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

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Guidance for Industry and Food and Drug Administration Staff

Document issued on October 25, 2017.

The draft of this document was issued on August 8, 2016.

This document supersedes *Deciding When to Submit a 510(k) for a Change to an Existing Device,* dated January 10, 1997.

For questions about this document regarding CDRH-regulated devices, contact the 510(k) Staff at 301-796-5640.

For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach, and Development (OCOD) at 1-800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration

Center for Devices and Radiological Health
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Preface

Public Comment

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

Guidance for Industry and Food and Drug Administration Staff

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or Office responsible for this guidance as listed on the title page.

I. Introduction

Almost from the enactment of the Medical Device Amendments to the Federal Food, Drug, and Cosmetic Act (the FD&C Act) in 1976, the Food and Drug Administration (FDA or the Agency) has attempted to define with greater clarity when a change in a medical device would trigger the requirement that a manufacturer submit a new premarket notification (510(k)) to the Agency. This document supersedes FDA's guidance *Deciding When to Submit a 510(k) for a Change to an Existing Device (K97-1)*, issued on January 10, 1997. This guidance is not intended to implement significant policy changes to FDA's current thinking on when submission of a new 510(k) is required. Rather, the intent of this guidance is to enhance the predictability, consistency, and transparency of the "when to submit" decision-making process by providing a least burdensome approach, and describing in greater detail the regulatory framework, policies, and practices underlying such a decision.

For the current edition of the FDA-recognized standards referenced in this document, see the FDA Recognized Consensus Standards Database at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word should in Agency guidance means that something is suggested or recommended, but not required.

II. Background

The regulatory criteria in 21 CFR 807.81(a)(3) state that a premarket notification must be submitted when:

> *(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.*

FDA issued the original guidance *Deciding When to Submit a 510(k) for a Change to an Existing Device (K97-1)* on January 10, 1997 to provide guidance on this regulatory language. As stated in that guidance, the key issue in the interpretation of 21 CFR 807.81(a)(3) 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 FDA and device manufacturers to different interpretations. The original guidance provided the Agency's interpretation of these terms, with principles and points for manufacturers to consider in analyzing how changes in devices may affect safety or effectiveness and determining whether a new 510(k) must be submitted for a particular type of change. The current guidance preserves the basic format and content of the original, with updates to add clarity. The added clarity is intended to increase consistent interpretations of the guidance by FDA staff and manufacturers and provide a more transparent framework for determining when submission of a new 510(k) is required.

The 510(k) Process and the Quality System Regulation

Any guidance on 510(k)s for changes to a legally marketed device should consider the role the Quality System (QS) regulation, 21 CFR Part 820, plays in changes to devices. For some types of changes to a device, the Agency believes that submission of a new 510(k) is not required and that reliance on existing QS requirements is the least burdensome approach to reasonably assure the safety and effectiveness of the changed device.

Regardless of whether a change requires premarket review, the QS regulation requires manufacturers of finished medical devices to review and approve changes to device design and production (21 CFR 820.30 and 820.70) and document changes and approvals in the device master record (21 CFR 820.181). Any process whose results cannot be fully verified by subsequent inspection and testing must be validated (21 CFR 820.75), and changes to the process require review, evaluation, and revalidation of the process where appropriate (21 CFR 820.75(c)).

The net effect of the QS regulation is to require that, when manufacturers of a finished medical device make a change in the design of a device, there is a process in place to demonstrate that the

manufactured device meets the change in design specifications (or the original specifications, if no change was intended). They must keep records, and these records must be made available to an FDA investigator upon request (see Section 704(e) of the FD&C Act). For many changes to a device, submission of a new 510(k) may not be required. In these cases, including for many design changes, compliance with the QS regulation can reasonably assure the safety and effectiveness of the changed device.

Least Burdensome Principles

The least burdensome provision concerning 510(k)s states that FDA "shall only request information that is necessary…" and "shall consider the least burdensome means of demonstrating substantial equivalence…" (see section 513(i)(1)(D)(i) of the FD&C Act). While not changing the standard for substantial equivalence, this provision states that FDA shall only request the "minimum required information" necessary to support a determination of substantial equivalence (see sections 513(i)(1)(D)(ii)-(iii) of the FD&C Act). The recommendations discussed in this guidance for evaluating when a change in a medical device would trigger the requirement that a manufacturer submit a new 510(k) to the Agency are consistent with least burdensome principles, and applies them in discussing the considerations that may affect the decision-making about when to submit a new 510(k) for a device change or modification.

III. Scope

This guidance will aid manufacturers of medical devices subject to premarket notification requirements who intend to modify a 510(k)-cleared device (or group of devices) or other device subject to 510(k) requirements, such as a preamendments device or a device that was granted marketing authorization via the De Novo classification process[1] under section 513(f)(2) of the FD&C Act (also referred to together as "existing devices"), during the process of deciding whether the change exceeds the regulatory threshold of 21 CFR 807.81(a)(3) for submission and clearance of a new 510(k). Note that any person required to register under 21 CFR 807.20 who plans to introduce a device into commercial distribution for the first time must, per 21 CFR 807.81(a)(2), submit a 510(k) if that device is not exempt from premarket notification requirements. Also note that devices with changes requiring submission of a new 510(k) may not be legally commercially distributed before FDA clears the changed device (21 CFR 807.100(a) and sections 513(f)(1) and 513(i) of the FD&C Act). This guidance is not intended to address changes to devices that are 510(k)-exempt or that require premarket approval (PMA). Also, the scope of key terminology used in this guidance, particularly intended use and indications for use, is limited to medical devices and not other FDA-regulated products.

This document incorporates concepts and recommendations from existing FDA guidance and policy, such as *Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile* (http://www.fda.gov/downloads/MedicalDevices/.../ucm109897.pdf), and device-specific final guidance documents that identify and characterize specific scenarios regarding when submission of new 510(k)s are required or not required based on changes to an existing device. In some

[1] This guidance applies to devices granted marketing authorization via the De Novo classification process that are not exempt from premarket notification requirements.

cases, FDA's thinking has derived from its experience in situations involving only a few manufacturers of a limited number of devices. In such instances, we have attempted to generalize the concepts to apply to a broader range of devices. However, special cases exist where FDA has established definitive final guidance for changes to specific devices, e.g., FDA's guidance on daily wear contact lenses, *Premarket Notification (510(k)) Guidance Document for Daily Wear Contact Lenses* (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080928.htm). This guidance is not intended to supersede such final device-specific guidance but may cover areas not addressed in such device-specific guidance.

Recalls: This guidance is also intended to apply to situations when a legally marketed existing device is the subject of a recall, correction, or removal, and a change in the device or its labeling is necessary. For more information on recommended procedures in a recall situation, please see *Blue Book Memorandum K95-1, 510(k) Requirements During Firm-Initiated Recalls* (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080297.htm). As stated in that guidance, if a correction alters a device rather than simply restoring it to its original specifications, submission of a new 510(k) may be required. FDA may use this guidance in determining whether submission of a new 510(k) is warranted in cases where the correction does alter the device.

Private Label Distributors and Repackagers: Private label distributors and repackagers are exempt from submitting a 510(k) if they satisfy the requirements of 21 CFR 807.85(b).

Software Changes: This guidance does not address software changes or modifications. Please refer to FDA's guidance *Deciding When to Submit a 510(k) for a Software Change to an Existing Device* (https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM514737.pdf) for recommendations regarding software changes.
This guidance does apply to non-software changes to devices containing software and non-software changes to software that is a medical device on its own. For example, labeling changes to software are covered by Section A of this guidance, and non-software technology changes and materials changes to existing devices that contain software are covered by Sections B through D of this guidance.

When there are multiple changes that affect labeling or hardware in addition to software, the manufacturer should assess the changes using both the general and software-specific modifications guidances. If use of either guidance leads to a "New 510(k)" conclusion, submission of a new 510(k) is likely required.

Combination Products: This guidance does not specifically address combination products, such as drug/device or biologic/device combinations; however, the general principles and concepts described herein may be helpful to manufacturers in determining whether submission of a 510(k) is required for changes to device constituent parts of combination products.

Remanufactured or Reprocessed Single Use Devices: This guidance is not intended to address whether submission of 510(k)s are required from remanufacturers of existing devices who do not hold the 510(k) for the device, such as reprocessors of single-use devices. This guidance does apply to reprocessors and remanufacturers who hold their own 510(k) and are addressing

changes or modifications. Remanufacturer is defined at 21 CFR 820.3(w) as "any person who processes, conditions, renovates, repackages, restores, or does any other act to a finished device that significantly changes the finished device's performance or safety specifications, or intended use."

IV. Guiding Principles

In using this guidance for deciding whether to submit a new 510(k) for a change to an existing device, a number of guiding principles should be followed. Some derive from existing FDA 510(k) policy and are widely known, and others are necessary for using the logic scheme contained in this guidance. Thus, anyone using this guidance should bear in mind the following Guiding Principles:

1. **Changes made with intent to significantly affect safety or effectiveness of a device –** If a manufacturer modifies their device with the intent to significantly affect the safety or effectiveness of the device (for example, to significantly improve clinical outcomes, to mitigate a known risk, in response to adverse events, etc.), submission of a new 510(k) is likely required. A change *intended* to significantly affect the safety or effectiveness of the device is considered to be a change that "*could* significantly affect the safety or effectiveness of the device" and thus requires submission of a new 510(k) regardless of the considerations outlined below. Changes that are not intended to significantly affect the safety or effectiveness of a device, however, should still be evaluated to determine whether the change could significantly affect device safety or effectiveness.

   If a manufacturer modifies their device to address a violation or recall, they should refer to FDA guidances *Blue Book Memorandum K95-1, 510(k) Requirements During Firm-Initiated Recalls* (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080297.htm) and *Distinguishing Medical Device Recalls from Medical Device Enhancements* (http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm418469.pdf).

2. **Initial risk-based assessment –** To determine whether a change or modification could significantly affect the safety or effectiveness of a device, the manufacturer should first conduct a risk-based assessment, using the guidance below, of whether the change could significantly affect the device's safety or effectiveness, either positively or negatively. This risk-based assessment should identify and analyze all new risks and changes in existing risks resulting from the device change, and lead to an initial decision whether or not submission of a new 510(k) is required.

   For the purposes of this guidance, we have chosen the term "risk-based assessment" to describe the analysis that should be completed to assist in the determination of whether or not a change could significantly affect safety or effectiveness of the device. Although common risk analysis methods define risk in terms of device harms and their effects on safety, it is important to note that whether submission of a new 510(k) is required depends on whether the change could significantly affect the safety *or effectiveness* of the device. Therefore, manufacturers should also consider the possible effects a device

change may have on device effectiveness. As such, we have chosen to use the distinct terminology of "risk-based assessment."

3. **Unintended consequences of changes** – After a manufacturer considers whether the change was made with the intent to significantly affect safety or effectiveness, the manufacturer should also consider whether the change could have unintended consequences. In order to fully assess device changes, manufacturers should consider the effects of the planned device changes and whether these changes create any intended and/or unintended consequences. For example, changes in sterilization may unintentionally affect device materials, or changes to materials may unintentionally affect the performance of the device. Any unintended consequences such as these should be evaluated according to the relevant flowcharts (and their companion text) to determine whether submission of a new 510(k) is required. For instance, a change in sterilization that may unintentionally affect device performance should be reviewed as a sterilization change under B3 and as a performance specification change under B5.

4. **Use of risk management –** A risk-based assessment as referred to throughout this document is based on the combination of multiple risk concepts that are important for managing the risks of medical devices. Hazards and hazardous situations, risk estimation, risk acceptability, risk control, risk/benefit analysis and overall risk evaluation are all concepts that can be applied during the design and development of a medical device. The concept of risk, as defined in ISO 14971: *Medical devices – Application of risk management to medical devices*, is the combination of the probability of occurrence of harm and the severity of that harm. Although the risk terminology used in this document is primarily derived from ISO 14971, we recognize that an individual manufacturer's terminology may differ. Because 21 CFR 807.81(a)(3)(i) requires submission of a new 510(k) when a change "could significantly affect safety or effectiveness," both safety and effectiveness should be considered in evaluating a device's risk profile and performing a risk-based assessment, as explained in Section E.

   This guidance states throughout that submission of a new 510(k) is likely required when a risk-based assessment of the changed device identifies any new risks or significantly modified existing risks. For the purposes of this guidance, a new risk is a new hazard or hazardous situation that did not exist for the original device (see discussion of appropriate comparative device below) and the pre-mitigation risk level associated with the new risk is not considered to be acceptable. For the purposes of this guidance, a device change could be considered to significantly modify an existing risk if it changes the risk score, risk acceptability category, or duration of risk. See Section E for further explanation.

5. **The role of testing (i.e., verification and validation activities) in evaluating whether a change could significantly affect safety and effectiveness** - If the initial decision following the risk-based assessment is that submission of a new 510(k) is not required, this decision should be confirmed by successful, routine verification and validation activities. If routine verification and validation activities produce any unexpected results, any prior decision that submission of a new 510(k) is not required should be reconsidered, as discussed in **B5.4** for non-IVD devices and **D4** for IVD devices. "Routine" activities in this context refer to the original design verification and validation activities that were done to assess the original device design. Because 21 CFR

807.81(a)(3) requires submission of a new 510(k) for a change that "*could* significantly affect safety or effectiveness," if the result of a risk-based assessment is that a change could significantly affect safety or effectiveness, submission of a new 510(k) is required even if routine verification and validation activities are conducted successfully without any unexpected results. Note that verification and validation requirements apply for all devices subject to 21 CFR 820.30, and must be conducted regardless of whether submission of a new 510(k) is required.

6. **Evaluating simultaneous changes to determine whether submission of a new 510(k) is required –** Because many simultaneous changes may be considered at once, each change should be assessed separately, as well as in aggregate.

7. **Appropriate comparative device and cumulative effect of changes –** In using this guidance to help determine whether a particular change requires submission of a new 510(k), manufacturers should conduct a risk-based assessment that compares the changed device to their device as previously found to be substantially equivalent in their most recently cleared 510(k), to their preamendments device (if the device was in commercial distribution before May 28, 1976 and there have not been changes to it subsequently cleared in a 510(k)), or to their device that was granted marketing authorization via the De Novo classification process (if there have not been changes to it subsequently cleared in a 510(k)). The appropriate comparative device is referred to as the "original device" throughout this guidance document. Of note, this comparison is different from a substantial equivalence comparison between the modified device and a legally marketed predicate device. Manufacturers may make a number of changes without having to submit a new 510(k), but each time they make a change, the modified device should be compared to the original device (i.e., the device described in their most recently cleared 510(k) for the device, their legally marketed preamendments device, or their device that was granted marketing authorization via the De Novo classification process). When the cumulative effect of individual changes triggers the regulatory threshold for submission, the manufacturer should submit a new 510(k). When it does not, the manufacturer must document the change(s) (see 21 CFR Part 820.30).

8. **Documentation requirement –** Whenever manufacturers change their device, they must take certain actions to comply with the QS regulation, 21 CFR Part 820, unless the device in question is exempt by regulation from the QS regulation. The QS regulation requires, among other things, that device changes be documented. The scope and type of documentation may vary, but the process of documenting the decisions described in this guidance should be established as part of the manufacturer's own quality system. See Appendix B for further explanation and recommendations on documentation.

