveform is modified to derive two additional parameters, or the device is modified to calculate standard deviation or variances of those parameters. Either of these changes would require submission of a new 510(k).</p> <p>Note: A new 510(k) may be required, even if the new patient assessment information is used as an aid or adjunct to other measures or is only considered additional information.</p>

Situation	New 510(k) Required?	Additional Considerations
Materials Changes⁷		
The material modification is made to device components that cannot have direct or indirect contact with the patient	Generally no	Note: A 510(k) may be required if the change affects the fundamental device technology or performance (e.g., preservatives, antibacterials, moving parts, structurally significant components, lubricants).
The change affects patient-contacting materials (either direct or indirect)	Yes	These changes may affect the biocompatibility or material properties of the device. Thus, a 510(k) is required for changes in material formulation for patient-contacting devices or device components. ⁸
The change involves the device surface	Likely yes	For example, changes to device coating or surface modification technique, chemical formulation, method of application, or surface preparation.
Clinical Data Necessary		
Clinical data is needed to determine substantial equivalence	Yes, if the manufacturer concludes testing or bench simulations are insufficient to evaluate the modified device's safety and effectiveness	Note: This does not necessarily apply to in vitro diagnostic devices, which have different testing requirements. Manufacturers should contact the appropriate review division within the Office of In Vitro Diagnostics for questions.

⁷ Materials changes could also lead to labeling or performance specifications changes, which should be considered first.

⁸ According to the draft guidance, material formulation includes the chemical composition of the material.

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