

# Welcome to Today's FDA/CDRH Webinar

*Thank you for your patience while we register all of today's  
participants.*

**If you have not connected to the audio portion of the webinar,  
please do so now:**

**U.S. Callers Dial: 888-455-9669**

**International Callers Dial: 1-415-228-4882**

**Passcode: 8211035**

**Conference Number: PWXW5928257**

# **Deciding When to Submit a 510(k) for a Change to an Existing Device**

**Final Guidance for Industry and FDA Staff  
and**

**Deciding When to Submit a  
510(k) for a Software Change to an Existing Device  
Final Guidance for Industry and FDA Staff**

**Published: October 25, 2017**

# Presenters

Rebecca Nipper & Linda Ricci  
Office of Device Evaluation  
Center for Devices and Radiological Health

# Agenda

- Background on 510(k) device modifications
- Development of FDA's modifications guidances
- FDA guidance goals
- General guidance highlights
- Software guidance highlights
- Questions and answers

# 510(k) Device Modifications Background

- Medical device innovation cycle requires continual modifications
- FDA's policy has two goals:
  1. Ensure patients and providers have timely access to modified devices; and
  2. Provide essential flexibility for industry and FDA to enable innovation and ensure effective public health oversight of modified devices

# Regulatory Basis for FDA's policy

- FDA's 510(k) device modifications policy is based on two regulations:
  - 21 CFR 807.81(a)(3)
    - Regulation that describes when a new 510(k) is required
  - 21 CFR 820
    - Quality System Regulation

# When a 510(k) is Required for a Change

21 CFR 807.81(a)(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.

# Quality System Regulation

- 21 CFR 820.30(i) *Design changes* - Each manufacturer shall establish and maintain procedures for the identification, documentation, validation or where appropriate verification, review, and approval of design changes before their implementation.
  - Robust documentation is helpful to both FDA and manufacturers



# Stakeholder Input

- Guidance content based on stakeholder feedback, including comments on draft guidances and FDA's 2013 Public Meeting
- Consensus around retaining the basic paradigm of original *Deciding When to Submit*:
  - No paradigm changes from original guidance
  - Clarification needed in certain areas
  - Rely on risk management and Quality System regulation (21 CFR 820) where possible

# FDA Guidance Goals

- FDA has made targeted changes to original *Deciding When to Submit* guidance from 1997:
  - Clarity, including interpretation of key regulation terms such as “could significantly affect”
  - Flowcharts – matched with text
  - Key principles
  - Materials changes
  - Examples to illustrate use of guidances
  - Documentation recommendations and examples
- Separate software guidance based on same key principles
- Addition of risk assessment paradigm

# Guidance Scope

- Both guidances apply to legally marketed devices subject to 510(k) requirements
  - Excludes PMA devices and 510(k)-exempt devices
- General Guidance and Software:
  - General guidance **does not** apply to software-specific changes
  - General guidance **does** apply to non-software changes to software devices or devices containing software (e.g., labeling)
  - Guiding principles are aligned between the guidances

# Guidance Scope

- Software Guidance
  - **Does not** apply to software for which FDA has stated in guidance that it does not intend to enforce compliance with applicable regulatory controls
  - **Does not** address:
    - the software lifecycle
    - what documentation should be included in a 510(k) for a software modification, or
    - the principles that are applicable to the validation of medical device software

# Evaluating Software and Non-Software Changes

- When multiple changes affect labeling/hardware in addition to software, assess the changes using both guidances.
  - If use of either guidance leads to a “New 510(k)” conclusion, submission of a new 510(k) is likely required.
- For example:
  - To add a new mode to software device (no hardware), use Software Mods. Only need to use General Mods for labeling revisions or if changes to indications for use are warranted (e.g., to explain new mode)
  - To add a new mode to an infusion pump, use Software Mods for the software revisions and General Mods for the change to pump specifications

# Guiding Principles

## (Applies to both General and Software 510(k) Modifications Guidances)

- Referred to as “Assumptions/Axioms” in the “Deciding When to Submit a 510(k) for a Change to an Existing Device (K97-1) published January 10, 1997
- Essential principles necessary for use of both guidances
- Principles should be used in conjunction with the more specific guidance sections