9. **510(k) submissions for modified devices –** When a new 510(k) is submitted for a device with multiple changes, that 510(k) should describe all changes that trigger the requirement for submission of a new 510(k). To help ensure that FDA has a complete understanding of the device under review, that 510(k) should also describe other changes since the most recently cleared 510(k) (i.e., those that did not require submission of a new 510(k)) that would have been documented as part of the first 510(k) for that device. For instance, 510(k)s typically include a listing of device warnings in the labeling, so if a warning in the device's labeling had been changed, that change should be described in

the new 510(k), even if that change did not itself trigger the requirement for submission of a new 510(k). However, a 510(k) would not typically identify or describe individual components of a circuit board, such as resistors, and therefore FDA would not expect changes to the resistors to be listed in the new 510(k) for a modified device because the first 510(k) would not have included information about the resistors.

If a manufacturer makes multiple changes to a device, but only one change triggers the requirement for submission of a new 510(k), the changes that do not require submission of a new 510(k) may be immediately implemented, so long as those changes can be implemented independently of changes that do require submission of a new 510(k). Any immediately implemented change should still be documented in accordance with applicable QS regulations and the manufacturer's documentation procedures. Those changes should, however, also be described in the new 510(k) for the change that does require submission.

10. **Substantial equivalence determinations –** Manufacturers should understand that, even though they may follow this guidance and submit a new 510(k), a substantially equivalent determination is not assured. See FDA's guidance *The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications (510(k))* (https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm284443.pdf) for more information on the decision-making process FDA uses to determine substantial equivalence.

V. How to Use This Guidance

This guidance uses flowcharts and text to guide manufacturers through the logic scheme we recommend to arrive at a decision on whether to submit a new 510(k) for a change to an existing device. A single logic scheme containing all the necessary steps would be large and cumbersome and could be quite daunting. Rather, for ease of use, the single scheme has been broken down into smaller sections that include:

- The main types of changes that might be made to a device (this section, Main Flowchart)
- Labeling changes (Section A, Flowchart A)
- Technology, engineering, and performance changes (Section B, Flowchart B)
- Materials changes (Section C, Flowchart C)
- Technology, engineering, performance, and materials changes for *in vitro* diagnostic devices (IVDs) (Section D, Flowchart D)
- Considerations for risk-based assessments of modified devices (Section E)

The main flowchart is provided in Figure 1 below and guides the manufacturer to the appropriate specific section(s) and flowchart(s) to assess their specific change(s).
When using the flowcharts, the reader should interpret "new 510(k)" as **submission of a new 510(k) is likely required** and "documentation" as **submission of a new 510(k) is likely not required, document your analysis and file it for future reference**. Please refer to Appendix C: Significant Terminology for the meaning of terms used in the guidance, including in the flowcharts.

Note that the first question is whether the change is being made with the intent to significantly improve the safety or effectiveness of the device, for example, to significantly improve clinical outcomes, to mitigate a known risk, in response to adverse events, etc. (Figure 1 – Main Flowchart). If so, the change likely could significantly affect safety or effectiveness and submission of a new 510(k) is likely required. If not, you should continue to follow the logic scheme shown in Figure 1, below.

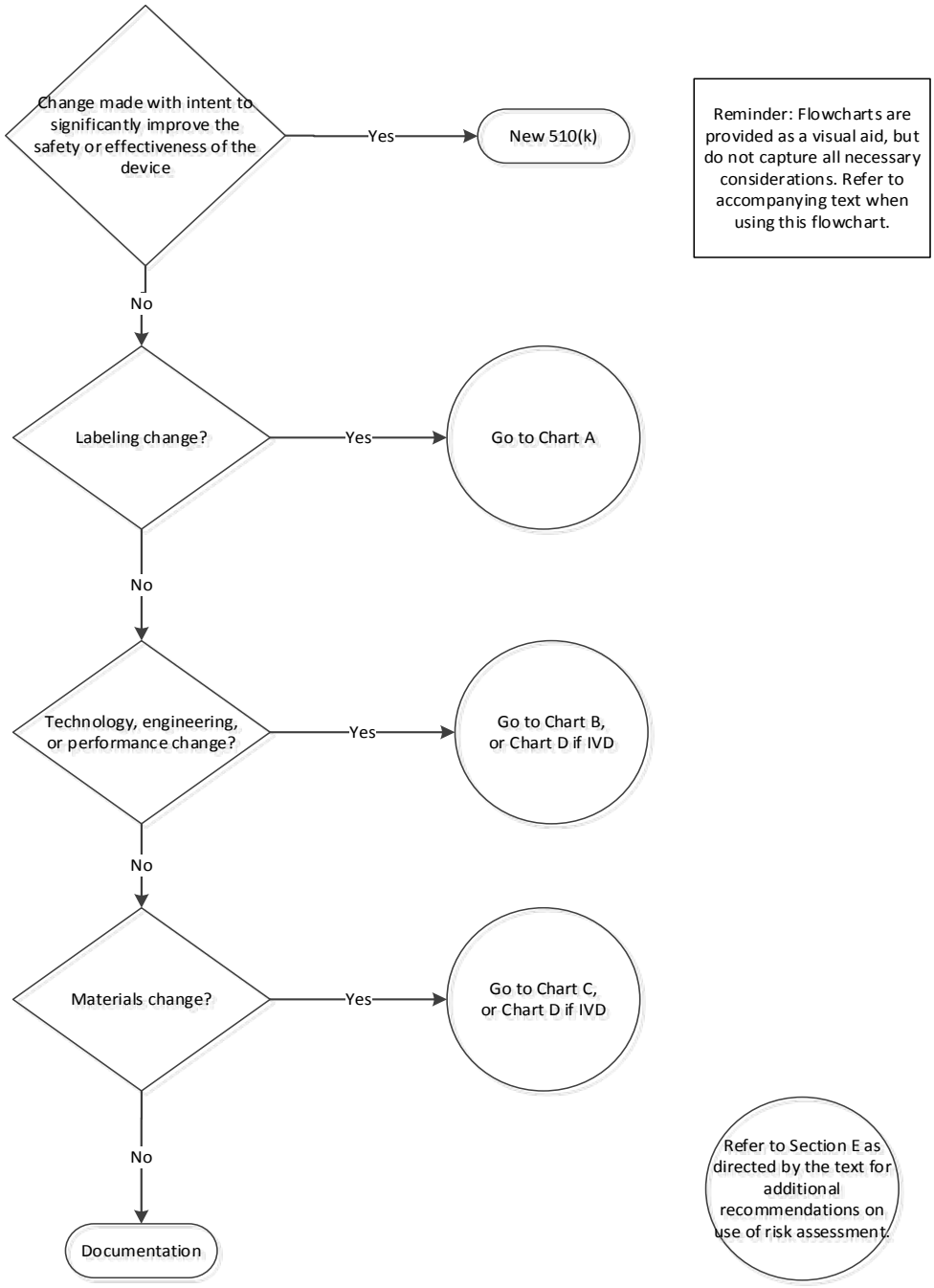

Figure 1 - Main Flowchart

Note that sections B and C are only applicable to non-IVDs, and section D is only applicable to IVDs. All other sections apply to both IVDs and non-IVDs.

Each of the questions listed on the detailed flowcharts are identified by the flowchart letter (A through D) and a sequential number. Those questions on the main spine of the flowcharts relate to major questions to be answered. Subsidiary questions are identified by the flowchart letter, the question number, a decimal point, and another sequential number (e.g., B4.1 is a decision point containing a follow-up question that builds off a determination made in decision point B4).

Manufacturers should use the flowcharts in concert with the Guiding Principles above, the recommendations in the sections below, and the examples provided in Appendix A. Manufacturers should follow all the applicable flowcharts and use their companion text to answer the questions posed for each individual type of change (e.g., performance change, material change) until a decision is made either to submit a new 510(k), or to document the basis for concluding that submission of a new 510(k) is not required. As mentioned above, when making the decision on whether to submit a new 510(k) for changes, the manufacturer's basis for comparison of any changed device should be the original device. Manufacturers are required to submit a new 510(k) when a change (or changes) exceeds the 21 CFR 807.81(a)(3) threshold, "could significantly affect the safety or effectiveness of the device," or constitutes a "major change or modification in the intended use of the device." This significant effect could be positive or negative. One must keep in mind that what may on the surface appear to be one discrete change to a device may involve multiple changes of various types.

Although this guidance does not specifically discuss manufacturing changes, a manufacturer should consider the impact of all manufacturing changes on device labeling, technology/engineering/performance, and/or materials. If the manufacturing change affects any of these three areas, manufacturers should evaluate the impact of the resulting labeling, technology/engineering/performance, or material change using the appropriate flowcharts and companion text. Specifically, consideration should be given to those devices for which manufacturing information was submitted in the most recently cleared 510(k) in order to assist in the characterization of the device and technology, such as bioresorbables, polymers, and biological fixation type devices. When manufacturing changes do not impact device labeling, technology/engineering/performance, and/or materials, there is no need to use the flow charts and their companion text to document the decision not to submit a new 510(k).

In cases with multiple changes, manufacturers should use all applicable flowcharts and companion text, including the Guiding Principles in Section IV of this guidance. Consider the following examples:

Example 1: Multiple changes caused by a manufacturing process change

> A manufacturer decides to change the manufacturing process for a patient-contacting part from a machining process to a stamping process. The use of the stamping process requires a change in the grade of stainless steel and also results in a change of the dimensional tolerances. To evaluate the impact of this change, the manufacturer should use both Sections B (Technology, Engineering, and Performance) and C (Materials).

Example 2: Multiple changes related to a change in shelf-life

> A manufacturer changes one or more materials in a device to improve the shelf-life of the product. The material change also affects some of the performance characteristics, resulting in the need to update the labeling. To evaluate the impact of the change, the manufacturer should use Sections A (Labeling), B (Technology, Engineering, and Performance) and C (Materials) or D (Technology, Engineering, Performance, and Materials Changes for IVD Devices).

Changes not addressed in Sections A through D should be evaluated with a risk-based assessment using the recommendations provided in Section E. In instances where the specific flowcharts do not address a given change, Section E provides recommendations for how manufacturers should utilize risk management principles to evaluate their own specific changes and modifications. Because 21 CFR 807.81(a)(3)(i) requires submission of a new 510(k) when a change "could significantly affect safety or effectiveness," both safety and effectiveness should be considered in evaluating a device's risk profile, as explained in the Guiding Principles and Section E. For those circumstances where the proposed change is not addressed in this guidance or in a device-specific guidance document, manufacturers are encouraged to contact CDRH staff or CBER staff.

A. Labeling Changes

As noted above, the guidance focuses on the following types of changes: labeling changes, technology, engineering, or performance changes, and materials changes. This guidance identifies several types of labeling changes or modifications to an existing device, including certain changes to the indications for use, that can have a major impact on intended use and thus require submission of a new 510(k) under 21 CFR 807.81(a)(3).[2] All labeling changes should be evaluated using a separate logic scheme that concentrates on changes in indications for use and applies a risk-based assessment framework for determining whether submission of a new 510(k) is required. Focusing on indications for use and using a risk-based assessment for labeling changes will also help identify those changes that are more frequently recommended for documentation only.

Flowchart A describes the logic scheme to be used when determining when submission of a new 510(k) is required for a labeling change. Changes in device labeling often pose the most difficult questions to be addressed by device manufacturers when deciding whether submission of a new 510(k) is required. Frequently, an apparently subtle change in a device's labeling can have a significant impact on the safe and effective use of the device.

Confusion often results when discussing the distinction between "indications for use" and the "intended use" of the device. For purposes of substantial equivalence, and for the purposes of this guidance, the term intended use means the general purpose of the device or its function, and encompasses the indications for use.[3] The indications for use generally describe the disease or

[2] Labeling changes are not the only type of changes that could result in a major change in intended use. See 21 CFR 801.4.

[3] When submitting a 510(k) premarket notification to FDA for review, an applicant must submit, among other things, information concerning a device's intended use(s), as described in the proposed labeling (21 CFR 807.92(a)).

condition the device will diagnose, treat, prevent, cure or mitigate, including a description of the patient population for which the device is intended.[4] The indications include all the labeled patient uses of the device. As it relates to medical devices, the indications for use statement is a factor in determining a device's intended use; however, a change in indications for use that requires the submission of a new 510(k) does not necessarily mean that the device has a new intended use (such that the device would not be substantially equivalent under section 513(i) of the FD&C Act).[5]

FDA looks to this aspect of the submission to make a substantial equivalence determination under section 513(i) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), which requires FDA to evaluate whether, based on the proposed labeling, the device and a predicate device have the same intended use. If a particular labeling change results in an intended use of the device that is not the same as the intended use of the original device, the device would not be substantially equivalent. See also FDA's guidance *The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications (510(k))* (https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm284443.pdf) Although, in evaluating substantial equivalence in reviewing a 510(k), FDA must determine the intended use of a device based on the proposed labeling, see 21 USC 513(i)(1)(E), FDA may consider other evidence of intended use in determining whether there has been a major change or modification in the intended use of the device under 21 CFR 807.81(a)(3).

[4] See FDA's guidance *The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications (510(k))* (https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm284443.pdf)

[5] *Ibid*.

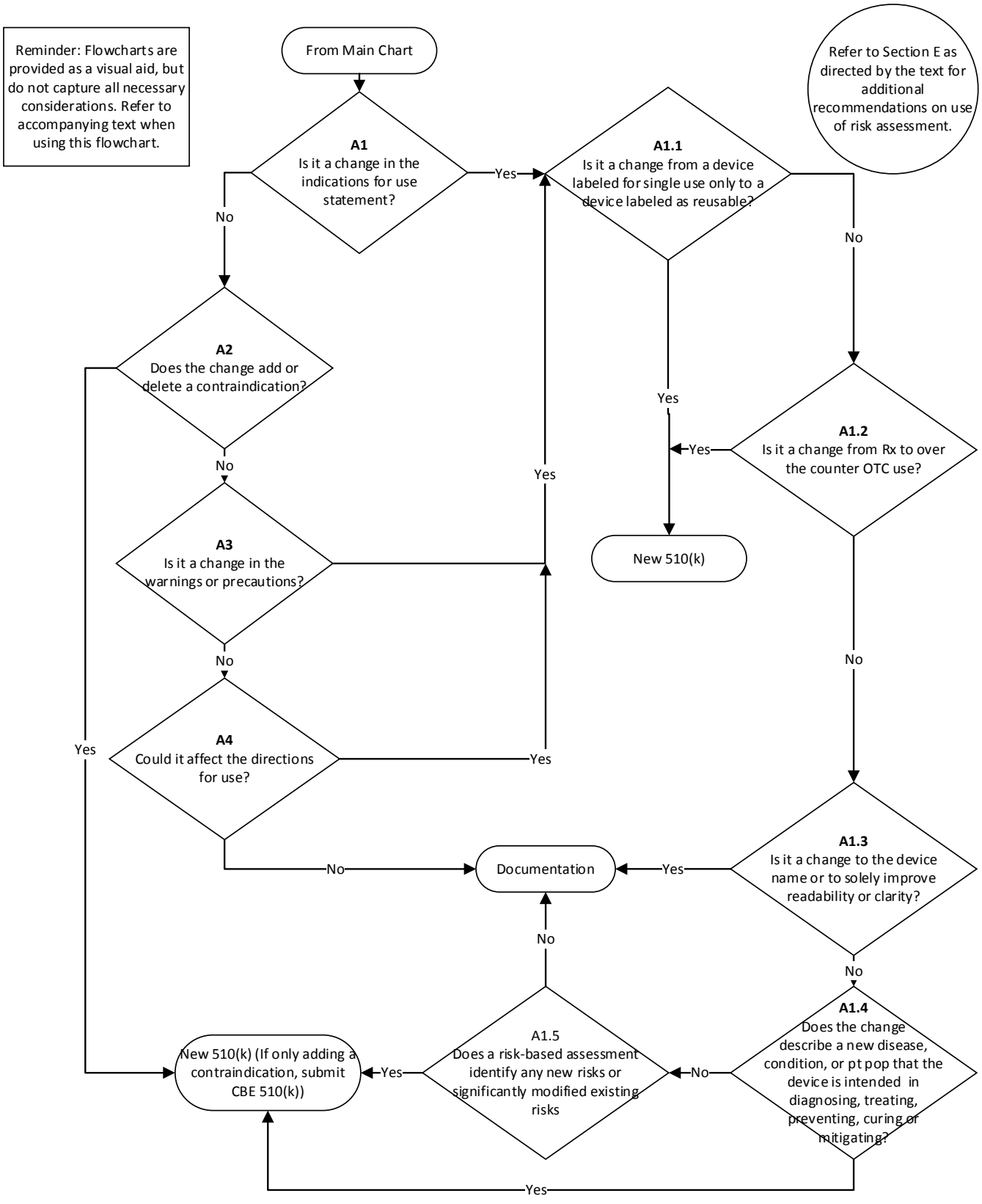

Figure 2 - Flowchart A: Labeling Changes

A1. Is it a change in the indications for use statement? Changes in the indications for use statement raise more Agency concern than any other aspect of labeling. In fact, most labeling changes that affect the substance, meaning, or scope of the indications for use could significantly affect safety or effectiveness and will require submission of a new 510(k). Changes that clarify the indications without affecting the substance or meaning of the indications usually do not require submission of a new 510(k). In addition, some changes in the indications for use that limit use within the currently cleared indication may occur without submission of a new 510(k). For example, if a device was cleared for use with three specific indications and the firm decides to market the device for only two of those indications, this change would not likely require submission of a new 510(k).

If the labeling change is to the indications for use statement, proceed to **A.1.1**. Otherwise, proceed to **A.2**.

It should be noted the decision points in **A1.1-A1.5** may apply not only to changes to the indications for use statement of the labeling, but also to changes to other sections of the labeling, such as the directions for use of the device. You should review these decision points when directed by the text of this guidance and Flowchart A: Labeling Changes.

A1.1 Is it a change from a device labeled for single use only to a device labeled as reusable?

FDA has found that the performance and risks associated with a reusable device can be significantly different from the performance and risks associated with that same device when it is labeled for single use only. Therefore, changing a device labeled for single use only to a device that is labeled as reusable typically could significantly affect the safety or effectiveness and would likely require submission of a new 510(k). Changing a device labeled for reuse to single use only, however, would likely not require submission of a new 510(k) because a single use is a limitation of the previously cleared indications for multiple uses, and the risks of single use were inherently considered within the risks of multiple uses.

If it is not this type of labeling change, proceed to **A.1.2**.

A.1.2 Is it a change from prescription (Rx) to over the counter (OTC) use?

FDA has found that the directions for use necessary for health care professionals to use a device safely and effectively can be significantly different from the directions for use necessary for lay users to use that same device safely and effectively. Therefore, changing a device labeled for prescription use only to a device that is labeled for OTC use typically could significantly affect the safety or effectiveness and would likely require submission of a new 510(k). Changing a device labeled for OTC use to prescription use, however, would likely not require submission of a new 510(k) because it is unlikely that the associated labeling changes could significantly affect the safety or effectiveness of the device.

If it is not this type of labeling change, proceed to **A.1.3**.

A.1.3. Is it a change to the device name or a change solely to improve readability or clarity?

Changes to the device name or description that are consistent with the cleared indications for use typically do not significantly affect the safety or effectiveness and would likely not require submission of a new 510(k). Changes that are solely to improve readability or clarity that are consistent with the cleared indications for use typically do not significantly affect the safety or effectiveness and likely would not require submission of a new 510(k).

If it is not this type of labeling change, proceed to **A.1.4**.

A.1.4 Does the change describe a new disease, condition, or patient population that the device is intended for use in diagnosing, treating, preventing, curing or mitigating?

Differences in indications for use should be analyzed to explain how they are or are not critical to the intended therapeutic, diagnostic, prosthetic, or surgical use of the device, and how the differences do or do not affect the safety and effectiveness of the device. Specific changes that could significantly affect the safety and effectiveness include describing a new disease, condition, or patient population that the device is intended for use in diagnosing, treating, preventing, curing or mitigating (or an anatomical site from which a new disease, condition, or population may be inferred). The criticality of these types of changes and their direct effect on safety and effectiveness means that a change to add a new disease, condition, or patient population likely requires submission of a new 510(k).

As introduced prior to Section A.1.1., not all changes that describe a new disease, condition, or patient population that the device will diagnose, treat, prevent, cure or mitigate are necessarily made in the indications for use section of the labeling. These types of changes could also result from a change to other sections of the labeling, such as the directions for use of the device. For example, a device's directions for use may be revised from providing that the device is to be used when symptoms occur (i.e., use in the treatment of a disease or condition) to providing that the device is to be used once per day, even in the absence of symptoms (i.e., use in the prevention of a disease or condition). In this example, the patient population has changed from patients who have been previously diagnosed with a disease or condition to asymptomatic or healthy individuals. Because this change describes a new patient population, submission of a new 510(k) is likely required.

To evaluate whether a change in patient population is a new and distinguishable patient population, manufacturers should compare the demographics, diagnosis, prognosis, comorbidity, and potential for complications of the patient population described in the previously cleared 510(k) to those of the modified patient population. If the change describes a patient population with similar demographics, diagnosis, prognosis, comorbidity and potential for complications, then submission of a new 510(k) is likely not required. However, if any of these factors differ between patient populations, submission of a new 510(k) would likely be required.

One method for determining whether changes to the demographics, diagnosis, prognosis, comorbidity, and potential for complications of the previously cleared patient populations result in a new and distinguishable patient population is to assess if the changes could significantly affect a device's risk profile through a risk-based assessment as described in A.1.5 and Section E. For example, if the most recently cleared patient population included only individuals with Stage IV carcinoma, and the modified patient population added individuals with Stage III carcinoma, a risk-based assessment considering the factors outlined in section A.1.5 could help determine whether there are any new risks or significantly modified existing risks that would require submission of a new 510(k).

If it is not this type of labeling change, you should proceed to **A.1.5.**

A.1.5. Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks?

For changes that are not addressed by the previous questions in this section, thus necessitating the use of a risk-based assessment as described in Section E, the factors discussed below should be considered as part of such an assessment for a labeling change.

As discussed in Question 1 of the Main Flowchart, if a change is intended to significantly affect safety or effectiveness, particularly those meant to significantly improve clinical outcomes, to mitigate a known risk, or in response to adverse events, that change likely requires submission of a new 510(k); this includes changes to the indications for use. For labeling changes that are not intended to significantly affect safety or effectiveness, manufacturers should consult Flowchart A and Section E and consider whether the change creates new risks or significantly modifies existing risks.

Changes to the labeling can affect a device's risk profile by affecting how, when, where, or by whom the device is used. As part of the risk-based assessment of a labeling change, manufacturers should consider whether the change could introduce human factors or usability issues that could significantly affect users' understanding of the labeling and use of the device. Changes that significantly affect a device's risk profile likely require submission of a new 510(k).

As further described in Section E, the risk-based assessment should include an analysis of both safety and effectiveness. A risk-based assessment will help manufacturers determine whether changes such as the following could significantly affect safety or effectiveness and would require submission of a new 510(k).

Changes to the type of joint, organ, bone, vasculature, or tissue applied to or interacted with, regardless of the section of labeling in which this information is contained: Although some changes to the type of joint, organ, bone, vasculature, or tissue applied to or interacted with would involve a new disease, condition, or patient population, and thus lead to a decision to submit a new 510(k) under A.1.4, a risk-based assessment would be appropriate for other changes in this category. How a change to the type of joint, organ, bone, vasculature, or tissue applied to or interacted with affects a device's risk profile depends on the specific change. For example, a change from use of a

bone fixation system – plates, screws, and wires – in an extremity to use in the skull is likely to significantly affect the device's risk profile and require submission of a new 510(k). Alternatively, a bone fixation system used on one type of long bone changed to use on a different type of long bone may not significantly affect the device's risk profile and is less likely to require submission of a new 510(k).

Changes in user or use environment: How a change of this type affects a device's risk profile depends on the differences in use environment and environmental specifications. For example, a change from use in a surgical suite to use in a hospital recovery room, both of which will have professional healthcare supervision, may not significantly affect the device's risk profile. Similarly, changes between users with similar training on a specific device, such as changes between a general physician and a specialist using basic medical equipment may not significantly affect a device's risk profile. However, changes from professional use to home use[6] or hospital use to ambulatory transport are more likely to affect the device's risk profile and require submission of a new 510(k) because the different environments have different levels of professional healthcare supervision and offer different environmental challenges, such as presence of other electronic devices that can cause electromagnetic interference, different levels of cleanliness, or shocks and vibrations associated with patient travel or ambulatory use. Similarly, changes from professional use to home use, hospital use to ambulatory transport, or between any other healthcare providers with different levels of training on specific devices are more likely to affect the device's risk profile and require submission of a new 510(k) because the different level of training could significantly affect the safe and effective use of the device.

Changes in frequency or duration of use: Changes in the frequency or duration of use of a device include changes indicating that a device can or should be used more or less often, changes indicating that a device can perform a task or treat a condition in or for a different duration of time, or changes between periodic and continuous monitoring. Manufacturers should evaluate the effect such changes could have on the performance of a device, and whether such changes significantly affect the device's risk profile.

Changes concerning the compatibility or interoperability of a device with other devices, components, or accessories: Two examples of such changes would include 1) changes indicating an IVD reagent for use with a new system, and 2) changes that describe how to use an infusion pump with inputs from other devices not described in the previously cleared 510(k), such as a pulse oximeter or blood pressure monitor.

To evaluate whether these changes significantly affect the device's risk profile, manufacturers should carefully consider the following factors:

[6] A home use medical device is a medical device intended for users in any environment outside of a professional healthcare facility. This includes devices intended for use in both professional healthcare facilities and homes. See FDA's Home Use Devices website for more information: http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/HomeHealthandConsumer/HomeUseDevices/default.htm.

- Differences between the other devices, components, or accessories referred to in the previously cleared indications and the ones referred to in the modified indications. Manufacturers should be able to clearly identify and analyze the risks associated with such differences, including whether the change may affect biocompatibility, performance, connectivity, etc. If the change is to indicate compatibility with a type of device, component, or accessory that was not indicated as compatible previously, that change will likely require submission of a new 510(k).
- The criticality of the other device, component, or accessory; the more critical the other device, component, or accessory is to overall system function, the more likely a labeling change regarding compatibility or interoperability could significantly affect safety or effectiveness.
- The labeling of the other device, component, or accessory. If the change is to indicate compatibility or interoperability with another device that is labeled for use with the subject device or device type, it is less likely that the change introduces a compatibility or interoperability issue that could significantly affect safety or effectiveness.

IVD manufacturers should see also FDA's guidance *Replacement Reagent and Instrument Family Policy* (http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm071465.pdf).

Changes from a general use to a more specific use: These types of changes include those changes made to identify a specific use when the cleared device has a general indication for use. These changes are among the most difficult to assess. FDA's *Guidance for Industry: General/Specific Intended Use* (https://www.fda.gov/RegulatoryInformation/Guidances/ucm073944.htm) provides information on when a specific indication for use is reasonably included within a general indication for use for purposes of determining substantial equivalence, i.e., whether a 510(k) can be cleared or whether, instead, a PMA or De Novo request is required. The factors discussed therein – particularly those discussing the risk and public health impact of an indications for use change – may be helpful to consider in deciding whether to submit a new 510(k) for a change to an existing device, but that guidance should not be used in and of itself to justify that submission of a new 510(k) is not required. The General/Specific guidance is not intended to provide guidance on when submission of a new 510(k) is required for changes to an existing device.

If a risk-based assessment indicates that the change leads to a significant change in the device's risk profile, submission of a new 510(k) is likely required.

A2. **Does the change add or delete a contraindication?** Changes in the labeled contraindications for device use generally could significantly affect safety or effectiveness of a device and should typically be reviewed by the Agency; however, FDA recognizes that, in general, the addition of a contraindication based on new information is important to public health. Thus, FDA does not intend to object if manufacturers add new contraindications to their labeling and notify existing users of their device as expeditiously as possible whenever a pressing public health need arises. In this situation,

the new labeling should be submitted to FDA as part of a new 510(k) that is prominently labeled "change being effected" (CBE, in Figure 2- Flowchart A). Manufacturers should ensure they are thoroughly familiar with the definition of a contraindication in such situations.

Deletion or modification of a contraindication also usually requires submission of a new 510(k) prior to effecting the change, because this type of labeling change typically changes the indications for use in a way that could significantly affect safety or effectiveness. Deletions of contraindications would expand the indications for use. For example, if a physical restraint was contraindicated for use with individuals weighing less than 100 pounds because of established life-threatening and other serious adverse events, and the manufacturer subsequently wishes to remove this contraindication, submission of a new 510(k) is likely required.

Similar to changes in indications for use, minor changes that clarify or reword a contraindication without changing the meaning of the contraindications would not typically require submission of a new 510(k).

If the change adds or deletes a contraindication, submission of a new 510(k) is likely required. Otherwise, proceed to **A3.**

A3. **Is it a change in warnings or precautions?** In order to facilitate a continuous upgrading in device labeling, manufacturers should monitor device usage and promptly revise the warnings and precautions section(s) based on user experience. Events that precipitate changes of this type may be those reported under the medical device reporting regulation (MDR), 21 CFR Part 803. Submission of new 510(k)s for such labeling changes are generally not required. However, to determine whether the change in warnings or precautions requires submission of a new 510(k), manufacturers should proceed to **A.1.1** and follow Flowchart A through **A.1.5**. If it is not a change in warnings or precautions, manufacturers should proceed to **A4**.

A4. **Could the change affect the directions for use of the device?** Device labeling may be changed for a multitude of reasons. Many labeling changes result from attempts to clarify labeling. Manufacturers should consider whether the change is intended to or could affect how the device is used in practice.

Manufacturers should evaluate labeling changes to determine whether the change affects the directions for use of the device, including IVD labeling required under 21 CFR 809.10. If the change affects the directions for use, the change should subsequently be analyzed under **A.1.1** through **A.1.5.** If the change could not affect the directions for use of the device, submission of a new 510(k) is likely not required based on the labeling change.