## Guiding Principles Cont.

- Modifications made with intent to significantly affect safety or effectiveness of a device
  - Per 21 CFR 807.81(a)(3)(i), a change that could significantly affect safety or effectiveness requires a 510(k)
  - Change that's intended to significantly affect safety or effectiveness (e.g., to address adverse events) requires a 510(k)
  - Changes not intended to significantly affect safety or effectiveness should still be evaluated using this guidance

## Guiding Principles Cont.

- “Could significantly affect” and the role of testing
  - Risk-based assessment should be used to make initial determination of whether a 510(k) is necessary
    - Assessment should cover new risks and changes in known risks resulting from device modification
  - Risk-based determinations not to submit should be confirmed by verification and validation (V&V)
    - If V&V activities produce unexpected results, decisions not to submit should be reconsidered
- Unintended consequences of changes
  - Manufacturers should consider whether there are unintended consequences or effects of device modifications
  - Example: sterilization changes may affect device materials



# Guiding Principles Cont.

- Use of risk management
  - Plays a central role in determining when a change “could significantly affect” safety or effectiveness
  - Guidances intended to leverage manufacturers’ existing risk processes to determine when change requires a 510(k)
  - Risk terminology in guidance primarily based on ISO 14971, but an individual manufacturer’s terminology may differ
  - Because 21 CFR 807.81(a)(3)(i) requires 510(k) for change that “could significantly affect safety or effectiveness,” both safety and effectiveness should be considered

# Guiding Principles Cont.

- Evaluating simultaneous changes
  - Changes should be assessed separately and together
- Appropriate comparative device and cumulative effect of changes
  - To determine whether changes “could significantly affect safety or effectiveness,” manufacturer should compare modified device to unmodified device, as most recently cleared by FDA
  - For purposes of determining whether a 510(k) is necessary, changes should not be compared to other predicate devices (this is not a substantial equivalence (SE) determination)
- Documentation requirement
  - Quality system regulation requires documentation of design changes

## Guiding Principles Cont.

- 510(k) submissions for modified devices
  - When a 510(k) is required, 510(k) should describe all changes that trigger the requirement
  - Changes that do not trigger the requirement should also be described, if they would have been described in the original 510(k) for that device
  - Example: labeling changes should be described, even if they do not trigger 510(k) requirement, to ensure complete understanding of changes for a substantial equivalence (SE) comparison
- Substantial equivalence determinations
  - Following this guidance does not ensure SE determination

# How to Use The 510(k) Modifications Guidances

- Guidances describe a logic scheme for determining when a 510(k) is required
- Include flowcharts for ease of use, but flowcharts are not intended to be used alone

Reminder: Flowcharts are provided as a visual aid, but do not capture all necessary considerations. Refer to accompanying text when using this flowchart.

# Labeling Changes

- Focuses on changes to indications for use, and changes to other pieces of labeling that could affect indications for use
  - Rather than refer to intended use, K97 and new guidances refer to changes that have *major impact on intended use*, including certain indications for use changes (new intended use would be NSE)
- Describes common indications changes that likely do/don't require 510(k)s
- Describes indications changes that depend on various factors, and provides factors to consider
  - Example: For changes in use environment, consider whether the device user changes, whether the environment presents different challenges such as a lower level of cleanliness, etc.
- For labeling changes that do not affect the indications for use, does a risk assessment identify any new or significantly modified existing risks?

# Technology, Engineering, and Performance Changes

- Begins with recommendations on a few specific changes:
  - Fundamental device changes that almost always require 510(k)s, such as operating principle changes
  - Sterility and packaging changes, which depend on described factors
- For all other technology changes:
  - Does the change significantly affect the use of the device?
  - Does risk assessment identify new or significantly modified existing risks?
  - Is clinical data necessary?
  - Any unexpected results from V&V activities?