Examples of changes that affect the directions for use of the device, and that should be analyzed under **A1.1** through **A1.5** include:

- Adding additional or new instructions on how to interpret diagnostic data from a diagnostic device.
- Adding a new procedural technique not described in the original labeling.
- Use of a product for a duration/frequency that is different than what is described in the labeling of the cleared device.
- Changing from labeling a device as non-sterile to labeling it as sterile or vice versa.
- Adding instructions for device use in a new patient population not described in the original indications for use.
- Adding instructions for device use in a different type of joint, organ, bone, vasculature, or tissue.

FDA believes that, if manufacturers follow this approach to changes in device labeling, only necessary new 510(k)s (those changes that could significantly impact safety and effectiveness) will be submitted, while the submission of unnecessary new 510(k)s (those that could not significantly affect safety and effectiveness) will be minimized. At the same time, manufacturers should be able to retain the flexibility to improve their labeling to assure safe and effective use of their devices.

B. Technology, Engineering, and Performance Changes

These types of changes encompass a broad span of design activities, from minor engineering changes in a circuit board layout to a change from electromechanical to microprocessor control of device function. Flowchart B illustrates the decision-making logic scheme for such technology, engineering, and performance changes to a device. These changes should be evaluated using this scheme, and then the changes should be verified and/or validated according to the QS requirements (21 CFR 820.30(i)). If the results of the verification and/or validation raise any unexpected issues, the decision of whether submission of a new 510(k) is required should be re-evaluated per B5.4.

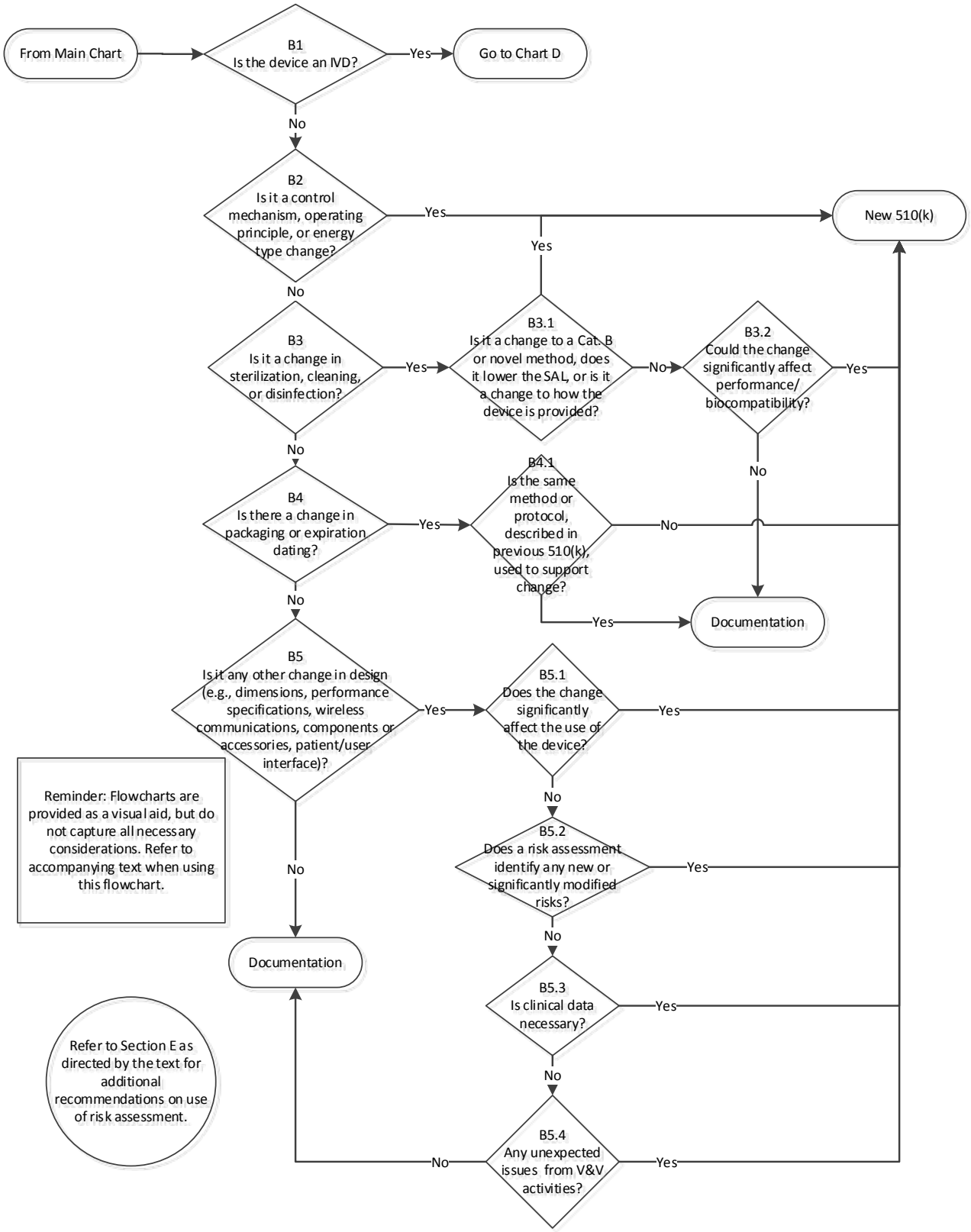

Figure 3 - Flowchart B: Technology, Engineering, and Performance Changes

B1. Is the device an *in vitro* diagnostic device? If the device is an IVD, refer to the later section of this guidance which is specific to technology, engineering, and performance changes in IVDs (Section D – Technology, Engineering, Performance, and Materials Changes for *In Vitro* Diagnostic Devices).

B2. Is it a control mechanism, operating principle, or energy type change?

Control mechanism changes: A control mechanism, for the purpose of this guidance, is the manner by which the actions of a device are directed. Almost all changes in the control mechanism for a device could significantly affect safety and effectiveness. Therefore, such changes will usually require submission of a new 510(k). This is also true for changes in operating principle as well as for changes in energy type (discussed below). Changes of these types tend to be more revolutionary than evolutionary.

One example of a control mechanism change would be a change from analog to digital control of a medical device. While the change to digital control can markedly improve device performance specifications and effectiveness, the integration of a digital control into a previously all-analog system is complex and usually undertaken only as part of a major redesign of a product. Thus, it would be rare that submission of a new 510(k) would not be required. Most often, such changes in control mechanism represent the introduction of a new product line. Another example of a change that would likely require submission of a new 510(k) is the change from pneumatic to electronic control of a respiratory care device.

Operating principle changes: Similar to a control mechanism change, a change in operating principle would also usually require submission of a new 510(k). An example of a new operating principle for a device would be changing the image reconstruction algorithm used in a computed tomography x-ray system from simple back projection to a new, more radiation-efficient method. In this case, testing both at the bench and in the clinic would be necessary to support a finding of substantial equivalence for the new device. Another example would be a change in a water droplet dispersal method used by a respiratory gas humidifier from piezoelectric material to a wick and fan method. The two mechanisms use the same design principle, but apply it in different ways. The differences between the two could significantly affect safety and effectiveness.

Such changes may also be accompanied by significant labeling changes and, sometimes, by a need for operator retraining to ensure continued safe and effective operation.

Energy type changes: Submission of a new 510(k) will usually be required for energy type changes. These changes include both energy output and input changes. A change from emitting microwave energy to radiofrequency (RF) energy would be an example of an energy output change; this type of change would likely be part of a significant redesign. An example of an energy type input change is a change from AC to battery power; this type of change is usually part of a redesign to provide a portable device that can be used under different environmental conditions than the original device. Such a change would normally be accompanied by significant labeling changes, including a new or expanded indication for use. Note that this type of change does not include a change in

voltage, such as from 3V to 9V operation or a change between different types of batteries, such as from NiCad to lead acid storage batteries. Such changes should be considered changes in performance specifications or device design, as discussed at decision point **B5**.

B3. **Is it a change in sterilization, cleaning, or disinfection?** Changes in sterilization, cleaning, or disinfection should be carefully assessed. If there is a change of this type, proceed to **B3.1**.

B3.1 **Is it a change to an "established category B" or "novel" sterilization method, does the change lower the sterility assurance level, or is it a change to how the device is provided?** Changes from "established category A" sterilization methods to "established category B" or "novel" sterilization methods generally require submission of a new 510(k). Changes from one "established category A" method to another "established category A" method, or from an "established category B" or "novel" method to an "established category A" method, should be evaluated under **B3.2**. See FDA's guidance *Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile* (https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm109897.pdf) for a discussion of sterilization methods and their categorization (e.g., established A, established B, or novel).

If the sterility assurance level (SAL) is lowered, manufacturers should consider whether device safety or effectiveness may be compromised by the new level. In general, reductions in SAL require submission of a new 510(k) unless the SAL remains better than 10^{-6}. Note that changes to cleaning and disinfection processes for reprocessed devices can also affect the bioburden levels on a device, which may invalidate subsequent processing steps such as sterilization; manufacturers should carefully consider whether these changes could significantly affect the safety or effectiveness of the device. It is likely that changes to reprocessing procedures for devices listed in Appendix E of FDA's guidance *Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling* (https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm253010.pdf), could significantly affect safety or effectiveness. FDA has identified the devices there as a subset of medical devices that pose a greater likelihood of microbial transmission and represent a high risk of infection (subclinical or clinical) if they are not adequately reprocessed.

Some changes to how a device is provided to the user or patient could also significantly affect safety or effectiveness. For the purposes of this question, "how the device is provided" refers to whether the device is provided sterile or non-sterile, and to whether the device is provided for (1) single-patient, single-use, (2) single-patient, multi-use, or (3) multi-patient, multi-use. If a device is changed from (1) to (2), (1) to (3), or (2) to (3), i.e., provided for more patients and/or more uses, submission of a new 510(k) is likely required. However, the reverse would not be true; it would be unlikely that a change from (3) to (2), (3) to (1), or (2) to (1) could significantly affect safety or effectiveness and therefore would not likely require submission of a new 510(k). In addition, if a device that was originally provided sterile is modified to be provided non-sterile – either to be

sterilized by the user or to be used without sterilization – submission of a new 510(k) is likely required. Submission of a new 510(k) is also likely required if a device originally provided non-sterile is modified to be provided sterile.

If the answer to this question is yes, submission of a new 510(k) is likely required. If the answer is no, proceed to **B3.2**.

B3.2 Could the change significantly affect the performance or biocompatibility of the device? Changes in the method of sterilization, cleaning, or disinfection have the potential to change material or performance characteristics of a device. This is particularly true of the properties of polymeric materials or surface coatings, resorbable materials, or animal-derived materials. When manufacturers make changes in sterilization, cleaning, or disinfection methods, they should consider whether the properties or specifications of the device could be significantly affected.

To determine whether the cleaning, disinfection, and/or sterilization change could significantly affect device performance, the manufacturer should consider known information on the sterilization, cleaning or disinfection method, its parameters, and the material being sterilized, cleaned, or disinfected, and determine if there are any new or significantly modified existing risks associated with using the proposed method and its parameters with the device's materials of construction. If there are new or significantly modified existing risks (see Section E), this likely indicates that the change could significantly affect the device's safety or effectiveness. Note also that if verification and/or validation of the new methods show any unexpected results, manufacturers should re-evaluate whether submission of a new 510(k) is required (see **B5.4**).

Cleaning, disinfection, and/or sterilization changes may also affect the biocompatibility of a device. For instance, changes to an ethylene oxide sterilization process may leave increased ethylene oxide residuals on the device surface, or changes to a cleaning process may incorporate chemicals that are inappropriate for use with a patient-contacting device. Manufacturers should consider whether sterilization, cleaning, or disinfection changes could significantly affect the biocompatibility of their device. If a manufacturer determines their cleaning, disinfection, or sterilization change could significantly affect the performance or biocompatibility of the device, submission of a new 510(k) is likely required. Otherwise, it is unlikely submission of a new 510(k) is required as a result of this type of change.

B4. Is there a change in packaging or expiration dating? If yes, proceed to **B4.1**.

B4.1 Is the same method or protocol, as described in a previously cleared 510(k), used to support the change? Generally, changes in device packaging or changes in the expiration date for use of a device do not require submission of a new 510(k). FDA relies on the QS regulation (21 CFR Part 820) to reasonably assure the safety and effectiveness of devices with these types of changes. This is true whether or not the manufacturer applies an expiration date because of package integrity considerations, e.g., sterility, or because of a finite shelf-life of the device. However, where methods or protocols that are not described in a previously cleared 510(k) are used to support new package integrity or shelf-life claims, submission of a new 510(k) is likely required. FDA recognizes that

methods or protocols may be updated to reflect newly recognized versions of consensus standards. Submission of a new 510(k) is likely not required in such circumstances.

B5. Is it any other change in design (e.g., dimensions, performance specifications, wireless communication, components or accessories, or the patient/user interface)? These types of design or engineering changes encompass everything from the routine specification changes necessary to maintain or improve device performance as a result of feedback from users, field or plant personnel, etc., up to and including significant product redesign. The bullets below highlight some, but not all, of these changes, and provide points to consider for each type of change.

- **Dimension changes:** In determining whether submission of a new 510(k) is required for these types of changes, per **B5.1**-**B5.4**, the manufacturer should consider not only the magnitude of the dimension or dimensional specification change, but the criticality of the modified dimension. The more critical the dimensions being modified are to the safe and effective operation of the device, the more likely it is that the change could significantly affect safety or effectiveness. For instance, a 1 mm change to the diameter of a working channel of an endoscope is more likely to significantly affect safety or effectiveness than a 1 mm change to the length of an endoscope.

  If a modified dimension is within a range of dimensions previously cleared for the original device, submission of a new 510(k) would not typically be required. For instance, if the original device was cleared with two models that were 2 and 4 mm in diameter, and the modified device of the same length has a diameter of 3 mm, submission of a new 510(k) is likely not required for this change.

- **Device performance changes:** This category covers a broad range of changes. As discussed in the Main Flowchart, Question 1, changes that are intended to significantly affect device safety or effectiveness likely require submission of a new 510(k). Changes that are not intended to affect device safety or effectiveness should be considered per **B5.1**-**B5.4**.

- **Wireless communication changes:** Changes to device communication between device components or between the modified device and other products, particularly from wired to wireless, may change a device's risk profile by introducing or modifying risks regarding data transmission or cybersecurity.[7] Changes to employ wireless communication in devices where it was previously not used are likely to significantly affect safety or effectiveness and likely require submission of a new 510(k). This is particularly true when wireless communication is used to control device operations. When evaluating other changes, including a change to a different wireless communication protocol, the factors in **B5.1**-**B5.4** should be taken into account in determining whether submission of a new 510(k) is required.

[7] See FDA's webpage on cybersecurity in medical devices, http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ConnectedHealth/ucm373213.htm.

- **Components or accessories:** Changes to components or accessories could, in some cases, significantly affect the safety or effectiveness of the device as a whole. In **B5.1**, manufacturers should consider whether changes to the device or any of its components or accessories affect the use of other components or accessories, or if changes to a component or accessory could lead a device to be used in a new way. In **B5.2**, manufacturers should consider whether changes to the device or any of its components or accessories could disrupt compatibility between the device and its components or its accessories, and whether these changes could lead to a significant change in the device's risk profile.