# Technology, Engineering, and Performance Section

- Role of verification and validation (V&V) activities
  - Concept from K97. Reconsider the significance of a change if:
    - A change drives need for new V&V activities because activities used on previous versions are no longer applicable
    - “Unexpected issues” are encountered during V&V. e.g., acceptance criteria cannot be met

# Materials Changes

- Focuses on risk assessment of material changes
  - Does the new material have new or increased biocompatibility concerns compared to the unmodified material?
  - If so, has manufacturer used same material previously in a similar device?
    - If yes, manufacturer may be able to determine the new material could not significantly affect safety or effectiveness
    - If no, a 510(k) is likely required
- If there are no new or increased concerns, or material doesn't have direct/indirect contact, could the change affect device performance?
  - If so, evaluate as technology change



# Technology, Engineering, Performance, and Materials Changes for In Vitro Diagnostics (IVD)

- Modifications to IVDs other than labeling are handled in an IVD-specific section
- Analysis is similar to that found in non-IVD Technology and Materials sections, but is tailored to use language relevant to IVDs in explaining how decisions should be made for IVDs
  - Focuses on risk-based assessment and changes that can affect IVD performance
- Guiding Principles, Labeling, and Risk Assessment sections also apply to IVDs

# Considerations for Risk-Based Assessments of Modified Devices

- Provides general recommendations on how to use risk-based assessment to evaluate device modifications
  - Thought process to consider changes not directly addressed by the guidance
  - Based on principles of ISO 14971 and benefit-risk principles
- Risk likelihood or probability (*could* the change affect?)
  - If it's determined that the likelihood of a risk occurring due to a change is negligible, that change probably could not significantly affect safety or effectiveness
- Risk severity (*could* the change *significantly* affect?)
  - New risks, changes in risk acceptability or risk score, and duration of risk should be considered to determine if risk is significant

# Considerations for Risk-Based Assessments of Modified Devices Cont.

- Effectiveness concerns should also be considered
  - 21 CFR 807.81(a)(3)(i) requires 510(k) for change that “could significantly affect safety or effectiveness”
  - Therefore, manufacturers should consider the possible effects modifications may have on device effectiveness
    - What’s the likelihood or probability that a change will affect device effectiveness?
    - If the change could affect effectiveness, could that affect be significant?
  - Consider the criticality of the device feature (labeling/design aspect/material/etc.) being modified
    - If a feature is critical to the effective operation of the device, changing it is more likely to be significant

# Appendix A: Examples

- Appendix A includes hypothetical examples intended to illustrate process of determining whether a 510(k) is required
- Each example includes an explanation of why it would/wouldn't require a 510(k)
- Important to note: examples can't account for every possible detail and are not intended to be definitive

# Appendix A: Examples



**19. Change:** The grip portion of a diagnostic ultrasound transducer is redesigned to improve user comfort.

**Relevant questions:**

*B5 – Is it any other change in design (e.g., dimensions, performance specifications, wireless communication, components or accessories, or the patient/user interface)?* Yes. This is a change to the device’s user interface.

*B5.1 – Does the change significantly affect the use of the device?* No. In this example, the redesign of the grip would not significantly affect the use of the device.

*B5.2 – Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks?* No. While the change to the transducer grip of the device could affect certain risks, such as the user potentially mishandling the device, the severity of these risks for this device is low.

*B5.3 – Are clinical data necessary to evaluate safety or effectiveness for purposes of design validation?* No. The manufacturer determines clinical data are not necessary for their specific change. They make the initial decision at this point to document the change to file.

*B5.4 – Do design verification and/or validation activities produce any unexpected issues of safety or effectiveness?* No. In this example, routine verification and validation activities are conducted successfully.

**Decision:** Documentation

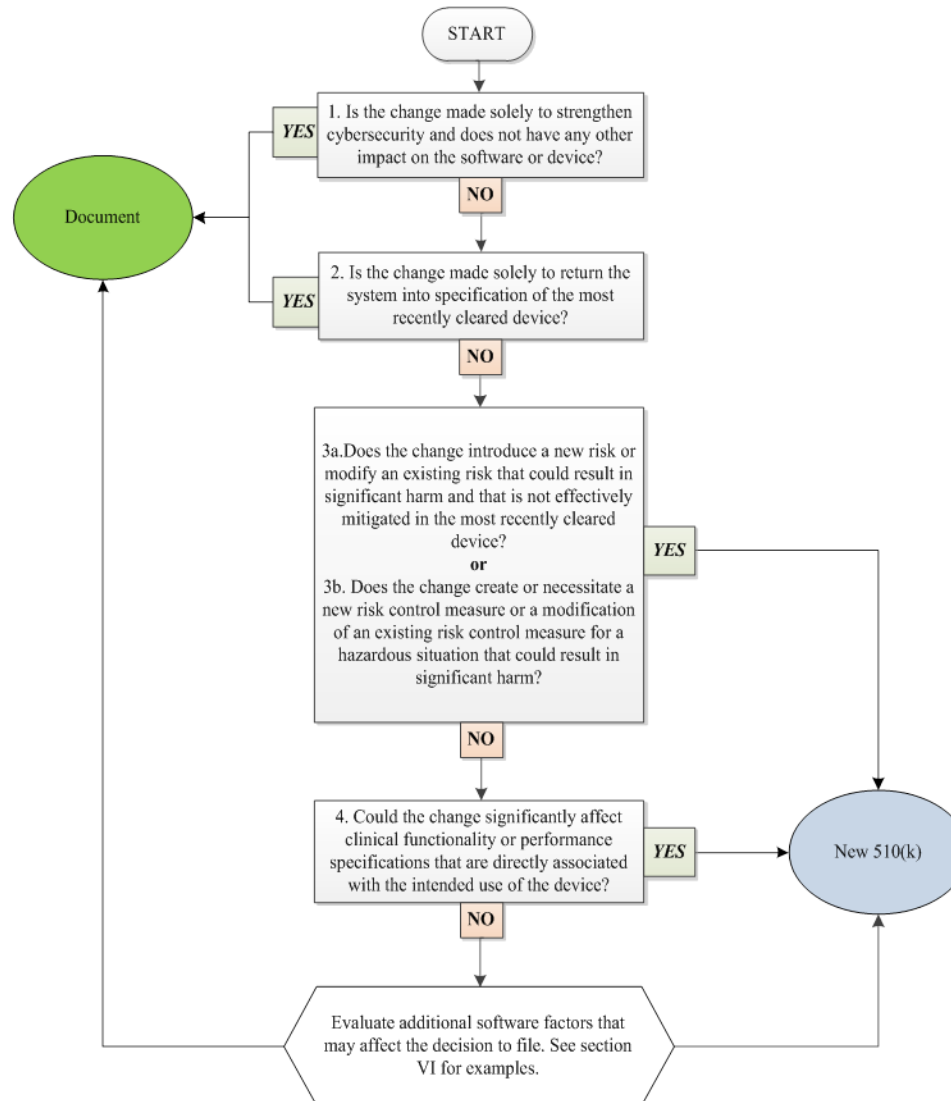
# Appendix B: Documentation

- Most 510(k) devices must comply with quality system regulation, which requires documentation of design changes prior to implementation
- Documentation is particularly important when manufacturers determine a 510(k) is not required
- Appendix B recommends basic elements of good documentation that every manufacturer should use
  - Also provides examples of documentation that can be adapted to the complexity of a given change (manufacturers can use these or adapt these as needed)

# Software Modifications

- Same General Principles as with the General Guidance
- Software-specific policy
  - 4 Questions
  - Additional considerations
- Software-specific examples in appendix of Software Modifications Guidance only

# Decision Making Process





## Question #1

Is the change made solely to strengthen cybersecurity and does not have any other impact on the software or device?

- To answer yes:
  - No other changes to the software or architecture are included
  - The change does not have impact on the device
    - e.g. Adding encryption where it was not used before may have impact on software or device
- If the answer to this question is yes, document the change and the rationale as discussed previously.
- If the answer is no, continue to Question 2

## Question #2

Is the change made solely to return the system into specification of the most recently cleared device?