- **Changes in the human factors of the patient or user interface:** A device user interface includes all points of interaction between the product and the user, including elements such as displays, controls, and packaging. User interface changes refer to changes in the way in which a patient or user interacts with a device, including, for example, the way in which the device presents alarms to the user, the layout of the control panel, the mode of presentation of information to the user or patient, and the way in which the device physically interacts with the user and/or patient (e.g., the way in which a CPAP mask attaches to a patient's face, or the way a surgical instrument is designed to fit in a surgeon's hand). Note that this type of change includes changes that modify a user workflow (tasks performed by a user in order to complete their work). Manufacturers should consider the risk impact of changes in user workflow; for example, providing new information to the user or modifying the manner in which information is presented may impact user comprehension. In addition, changing the layout of device controls may impact device use differently in different use scenarios. For more information on applying human factors in medical devices, see FDA's guidance *Applying Human Factors and Usability Engineering to Optimize Medical Device Design* https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/UCM259760.pdf .

  Changes intended only to increase user or patient comfort when interacting with the device may be particularly difficult to evaluate. Changes to increase user or patient comfort will typically not require submission of a new 510(k), but some changes made for the comfort of the user or patient could also change the way the device functions or performs and therefore could significantly affect safety or effectiveness. For example, if a surgical handpiece is redesigned to move a motor closer to the surgeon's hand or the surgical site, any heating of the motor will be more likely to affect the surgeon or patient and could result in burns. Manufacturers should evaluate changes to a user interface and whether they significantly affect safety or effectiveness in answering **B5.1-B5.4**.

Changes in design should be considered, along with the above bulleted points, in answering **B5.1-B5.4**.

B5.1 **Does the change significantly affect the use of the device?** As with a labeling change, if a design change significantly affects how a device may be used, submission of a new 510(k) is likely required. In the risk-based assessment, manufacturers should consider whether the design change increases the likelihood that the device will be used by a

broader or different group of users who have less training regarding safe and effective use of the device (e.g., lay users instead of clinicians, or general practitioners instead of surgeons) and whether that design change affects the risk profile of the device. If the change significantly affects the risk profile (see Section E), submission of a new 510(k) is likely required.

Manufacturers should also consider whether the design change increases the likelihood that the device will be used in a new environment, and whether the new environment affects the risk profile of the device. If the change facilitates use in a completely different environment (e.g., from hospital to home use, or from hospital to ambulance transport), this typically will introduce new or significantly modified existing risks and will likely require submission of a new 510(k). If the change facilitates use only in similar environments, the risk profile of a device may also be changed, but this is less likely to require submission of a new 510(k). In deciding whether a design change that allows use of the device in a new environment could significantly affect the safety or effectiveness of the device, manufacturers should consider differences in environmental specifications such as:

- temperatures and humidity that might affect device operation;
- noises that might drown out the sound of auditory alarms;
- exposure to water, soils, or light that might affect device operation;
- presence of other devices or equipment that may cause electromagnetic interference; and
- possible use in magnetic resonance imaging (MRI).

If the design change introduces new or significantly modified existing risks, submission of a new 510(k) is likely required.

If the design change significantly affects use of the device, submission of a new 510(k) is likely required. If it does not, proceed to **B5.2**.

B5.2 Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks? As discussed in the Guiding Principles and Section E, the manufacturer should conduct a risk-based assessment for any modified device. New risks, changes to the acceptability of previously identified risks, or changes to device features that may be critical to the device's safe or effective operation will likely require submission of new 510(k)s.

Manufacturers should carefully consider whether changing one aspect or feature of a device's design might affect a seemingly unrelated aspect or feature. For instance, a dimensional or component change may affect the ability to reprocess a device or the ability to regulate the temperature of an electronic device. Manufacturers should evaluate these impacts of the change as part of their risk-based assessment.

If a risk-based assessment does not identify any new risks or significantly modified existing risks per Section E, proceed to **B5.3**.

B5.3 Are clinical data necessary to evaluate safety or effectiveness for purposes of design validation? Whenever a manufacturer recognizes that clinical data are needed because bench testing or simulations are not sufficient to assess the impact of the change on safety or effectiveness to validate the design change, submission of a new 510(k) is likely required. For the purposes of this question, clinical data does not include data used for purposes other than design validation, such as user or patient preference testing.

If clinical data are unnecessary to evaluate safety and effectiveness for purposes of design validation, proceed to **B5.4**.

B5.4 Do design verification and/or validation activities produce any unexpected issues of safety or effectiveness? All changes to device design should undergo some level of design verification and/or validation or evaluation to ensure that the device continues to perform as intended. See 21 CFR 820.30. As discussed in the Guiding Principles, manufacturers should make an initial risk-based assessment of whether a change requires submission of a new 510(k). If the manufacturer determines after an initial assessment that submission of a new 510(k) is not required, the manufacturer should conduct routine verification and validation activities to ensure that no new issues of safety or effectiveness are raised. If successful application of routine verification and validation activities confirms the initial assessment, manufacturers should proceed with the design change and document their assessment.

Occasionally, routine verification and validation activities may either produce unexpected results or otherwise prove to be inadequate to verify and/or validate the modified design. In such instances, the manufacturer likely is required to submit a new 510(k).

If a manufacturer encounters unexpected results performing routine verification and validation activities – for example, the device does not perform as expected, pre-specified acceptance criteria are not met, or testing demonstrates unexpected safety or effectiveness issues – the manufacturer should analyze the results carefully. The initial risk-based assessment should be re-evaluated, and if changes to that assessment are necessary, the manufacturer should re-evaluate whether the device change could significantly affect safety or effectiveness. If different verification and/or validation test methods or acceptance criteria are necessary to produce the expected results, it is likely that the change could significantly affect safety or effectiveness and thus submission of a new 510(k) is likely required.

If the manufacturer determines prior to conducting verification and validation activities that routine verification and validation activities are insufficient and the design change necessitates a different verification and/or validation scheme or new acceptance criteria, submission of a new 510(k) is likely required. This does not mean that manufacturers should not update test methods and acceptance criteria for verification and validation activities in accordance with advances in science or relevant voluntary consensus standards, but if the design change drives the need for a new testing scheme or acceptance criteria (as opposed to advances in science or standards), it is likely that the design change could significantly affect safety or effectiveness. Note that performing a subset of the original suite of tests is not considered a new test scheme.

If the initial assessment determines submission of a new 510(k) is not required, and verification and validation activities are substantially unchanged (i.e., use the same test methods and same acceptance criteria) and successful, as outlined in the examples below, then proceed to Section C.

For example, in order to better accommodate connection of a urinary drainage (Foley) catheter to a collection apparatus, the manufacturer increases the length of the catheter by several millimeters. The new length is outside of previously cleared lengths for this device, however, the length change is not far outside cleared lengths. Based on its risk-based assessment, the manufacturer does not expect the length change will create any new risks or significantly modify existing risks. The manufacturer therefore determines that the length change could not significantly affect the device's safety or effectiveness, and does not require submission of a new 510(k). The manufacturer subsequently conducts design control activities, and verifies that the catheter functions safely and effectively, as predicted, with no unexpected results. The manufacturer documents these efforts and proceeds to production.

In another example, a manufacturer of monitoring devices wants to use a more sensitive comparator circuit, and makes other design changes to accommodate the more sensitive component. The design change is similarly evaluated in an initial risk-based assessment based on models, calculations, etc., and a decision is made that the change could not significantly affect the device's safety or effectiveness, and therefore the changes do not require submission of a new 510(k). However, as part of routine verification and validation activities, tests with a simulator produce unexpected results, and additional work is necessary to understand how and why this outcome occurred. The manufacturer should carefully assess these results and whether new issues of safety or effectiveness have been uncovered.

C. Materials Changes

Firms making changes to the materials from which their device is manufactured should also consider the other types of changes discussed above and their impact on the decision regarding submission of a new 510(k). For example, a material change, as discussed below, might also lead to a change in the labeling of the device (e.g., the removal of a contraindication or the addition of a new warning), or a change in specifications (e.g., a reduction in the strength of the device). These collateral changes should be considered in addition to the logic scheme described in this section.

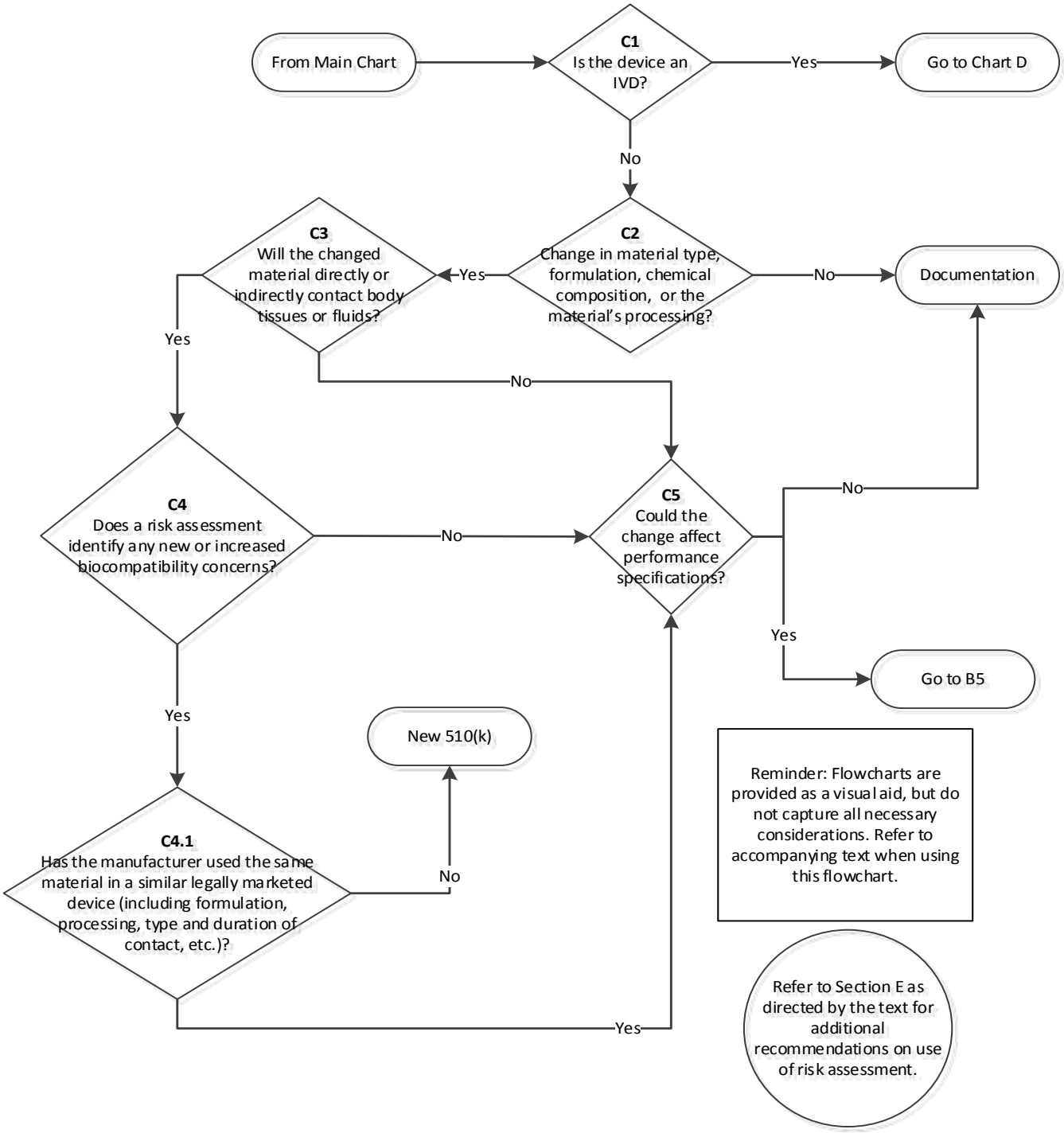

Figure 4 - Flowchart C: Materials Changes

C1. **Is the device an *in vitro* diagnostic device?** If the device is an IVD, refer to the later section of this guidance which is specific to materials changes in IVDs (Section D – Technology, Engineering, Performance, and Materials Changes for *In Vitro* Diagnostic Devices).

C2. **Is this a change in material type, material formulation, chemical composition, or the material's processing?** If there is any change in material type, formulation, or chemical composition, the answer to this question should be yes. Additionally, if there is any change in supplier or manufacturer material processing or finishing steps, the answer should also be yes. The biocompatibility and physical properties of a finished device depend not only on the materials, but also on the processing of the materials, manufacturing methods (including the sterilization process), and the manufacturing residuals that may be present on the finished device. Changes of this type should be further evaluated for their potential impact on safety and effectiveness. The subsequent questions, such as **C4** and **C4.1**, address whether the change is significant using the process of risk assessment.

Many material changes result from material supplier changes, including changes made by a material supplier, or changes from one supplier to another. When these types of changes occur, the manufacturer should utilize their quality system process to analyze the material and determine the extent of the change made, as this analysis might impact answers to subsequent questions, even when these changes result in materials that remain within the original material specifications.

If there is a change in material type, material formulation, chemical composition, or the material's processing as described above, proceed to **C3**. Otherwise it is unlikely submission of a new 510(k) is required as a result of a materials change.

C3. **Will the changed material directly or indirectly contact body tissues or fluids?** Both direct and indirect patient and user contact should be considered in answering this question. Direct contact is when a material comes into physical contact with a patient or user while the material is still in or on the patient or user. A material with indirect contact is a material through which a fluid or gas passes, prior to the fluid or gas coming into physical contact with body tissue (i.e., the device or device component itself does not physically contact body tissue).[8] For example, materials in a catheter hub (the part of the catheter which is external to the patient) can contact the patient indirectly if fluids or drugs are infused through the hub and directly into the patient.

While most implant materials contact patients, there are some exceptions. For example, the internal contents of spinal cord stimulators are not patient-contacting; they are hermetically sealed so that there is no material transfer, fluid transfer, or leeching out of any material internal to the device.

[8] See FDA's guidance *Use of International Standard ISO-10993, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process"* (https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm348890.pdf).

If the changed material directly or indirectly contacts body tissues or fluids, proceed to **C4**. If the changed material does not contact body tissues or fluids, proceed to **C5**.

C4. Does a risk assessment identify any new or increased biocompatibility concerns? Manufacturers should conduct a biocompatibility risk assessment, which may include an assessment of the device's toxicological and physical properties, of any changed materials that may contact the patient or user to determine if there are any new or increased biocompatibility concerns. An example of a new concern would be a material change that requires a new type of biocompatibility test, such as an implantation test, that was not required for the original device. An example of an increased concern would be where a new chemical component added to a material requires a genotoxicity analysis of that component (because, for instance, the particular component is noted in the literature as potentially genotoxic), but the original device already required a genotoxicity analysis. See FDA's guidance *Use of International Standard ISO-10993, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process"* (https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm348890.pdf) for detailed information regarding recommendations on how to conduct a biocompatibility risk assessment, including a specific chemical assessment.