- To answer yes:
  - Specification is for most recently cleared device
  - The change does not have an overall impact on the device that could significantly affect safety, effectiveness or intended use
- If the answer to this question is yes, document the change and the rationale as discussed previously.
- If answer is no, continue to Question 3

## Question #3

- Two-part question assessing the impact of changes to risk

3a: Does the change introduce a new risk or modify an existing risk that could result in significant harm and that is not effectively mitigated in the most recently cleared device?

- Criteria for assessing:
  - The change creates a new or modifies a hazard, hazardous situation, or cause in the risk management file
  - The level of harm associated with the new or modified hazard, hazardous situation, or cause is considered serious or more severe
  - The hazard, hazardous situation, or cause is not already effectively mitigated in the most recently cleared device
- If the all criteria are met, a new 510(k) is likely required.
- If answer is no, continue to Question 3a

## Question #3

3b: Does the change create or necessitate a new risk control measure or a modification of an existing risk control measure for a hazardous situation that could result in significant harm?

- Changes to or additions of risk control measures may be necessary due to new, modified, or previously unknown hazardous situations or causes thereof.
  - If the changes to risk controls are necessary to prevent significant harm, submission of a new 510(k) is likely required.
  - Submission is likely not required when implementing redundant risk control measures or enhancing existing risk control measures if the risk control measures in the most recently cleared device effectively mitigated the hazardous situation.
- If the answer to this question is no, continue to Question 4.

## Question # 4

Could the change significantly affect clinical functionality or performance specifications that are directly associated with the intended use of the device?

- Addition or change to clinical functionality or performance specifications
- Change is directly associated with intended use
  - If the intended use is changed, change is outside scope of this guidance.
- If the answer to this question is yes, a new 510k is likely required.
- If answer is no, continue to Additional Factors

# Evaluate additional software factors that may affect the decision to file

- **“Infrastructure”** modifications made to the software support system.
- **“Architecture”** modifications to the overall structure of the software.
- **“Core algorithm”** modifications made to an algorithm that directly drive the device’s intended use.

# Additional Factors Cont.

- **“Clarification of Requirements – No change to Functionality”** are changes made to clarify software requirements after a product has received premarket clearance.
- **“Cosmetic Changes – No change to Functionality”** are changes made to the appearance of the device that do not impact the clinical use of the device.

# Additional Factors Cont.

- **“Reengineering or refactoring”** SW maintenance techniques.

Reengineering - the examination and alteration of SW to reconstitute it in a new form, and includes the subsequent implementation of the new form.

Refactoring - is a disciplined technique for restructuring a SW program’s internal structure without changing its clinical performance specification, to improve a program structure and its maintainability.



# Software Example

## Adding a new diagnostic parameter

**Description:** An electroencephalogram (EEG) diagnostic monitor was cleared with spectral edge frequency (SEF) and peak power (PP) as quantitative parameters. The device’s intended use is to monitor brain electrical activity through electrodes placed on the surface of the head. A software modification is made to add Amplitude Integrated EEG (aEEG) as an additional quantitative parameter that was not included in the original premarket notification.

#	Question	Yes/No	Rationale
3a	Does the change introduce a new risk or modify an existing risk that could result in significant harm and that is not effectively mitigated in the most recently cleared device?	Yes	The hazardous situation most commonly associated with quantitative diagnostic parameters is the risk of incorrect or confusing information to the physician leading to a misdiagnosis, which could result in significant harm. While the causes of incorrect information for SEF and PP would be included in the original risk files, aEEG introduces a new cause related to an error in the aEEG calculation. Submission of a new 510(k) is required because the new cause is not effectively mitigated in the most recently cleared device and the hazardous situation, as discussed above, could result in significant harm.

**Outcome:** Submit the change in a new 510(k).

# Questions ?

Questions about the 510(k) device modifications guidances?

510(k) Staff: 301-796-5640

[510K\\_Program@fda.hhs.gov](mailto:510K_Program@fda.hhs.gov)

General questions about this webinar?

Contact Division of Industry and Consumer Education:

[DICE@fda.hhs.gov](mailto:DICE@fda.hhs.gov)

Slide presentation, transcript and webinar recording will be available at:

<http://www.fda.gov/training/cdrhlearn>

Under Heading: How to Study and Market Your Device; Sub-heading: Premarket Notification (510k)