The answer to **C4** may be no if a knowledgeable individual reviews the differences in chemical composition or physical properties and determines that the change is minor enough that there is no new concern about biocompatibility.

A supporting toxicological assessment can be based on an analysis of the chemical formulations or the results of chemical characterization tests if the detailed formulation is not available (i.e., when the material is provided by a supplier and the formulation is proprietary). If, however, this analysis identifies new chemical entities or other properties that are either novel or have the potential to generate adverse biocompatibility responses, such as genotoxicity, submission of a new 510(k) may be required.

If a risk assessment identifies any new or increased biocompatibility risks, consider the questions in **C4.1**. If no new or increased biocompatibility risks are identified, proceed to **C5**.

C4.1 Has the manufacturer used the same material in a similar legally marketed device?[9] Manufacturers who have identified possible biocompatibility concerns in their risk assessment (**C4**) should consider whether they have used the same material, in its final, finished state, in another one of its own legally marketed devices that has been cleared or approved by the FDA. If the manufacturer has used the same material in a similar device

[9] The term "similar legally marketed device" is not intended to refer to a predicate device as in the context of a substantial equivalence determination. The device is more akin to a reference device, as described in FDA's guidance *The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]* (https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/UCM284443.pdf.) For additional context, see Section III of FDA's guidance *Use of International Standard ISO-10993, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process"*(https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm348890.pdf).

that has been cleared or approved by the FDA (this would typically involve a biocompatibility evaluation), and there is no postmarket evidence of biocompatibility issues with the device, that may provide evidence that the material will be biocompatible in its new application in the changed device as well and the manufacturer can answer yes to this question.

It is important to note that in order to answer yes to this question, the material in question should have the same formulation or chemical composition and be subjected to the same processing, including sterilization (i.e., the comparison should be between materials as they are applied in the final finished device, not between raw materials). Note that the size and geometry of the changed device or component could affect the material properties (e.g., affect the curing of the polymer, or result in more material in the new device or component). Any change in chemical composition, manufacturing process, physical configuration (e.g., size, geometry, surface properties) or intended use of the device should be evaluated with respect to possible changes in biocompatibility and the need for additional biocompatibility assessment.

The previously cleared or approved device should have the same or a more risky type of contact and the same or a longer duration of contact. For example, if a manufacturer intends to use a new material in a limited exposure application (<24 hours), and the manufacturer has used that same material in a cleared or approved device for prolonged exposure (24 hours to 30 days), then it is unlikely that submission of a new 510(k) will be required for this change. If the modified device is intended to have a riskier category of contact (e.g., mucosal membrane contact is riskier than contact with intact skin, and blood contact is riskier than tissue/bone contact) or a longer duration of contact, then the manufacturer should answer no to this question. Contact may be either direct or indirect.

Manufacturers should not compare their changed material to materials in other manufacturers' legally marketed devices, unless the exact formulation and processing of the device, which may affect the safety and effectiveness of the final finished product, can be verified.

If the manufacturer has used the same material in a similar legally marketed device, proceed to **C5** to determine if the material change could affect device performance. If the manufacturer has not used the same material in a similar legally marketed device, submission of a new 510(k) is likely required.

C5. Could the change affect the device's performance specifications? Manufacturers should consider whether the material change could affect the performance of the device by affecting its mechanical properties, such as strength, hardness, etc. Manufacturers should also consider whether the new material could be affected by any labeled cleaning, disinfection, and/or sterilization process of the device. If the answer to this question is yes, manufacturers should proceed to **B5** above and consider whether the change could significantly affect the safety or effectiveness of the device. If the change could not affect the device's performance specifications, it is unlikely the change could significantly affect safety or effectiveness, and the manufacturer should document the change.

D. Technology, Engineering, Performance, and Materials Changes for *In Vitro* Diagnostic Devices

Changes in technology, engineering, performance, or materials of an IVD can include changes made to reagents or changes to a test method or protocol, among other things.
For IVDs, performance generally refers to the analytical and clinical specifications established as part of the most recent 510(k) clearance. Analytical performance refers to the documented ability of an IVD test or test system to measure or detect a target analyte or substance that the IVD is represented or purported to identify or measure.Clinical performance refers to the documented ability of an IVD to identify, measure, monitor, or predict the presence or absence of, or the future development of, a clinical condition or predisposition, for which the device is intended.

Firms making technology, engineering, performance, or materials changes to their IVD should also consider the other types of changes discussed above in Section A, Labeling Changes, and their impact on the decision regarding submission of a new 510(k). For example, a material change, as discussed below, might also be considered a design change and/or might engender a change in the labeling of a device (e.g., the removal of a contraindication, addition of a new warning, or a change in the measuring range). These collateral changes should be considered also when applying the logic scheme described in this section.

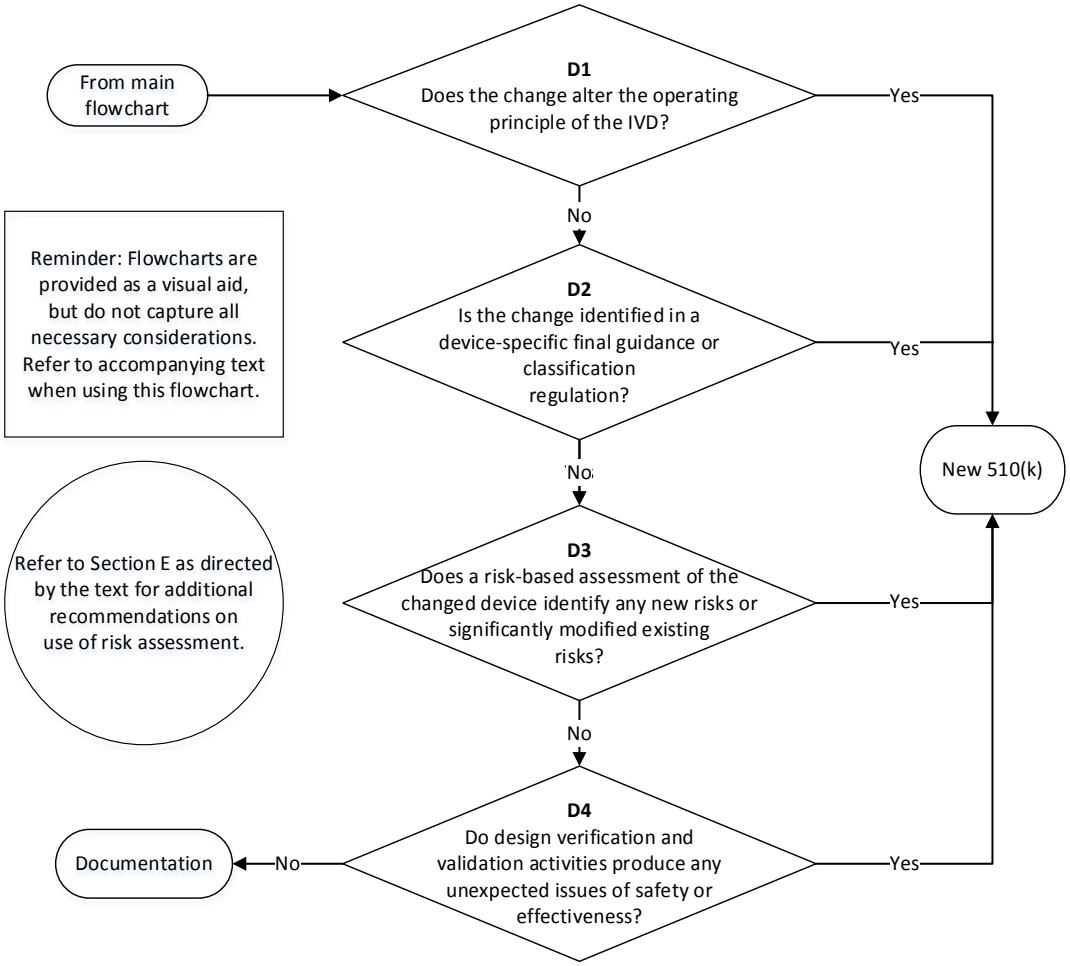

Figure 5 - Flowchart D: Technology, Engineering, Performance, and Materials Changes for *In Vitro* Diagnostic Devices

D1. Does the change alter the operating principle of the IVD?

In most cases, a technology, engineering, performance, or material change that alters the operating principle of an IVD could significantly affect safety and effectiveness, in which case submission of a new 510(k) is required. Submission of a new 510(k) is not necessarily required for all changes in technology, engineering, performance, or materials for IVDs that alter the operating principle of an IVD. However, when such changes introduce novel technology that could have an impact on the ability of the device to extract, isolate, or detect the analyte(s) and could therefore affect the value assigned to the specimen, or could produce deviations in device performance that would result in modified reporting of performance in labeling, submission of a new 510(k) is likely required.

Examples of changes in technology, engineering, performance, or materials that likely alter the operating principle of the IVD and for which a new 510(k) is likely required include:

- changes from radioimmunoassays (RIA) to non-RIAs;
- changes in the antibody;
- changes in detection reagents;
- changes in critical reaction components; and
- changes in conjugates.

Examples of changes in technology, engineering, performance, or materials that might alter the operating principle of the IVD include:

- changes from liquid to solid reagent;
- changes in calibration materials and quality control materials;
- changes in substrates;
- changes in specimen type;
- changes in specimen processing; and
- changes in incubation times and temperatures.

Examples of changes in technology, engineering, performance, or materials of an IVD which do not ordinarily affect the operating principle of the IVD include:

- changes to external packaging;
- changes to use a new lot or batch for the same antibody or enzyme;
- changes to a new vendor for the same reagent; and
- changes in concentrations of packaged reagents provided the same diluted concentration was used in the assay.

If such a change to an IVD does not alter the operating principle of the IVD, proceed to **D2**.

D2. Is the change identified in a device-specific final guidance or classification regulation?

In the case of some IVDs, FDA has published device-specific final guidance documents, which provides resources to manufacturers on specific issues related to those devices. A searchable listing of these device-specific guidances can be found on FDA's website at https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070274.htm. When a device-specific final guidance identifies a change or modification that FDA has determined could significantly affect safety or effectiveness, submission of a new 510(k) is generally required. Additionally, in the case of some IVDs, FDA has established specific requirements (e.g., special controls) that are identified in the classification regulation. If a classification regulation identifies a change that could significantly affect safety or effectiveness, submission of a new 510(k) is required. Where a change is not identified in a device-specific final guidance or classification regulation, proceed to **D3**.

D3. Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks?

As discussed in the Guiding Principles and Section E, the manufacturer of an IVD should conduct a risk-based assessment for any modified device. Changes in the technology, engineering, design, or material used in an IVD can affect the performance, including the analytical or clinical performance, of the device. Further, certain changes in an IVD could also present new or significantly modified existing risks that could affect the overall risk profile of the IVD, apart from the performance (e.g., transmission of pathogenic diseases, biocompatibility or sterility issues).

For IVDs, a manufacturer's risk-based assessment identifies new risks or significantly modified existing risks when the risk-based assessment (1) indicates that the performance of the modified test could significantly change from the previously cleared performance claims or (2) identifies new risks or significantly modified existing risks, apart from performance. If a change could affect the analytical performance of a device, particular attention should be paid to the effect on device performance around the clinical decision point(s) (i.e., cut-offs, cut-points). When new risks or significantly modified existing risks have been identified, in general, the change to the IVD could significantly affect safety or effectiveness of the device and submission of a new 510(k) is likely required. This includes a change that is clinically significant in terms of clinical decision making.

Changes to components or accessories could, in some cases, significantly affect the safety or effectiveness of an IVD as a whole. Manufacturers should consider in their initial risk-based assessment whether changes to the IVD or any of its components or accessories affect the use of other components or accessories, or if changes to a component or accessory could lead an IVD to be used in a new way. Manufacturers should also consider whether changes to the IVD or any of its components or accessories could disrupt compatibility between the device, its components, and/or its accessories, or whether these changes could significantly affect performance or the device's risk profile.

Changes in the human factors of a patient or user interface could, in some cases, significantly affect the safety or effectiveness of an IVD as a whole. Manufacturers

should evaluate in their initial risk-based assessment whether a change in the human factors of a patient or user interface could significantly change the performance of the IVD or presents new risks or significantly modified existing risks. A device user interface includes all points of interaction between the product and the user, including elements such as displays, controls, and packaging. User interface changes refer to changes in the way in which a patient or user interacts with a device, including, for example, the way in which the device presents alarms to the user, the layout of the control panel, the mode of presentation of information to the user or patient, and the way in which the device physically interacts with the user and/or patient. Note that these changes include those that modify a user workflow (tasks performed by a user in order to complete their workflow). Manufacturers should consider the risk impact of changes in user workflow, such as providing new information to the user or modifying the manner in which information is presented, which may impact comprehension, or changing the layout of device controls, which may impact device use differently in different use scenarios. For more information on applying human factors in medical devices, see FDA's guidance, *Applying Human Factors and Usability Engineering to Optimize Medical Device Design* https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/UCM259760.pdf.

Changes intended only to increase user or patient comfort when interacting with the device may be particularly difficult to evaluate. These changes will typically not present new risks or modified existing risks, but some changes made for the comfort of the user or patient could significantly affect safety or effectiveness. Manufacturers should evaluate the potential of changes to a user interface as to whether they could significantly affect safety or effectiveness.

If a risk-based assessment indicates that that the performance of the modified IVD could not significantly change from the previously cleared performance claims, or that the modified IVD does not present new or significantly modified existing risks apart from performance, proceed to **D4**.

D4. Do design verification and/or validation activities produce any unexpected issues of safety or effectiveness?

As discussed above in the Guiding Principles, manufacturers should conduct an initial risk-based assessment of whether a change requires submission of a new 510(k); if the initial decision following the risk-based assessment is that submission of a new 510(k) is not required, the manufacturer should conduct design verification and/or validation activities to confirm the decision.

Verification and validation activities should reevaluate the performance claims or performance specifications that were part of the original 510(k) clearance, as appropriate based on the manufacturer's routine quality processes. Submission of a new 510(k) is likely not required where:

1) standard methods and performance criteria that have been established for evaluation of the specific device, as appropriate (e.g., (a) protocols and criteria used to support the original 510(k) or (b) a protocol established in the original

510(k) that described how anticipated changes would be evaluated), are used to verify and validate the modification;
2) the results of verification and validation indicate that the performance is within the criteria;
3) the performance of the modified IVD has not significantly changed from the previously cleared performance claims; and
4) verification and validation do not reveal new risks or significantly modified existing risks apart from performance.

If all of these criteria are met, then the change is unlikely to significantly affect safety or effectiveness and manufacturers should proceed with the change making sure to document their assessment of whether submission of a new 510(k) is required.

If any of these criteria are not met, for instance, if verification or validation test methods or acceptance criteria other than those identified in item 1 immediately above are necessary to evaluate the change, it is likely that the change could significantly affect safety or effectiveness and that submission of a new 510(k) is required.

If the results of routine verification and validation produce any unexpected issues or otherwise prove inadequate to verify and/or validate the change—for example, pre-specified criteria are not met, the device fails to perform as expected, or testing demonstrates unexpected safety or effectiveness issues—it is likely that the change could significantly affect the IVD's safety and effectiveness, and submission of a new 510(k) is likely required.

E. Considerations for Risk-Based Assessments of Modified Devices

As discussed throughout this document, a device modification that leads to a significant change in the device's risk profile likely requires submission of a new 510(k). This section provides guidance on the principal factors to consider in conducting a risk-based assessment to determine whether a device change leads to a significant change in the device's risk profile. Manufacturers should use the risk-based assessment considerations discussed below in conjunction with the logic schemes and decision-making flowcharts outlined above.

Although FDA recommends that manufacturers use an accepted method of risk assessment, such as ISO 14971, an FDA-recognized standard that provides a framework for systematically managing risks of medical devices throughout the total product life cycle, this guidance uses terminology distinct from ISO 14971.

In general, the assessment of risk in deciding whether to submit a new 510(k) should identify all possible risks associated with the changed or modified device, and then focus on risks whose existence and characteristics are supported by objective scientific evidence. It is not necessary to focus on hypothetical risks that are not supported by scientific evidence or those that are determined to be negligible due to both the low probability of occurrence and low severity of harm. The manufacturer should then explore the severity and probability of occurrence of the harm to determine whether the device change could significantly affect safety or effectiveness and require submission of a new 510(k).

Relationship between hazards and harm

Risk assessment involves describing the relationships between a hazard (a potential source of harm) and the ultimate consequences in terms of physical injury or damage. For some devices, non-physical injury, such as psychological harm, should also be considered. As part of their risk assessment, manufacturers should analyze possible sequences of events, hazardous situations, and associated possible harm. This may include:

- initiating hazards, failure modes, or circumstances;
- the sequences of events that could lead to a hazardous situation occurring;
- the likelihood of such situations arising;
- the likelihood that the hazardous situations lead to harm; and
- the nature of the harm that could result.

The extent of risks and harms associated with a device change may be assessed by taking into account the following factors, individually and in aggregate:

1. Likelihood or probability of occurrence of harm

Various approaches may be employed to estimate probabilities of hazardous situations in assessing risk, including, but not limited to:

- use of relevant historical and real-world data;
- prediction of probabilities of risk using analytical or simulation techniques;
- reliability estimates;
- production data; or
- use of expert judgment.

The use of multiple approaches may be considered as this might serve to increase confidence in the results. Where uncertainty exists around these estimates, it may be useful to consider a qualitative approach to risk probability analysis. See, for instance, Section D.3 Risk Estimation of ISO 14971:2007 (second edition).

If it's determined that the likelihood of a harm occurring due to a device change is negligible, then that change is unlikely to require submission of a new 510(k). If it cannot be determined that a harm's likelihood is negligible, or the probability cannot be determined at all, then the below factors should also be considered.

2. Severity of harm

Manufacturers should consider the following points in analyzing the severity of a potential harm (refer to ISO 14971:2007 (second edition), Annex D, Sections D.3.3 and D.4 on severity and risk acceptability):

- New risks – If a device change creates a new risk – i.e., a new hazard or hazardous situation – that did not exist for the original device and the new risk cannot be determined

to be negligible, it is likely that the change could significantly affect the device's safety or effectiveness, and submission of a new 510(k) is likely required. An exception is a device change where the pre-mitigation risk level (the risk level before any risk mitigations or controls are accounted for or product specifications are set) associated with the new risk is considered to be acceptable.

- Changes in risk acceptability – If a device change positively or negatively changes the pre-defined acceptability level (e.g., tolerable, acceptable, insignificant) of an individual risk based on the risk-based assessment, either before or after risk mitigation or control, it is likely that the change could significantly affect the device's safety or effectiveness, and submission of a new 510(k) is likely required.
- Changes in risk score – In cases where there is no risk acceptability change for an affected risk, a major change to the severity score may still suggest potential significant impact to safety, depending on how the manufacturer determines their risk scores and defines risk acceptability. These types of changes will be very dependent on how a manufacturer conducts risk management and defines risk scores and risk acceptability.
- Duration – Some device features expose patients and/or users to temporary, minor harm; some can cause repeated but reversible harm; others can cause permanent, debilitating injury. Duration – that is, how long the adverse consequence lasts – should be considered along with the other factors described in this section.

Note that if a device change results in risk that could significantly affect the safety or effectiveness of a device, submission of a new 510(k) must be submitted, even if the risk can be mitigated.

3. Device effectiveness

Although ISO 14971 defines risk in terms of device harms and their effects on safety, it is important to note that whether submission of a new 510(k) is required depends on whether the change could significantly affect the safety *or effectiveness* of the device. Therefore, manufacturers should also consider the possible effects a device change may have on device effectiveness. As with safety risks, the manufacturer should consider the probability and severity (i.e., magnitude) of impacts to device effectiveness.

In considering a device change's effects on device effectiveness, manufacturers should understand the criticality of the device feature being modified to the safe and effective use of the device. Certain features are more critical than others. For instance, the outer case of a ventilator, although important to the overall design of the device and providing for connection of various parts, is not as critical to the safe and effective use of the ventilator as the pump that circulates air to the patient. Note that labeling changes, which affect user actions, can be critical as well.

Appendix A: Examples

The following are hypothetical examples of device changes with explanations as to why they likely would or would not require submission of a new 510(k). These examples are intended to be illustrative of the thought process for different types of changes. Note that these generalized examples do not necessarily account for every possible detail, risk, or consideration a manufacturer should evaluate, and should not be taken to mean that the changes described definitely do or do not require submission of a new 510(k). Real-world device modification decisions will depend on the particular details of the change and the specific device in question.

Labeling change examples

1. **Change:** The original indications for use for a radio frequency (RF) device is to treat mild-moderate wrinkles on the peri-orbital area. The indications for use are modified to also indicate the device for treatment of severe wrinkles on the decollatage.
   Relevant questions:
   A1- *Is it a change in the indications for use statement?* Yes. The indications for use are being expanded from treatment of mild-moderate wrinkles on the peri-orbital area of the face to treatment of the peri-orbital area and severe wrinkles on the decollatage. Proceed to A1.1 - A1.5.
   A1.4 – *Does the change describe a new disease, condition, or patient population that the device is intended for use in diagnosing, treating, preventing, curing or mitigating?* No. The manufacturer determined that the conditions and patient populations that the device is intended for use in treating are the same.
   A1.5 – *Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks?* Yes. A risk-based assessment identifies that while there are no new or increased safety risks associated with the use of the device on the decollatage, the new indication for use is associated with a risk of significantly reduced effectiveness on the decollatage due to the differences in skin types and the severity of the wrinkles, which could significantly affect safety and effectiveness.
   Decision: New 510(k).
   Note that if this type of change in labeling was also associated with a design change of higher RF output in order to address the risk of significant change in effectiveness, then the analysis under Section B would also apply.

2. **Change:** The manufacturer of an IVD updates their labeling by changing the device from prescription use only to over-the-counter use.
   Relevant questions:
   A1– *Is it a change in the indications for use statement?* Yes. The revised labeling is a change in the indications for use statementof the device. Proceed to A1.1 -A1.5.
   A1.2 – *Is it a change from prescription to over the counter (OTC) use?* Yes. The revised labeling expands the scope of intended users of the device to lay users, which could significantly affect the safety or effectiveness of the device.
   Decision: New 510(k).

3. **Change:** The manufacturer of a device adds a precaution stating that the device must be properly sterilized prior to use for patient safety. The modified labeling does not modify the previously validated cleaning, disinfection, or sterilization instructions.
   Relevant questions:
   A1– *Is it a change in the indications for use statement?* No. This is not a change in the indications for use statement of the device.
   A3 – *Is it a change in warnings or precautions?* Yes. Proceed to A1.1-A1.5.
   A1.5 – *Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks?* No. The added precaution simply emphasizes proper sterilization and does not affect the device's risk profile.
   Decision: Documentation.

4.
   a. **Change:** The manufacturer of an IVD removes a limitation contained in their labeling that informs users that heterophilic human anti-mouse antibodies (HAMA) cause interference in their assay, which can lead to false results that could harm the end-user. The manufacturer removes this limitation without making any changes to the assay itself.
      Relevant questions:
      A1- *Is it a change in the indications for use statement?* No. This is not a change in the indications for use statement of the device.
      A3– *Is it a change in warnings or precautions?* Yes. This change removed the statement from the limitation section of the labeling that HAMA may cross-react with the assay. Proceed to A1.1-A1.5.
      A1.5 – *Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks?* Yes. Removing an identified interference from the labeling could lead to falsely elevated or falsely low analyte concentration, depending on the site of the interference in the immunoassay reaction. The removal of the limitation may result in the user failing to be alerted to a known risk and may impact performance by changing the ability to accurately measure the analyte concentration.
      Decision: New 510(k).

   b. **Change:** The manufacturer of an IVD updates their labeling by adding a new limitation after identifying a newly approved drug as a potential interferent.
      Relevant questions:
      Main flowchart, question 1 – *Change made with intent to significantly improve the safety or effectiveness of the device?* No. The manufacturer is only aware that the newly approved drug may cause interference with their assay and has not received any reports of adverse events. The labeling change is made to add the new limitation.
      A1- *Is it a change in the indications for use statement?* No. This is not a change in the indications for use statement of the device.
      A3– *Is it a change in warnings or precautions?* Yes. The change adds a new limitation to the IVD labeling and the manufacturer has monitored device usage and updated the labeling accordingly. Proceed to A1.1-A1.5.
      A1.5 – *Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks?* No. The labeling change does not significantly affect the device's risk profile because no new risks or significantly modified existing risks are identified in the risk-based assessment.
      Decision: Documentation.

5. **Change:** The warning information in the labeling for an IVD is modified to account for recently revised hazardous material guidelines.
   Relevant questions:
   A1- *Is it a change in the indications for usestatement ?* No. This not a change in the indications for use statement of the device.
   A3 – *Is it a change in warnings or precautions?* Yes. A change is made to a warning about hazardous materials. Proceed to A1.1-A1.5.
   A1.5 – *Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks?* No. So long as the same risks are communicated to the device user, this change would not significantly affect the device's risk profile.
   Decision: Documentation.

6. **Change:** The manufacturer adds a foreign language translation of the directions for use to a device's labeling. The translation does not change the meaning of the instructions.
   Relevant questions:
   A1- *Is it a change in the indications for usestatement ?* No. This is not a change in the indications for use statement of the device.
   A4 – *Could the change affect the directions for use of the device?* Yes. Proceed to A1.1-A1.5.
   A1.5 – *Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks?* No. As long as the translation does not change the meaning of the instructions, this change would not affect the device's risk profile.
   Decision: Documentation.

7. **Change:** The directions for use of a catheter guidewire are modified to provide instructions on how to access different types of vasculature that were not previously addressed in the labeling.
   Relevant questions:
   A1- *Is it a change in the indications for usestatement ?* No. This is not a change in the indications for use statement of the device.
   A4 – *Could the change affect the directions for use of the device?* Yes. Proceed to A1.1 - A1.5.
   A1.4 -- *Does the change describe a new disease, condition, or patient population that the device is intended for use in diagnosing, treating, preventing, curing or mitigating?* No. The guidewire is intended for use in the treatment of similar patient populations with the same diseases, even if the access points differ.
   A1.5 – *Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks?* Yes. The revised instructions suggest that the device can be used in new vasculature, which would be considered an expansion of the device's indications for use. A risk-based assessment identifies that the new vasculature is more tortuous and significantly increases the risk of several device failure modes, which could significantly affect safety and effectiveness.
   Decision: New 510(k).

8.

a. Change: The original directions for use for a surgical laser intended to treat stones in the urinary tract only included instructions on lithotripsy modes. The instructions are modified to provide instructions on ablating soft tissue.

Relevant questions:

A1- *Is it a change in the indications for use statement?* No. This is not a change in the indications for use statement of the device.

A4 – *Could the change affect the directions for use of the device?* Yes. Proceed to A1.1 - A1.5.

A1.4 – *Does the change describe a new disease, condition, or patient population that the device is intended for use in diagnosing, treating, preventing, curing or mitigating?* Yes. The revised instructions would result in the device being intended for use for ablation of soft tissue, which is a new disease or condition that the device is intended for use in treating, preventing, curing or mitigating, as compared to the treatment of stones in the urinary tract.

Decision: New 510(k).

b. Change: The original directions for use for a surgical laser intended to treat stones in the urinary tract only included instructions on lithotripsy modes. The instructions are modified to provide additional instructions on the existing settings for lithotripsy on the cleared device, and does not modify instructions regarding compatible procedures or instruments.

Relevant questions:

A1- *Is it a change in the indications for usestatement ?* No. This is not a change in the indications for use statement of the device.

A4 – *Could the change affect directions for use of the device?* Yes. Proceed to A1.1 - A1.5.

A1.4 – *Does the change describe a new disease, condition, or patient population that the device is intended for use in diagnosing, treating, preventing, curing or mitigating?* No. The condition that the device is intended to treat remains the same.

A1.5 – *Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks?* No. The manufacturer's risk-based assessment concludes that the clarification of already existing settings does not introduce any new device risks, and the risk acceptability for the previously existing risks is not changed.

Decision: Documentation.

9. Change: A manufacturer changes the design of an IVD for diagnosing herpes simplex 1 and 2 to a less strict performance specification that decreases both the sensitivity and specificity of the device to increase production. The manufacturer updates the performance specifications found in the labeling of the device.

Relevant questions:

A1- *Is it a change in the indications for usestatement ?* No. This is not a change in the indications for use statement of the device.

A4 – *Could the change affect the directions for use of the device?* Yes. The change could affect the directions for use by adding new instructions on how to interpret diagnostic data from the device. Proceed to A1.1 -A1.5.

A1.5- *Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks?* Yes. The changes to the device result in significantly increased existing risks. This is due to a mathematically expected increase in false positive

results, which would, in turn, be expected to lead to an increase in harms such as mental anguish, delayed diagnosis for the true cause of any symptoms, and unnecessary treatment (e.g., pregnant women and newborns receiving unnecessary antiviral drugs or an unnecessary caesarean delivery of the fetus). Further, this would also significantly increase risks due to a mathematically expected increase in false negative results, which would, in turn, be expected to lead to an increase in harms such as delayed diagnosis that would in turn delay treatment of the underlying condition and could lead to unintended spread of the disease (e.g., through sexual partners, neonatal transmission during vaginal delivery, and transplanted organs).

Using only Flowchart A and the corresponding text, the decision based solely on the labeling change alone would be "New 510(k)." However, this type of change in labeling is in response to a design change. Accordingly, analyses under both Section A and Section D apply and the manufacturer is directed to D1.
D1 – *Does the change alter the operating principle of the IVD*? No. The change in design is not one that alters the operating principle of the IVD.
D3 – *Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks*? Yes. The manufacturer's risk-based assessment indicates that a change in the design of the IVD could significantly change the performance of the modified device compared to the previously cleared performance claims.
Decision: New 510(k).

10. Change: The manufacturer of an IVD indicated for use with patients who have symptoms and signs of a specified set of closely related diseases updates their labeling to indicate use for patients with signs and symptoms of another closely related disease not within the specified set cleared in its most recent 510(k).
Relevant questions:
A1- *Is it a change in the indications for usestatement* ? Yes. The labeling change is a change in the indications for use statement of the device. Proceed to A1.1 -A1.5.
A1.4 – *Does the change describe or suggest a new disease, condition, or patient population that the device will diagnose, treat, prevent, or mitigate*? Yes. The labeling change describes a new disease that the device is intended for use in diagnosing that was not previously described by the original device.
Decision: New 510(k).

11. Change: The manufacturer changes the material of the immediate container for an IVD reagent such that the shelf-life of the reagent is extended 3 months. As a result of the change in materials to the immediate container for the IVD, the labeling is updated to reflect the extended shelf-life.
Relevant questions:
A1- *Is it a change in the indications for usestatement* ? No. This is not a change in the indications for use statement of the device.
A3 – *Is it a change in warnings or precautions?* No. There is no precaution or warning pertaining to the shelf-life of the IVD.
A4 – *Could the change affect the directions for use?* Yes. The labeling change to update the shelf-life could affect the instructions and directions for using the device. Proceed to A1.1 - A1.5.
A1.5.– *Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks?* No. A risk-based assessment was performed, from

which it was determined that the labeling change does not significantly affect the device's risk profile because no new risks or significantly modified existing risks are identified.

Using only Flowchart A and the corresponding text, the decision based solely on the labeling change alone would be "documentation." However, this type of change in labeling is in response to a change in material of the immediate container of the IVD reagent. Accordingly, analyses under both Section A and Section D apply and the manufacturer is directed to D1.
D1 – *Does the change alter the operating principle of the IVD*? No. The change in design is not one that alters the operating principle of the IVD.
D3 – *Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks*? No. The manufacturer's risk-based assessment indicates that the change to the immediate container of the IVD reagent could not significantly change performance of the IVD from the previously cleared performance claims (for instance, the IVD performance could not be affected by an increase in exposure of the reagent to light) and that the modified IVD presents no new or significantly modified existing risks.
D4 – *Do design verification and/or validation activities produce any unexpected issues of safety or effectiveness?* No. Standard methods and performance criteria that have been established for evaluation of the device are used to verify and validate the modification and results of the verification and validation do not produce any unexpected issues of safety and effectiveness. In assessing the impact of the modified IVD immediate reagent container on the reagent shelf-life, the manufacturer uses the same protocols and criteria described in the original 510(k).
Decision: Documentation.

Design change examples

12. Change: A device is modified to use an internal battery instead of an external AC power source.
Relevant questions:
B2 – *Is it a control mechanism, operating principle, or energy type change?* Yes. This is an energy type change, which typically requires submission of a new 510(k) due to the likelihood of such a change to significantly affect safety or effectiveness.
Decision: New 510(k).

13. Change: The manufacturer changes the packaging for their device, which is provided sterile, from one variant of polyethylene to another due to a material supplier change. An analysis shows the new polyethylene has no impurities that could affect the device's biocompatibility. The manufacturer will use the same package integrity test protocol as the one described in its previously cleared 510(k) to support the change.
Relevant questions:
B4 – *Is there a change in packaging or expiration dating?* Yes.
B4.1 – *Is the same method or protocol, as described in a previously cleared 510(k) used to support the change?* Yes.
Decision: Documentation.

14.

a. Change: A biliary stent manufacturer adds a new larger stent diameter to a family of biliary stents, 2 mm outside of the range of the manufacturer's previously cleared stents. The stent lengths are unchanged.

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.

B5.1 – *Does the change significantly affect the use of the device?* The answer to this question depends on the original diameter of the stent and the extent of change in the diameter.

B5.2 – *Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks?* Yes. The diameter of a biliary stent is critical to the device's safety and effectiveness. A risk-based assessment identifies that the changes to the device result in significantly increased existing risks, such as rupture of the duct and difficulty reaching the deployment area. Therefore, the greater stent diameter significantly affects existing device-related safety risks.

Decision: New 510(k).

b. Change: A biliary stent manufacturer adds a new stent diameter to a family of stents, within the range of the diameters of the manufacturer's previously cleared stents. The stent lengths are unchanged. The previously cleared 510(k) for the stents objectively demonstrated that the smallest and largest stent diameters (the minimum and maximum ends of the diameter size range) were the worst-case scenarios in terms of the safety and effectiveness risks.

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.

B5.1 – *Does the change significantly affect the use of the device?* No. Because the new diameter is within the range of the previously cleared stents, the manufacturer determines that the change does 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. Since the new stent diameter is within the range of the manufacturer's previously cleared stents of the same lengths, and the previously cleared 510(k) objectively demonstrated that the smallest and largest diameter sizes represented worst-case scenarios in terms of the safety and effectiveness risks for this stent length, the new diameter would not significantly affect the risk profile of the device.

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.

c. Change: A biliary stent manufacturer adds a family of stents made of a different material to their existing line of stents, within the range of the length and diameter combinations of the manufacturer's previously cleared stents. Through the use of Flowchart C and its

companion text, the manufacturer determined that there are no biocompatibility concerns that would require submission of a new 510(k), but the performance of the stents could be affected.

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.

B5.1 – *Does the change significantly affect the use of the device?* No. Because the new stent is within the size range of the previously cleared stents and is deployed using the same method, the manufacturer determines that the change does 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?* Yes. Certain performance characteristics of a biliary stent are critical to the device's safety and effectiveness. A risk-based assessment identifies that the changes to the device material have resulted in significantly increased existing risks, such as stent migration or stent fracture. Therefore, the new stent material could significantly affect safety and effectiveness.

Decision: New 510(k).

15. Change: In order to better accommodate connection of a urinary drainage (Foley) catheter to a collection apparatus, the length of the catheter is increased by several millimeters. The new length is outside of previously cleared lengths for this device.

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.

B5.1 – *Does the change significantly affect the use of the device?* No. The device's increased length would not suggest use of the device for purposes, locations, or populations other than those for which it was cleared, so the manufacturer determines that the change does 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?* Extreme length changes may affect the risk profile of a urinary drainage catheter (e.g., for biocompatibility), but in general, length changes for this device are unlikely to create new risks or significantly affect existing risks by affecting the acceptability of those risks. Device specifics will be important in this example, however, in this example the change does not significantly affect the device's risk profile.

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

16.

a. Change: The manufacturer of a urinary drainage (Foley) catheter reduces the diameter of the catheter to supplement a family of catheters. The new diameter is within the range of previously cleared diameters for this device, and the previously cleared 510(k) objectively demonstrated the smallest and largest diameters to be worst-case scenarios in terms of the

safety and effectiveness risks. The new diameter is within the range of sizes used for smaller adult patients for increased 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.
B5.1 – *Does the change significantly affect the use of the device?* No. This new catheter size would be expected to be used in the same patient population as the previously cleared devices.
B5.2 – *Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks?* No. Since the modified device is within the currently cleared range of dimensions and the smallest and largest previously cleared sizes were demonstrated to be worst-case scenarios in terms of the safety and effectiveness risks, this change would not significantly affect the risk profile of the device.
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.

b. Change: The manufacturer of a urinary drainage (Foley) catheter reduces the diameter of the catheter. The new diameter is outside of the range of previously cleared diameters for this device. The new diameter is also smaller than what is typically used or has been shown to be functionally appropriate for adult patients, and is of a size that is typically used and shown to be functional for pediatric patients. The device is not cleared for pediatric use.
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.
B5.1 – *Does the change significantly affect the use of the device?* Yes. Even if the indications for use and labeling are not changed, this new diameter significantly affects the use of the device by rendering the device non-functional in an adult and changing it from adult use to pediatric use. This could significantly affect the safety and effectiveness of the device.
Decision: New 510(k).

17. Change: The manufacturer of a biliary stent increases the thickness of the nitinol wire in the stent from that used in the previously cleared device to reduce potential for stent fractures.
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.
B5.1 – *Does the change significantly affect the use of the device?* No. The thickness of the nitinol wire of the device would not significantly affect its use.
B5.2 – *Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks?* Yes. The thickness of the wire is critical to the

performance of the stent, so an increase could significantly affect the risk profile and the safety or effectiveness of the device.
Decision: New 510(k).

18. **Change:** The manufacturer adds a foot switch to control an endoscopic electrosurgical unit. The previously cleared device did not have a foot switch.
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. The addition of a foot switch 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?* Yes. The risk analysis identified human factors and compatibility risks for the footswitch that did not exist for the previously cleared device. At least some of these risks were associated with the potential for unintentional activation of energy, which could result in a serious harm.
Decision: New 510(k).

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

20. **Change:** A particular device heats fluid in order to achieve its intended effect. The most recently cleared device had a low-power heater and the maximum fluid temperature was low enough that the severity of the worst-case thermal injury was low to moderate. In the risk analysis for the design of the most recently cleared device, the risk score/rating for thermal injury was therefore in a range identified in the risk management document as "tolerable but undesirable," before risk control measures were added. After receiving input from customers that the fluid heating process was too slow, the device was changed to use a higher-powered heater, which increased the maximum possible fluid temperature.
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.
B5.1 – *Does the change significantly affect the use of the device?* No. This change 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?* Yes. When the manufacturer performed a risk analysis on the new design, the severity of potential thermal injury increased and the risk of thermal injury became "unacceptable," before application of additional risk control measures. This risk analysis showed that the design change had a potentially significant impact on safety by changing the pre-mitigation acceptability of the risk. Therefore, submission of a new 510(k) is likely required. This same conclusion holds whether or not the manufacturer needed to add new risk control measures to bring the final risk into the acceptable range.
Decision: New 510(k).

21. Change: A portable medical device receives its power through a removable, rechargeable battery. The device manufacturer provides a battery charging station for the battery. The proposed change is to the design of the battery charging station. There is no change in the battery itself, only the means by which it is charged. The device is not life-sustaining or life-supporting.
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.
B5.1 – *Does the change significantly affect the use of the device?* No. This change 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. Because the device can operate without the battery charging station, the battery itself is easily replaced, and the device is not life-sustaining or life-supporting, the severities of risks surrounding the battery charging station are low. Unless any new risks are associated with the change or the likelihood of risks associated with the battery charging station are significantly increased, this change would not significantly affect the device's risk profile.
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.

22. Change: A manufacturer changes the surface of a titanium dental implant from an untreated surface to one that is acid-etched. The surface is in direct contact with the patient's bone. The manufacturer has not previously used the acid-etching process, and a cleaning process is necessary to remove acid from the device surface.
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 design change because the implant's surface properties are changed.

B5.1 – *Does the change significantly affect the use of the device?* No. This change 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?* Yes. Surface changes can significantly affect the safety and effectiveness of an implant by, for example, significantly modifying the likelihood of implant instability. This can be considered a safety risk, and since the interaction between the implant and the *in vivo* environment is critical to the stability of the implant and therefore its effectiveness, this could also be considered a significant impact on the device's effectiveness.
Decision: New 510(k).
Note: This change could also be evaluated as a materials change. See Example 26.

Materials change examples

23.

a. Change: The manufacturer of a catheter changes the material of its catheter from polymer A to polymer B. The manufacturer has not previously used polymer B in any of its devices, but knows of another catheter on the market from a different manufacturer with the same cleared indications for use that uses polymer B.
Relevant questions:
C2 – *Is this a change in material type, material formulation, chemical composition, or the material's processing?* Yes.
C3 – *Will the changed material directly or indirectly contact body tissues or fluids?* Yes.
C4 – *Does a risk assessment identify any new or increased biocompatibility risks?* Yes. Polymer B has a different chemical formulation than polymer A. The risk assessment identifies that the new formulation presents a new biocompatibility risk.
C4.1 – *Has the manufacturer used the same material in a similar legally marketed device?* No, the manufacturer has not used the same material before. Even though there is another catheter from a different manufacturer on the market made of polymer B, the other device may have a different formulation or different manufacturing or finishing processes that could affect the biocompatibility or performance.
Decision: New 510(k).

b. Change: The manufacturer of a catheter changes the material of its catheter from polymer A to polymer B. The manufacturer has used the same polymer B, with the same formulation and processing, in another cleared model of catheter with the same type and duration of contact and the same performance specifications.
Relevant questions:
C2 – *Is this a change in material type, material formulation, chemical composition, or the material's processing?* Yes.
C3 – *Will the changed material directly or indirectly contact body tissues or fluids?* Yes.
C4 – *Does a risk assessment identify any new or increased biocompatibility risks?* Yes. Polymer B has a different chemical formulation than polymer A. The risk assessment identifies that the new formulation presents a new biocompatibility risk.
C4.1 – *Has the manufacturer used the same material in a similar legally marketed device?* Yes. The manufacturer has used the same polymer B, with the same formulation and processing, in another model of catheter with the same type and duration of contact. This addresses the possible biocompatibility concerns identified in the risk assessment covered in C4.

C5 – *Could the change affect the device's performance specifications?* No. The manufacturer has used the same polymer B in another model of catheter with the same performance specifications.
Decision: Documentation.

c. Change: A manufacturer changes the material of its catheter, intended for prolonged blood contact, from polymer A to polymer B. The manufacturer has used the same polymer B in another cleared device; however, this other device was indicated for a use with limited duration and skin contact only.
Relevant questions:
C2 – *Is this a change in material type, material formulation, chemical composition, or the material's processing?* Yes.
C3 – *Will the changed material directly or indirectly contact body tissues or fluids?* Yes.
C4 – *Does a risk assessment identify any new or increased biocompatibility risks?* Yes. Polymer B has a different chemical formulation than polymer A. The risk assessment identifies that the new formulation presents a new biocompatibility risk.
C4.1 – *Has the manufacturer used the same material in a similar legally marketed device?* No. The manufacturer has used the same polymer B, with the same formulation and processing, in another device, however, the other device was subject to a less risky type and duration of contact. The modified device will be subjected to additional biocompatibility risks compared to the other polymer B device, and therefore the use of polymer B in the other device does not address the biocompatibility concerns identified in the risk assessment covered in C4.
Decision: New 510(k).

d. Change: A manufacturer changes the material of a device intended for limited skin contact from polymer A to polymer B. The manufacturer has used the same polymer B in another cleared device that was intended for prolonged blood contact and had the same performance specifications.
Relevant questions:
C2 – *Is this a change in material type, material formulation, chemical composition, or the material's processing?* Yes.
C3 – *Will the changed material directly or indirectly contact body tissues or fluids?* Yes.
C4 – *Does a risk assessment identify any new or increased biocompatibility risks?* Yes. Polymer B has a different chemical formulation than polymer A. The risk assessment identifies that the new formulation presents a new biocompatibility risk.
C4.1 – *Has the manufacturer used the same material in a similar legally marketed device?* Yes. The manufacturer has used the same polymer B, with the same formulation and processing, in another cleared device with a riskier type and duration of contact, and the size and geometry of the new device would not affect curing of the polymer or result in more material in the new device. The riskier use of the material in the other cleared device shows that the polymer B can be expected to be biocompatible in its new application.
C5 – *Could the change affect the device's performance specifications?* No. The manufacturer used the same polymer B in another model of catheter with the same performance specifications.
Decision: Documentation.

24. Change: A manufacturer changes the material of a catheter from material A to material B, which is used in another of the manufacturer's cleared catheters. Material A is molded, and material B, used in the other catheter, is extruded.

Relevant questions:

C2 – *Is this a change in material type, material formulation, chemical composition, or the material's processing?* Yes.

C3 – *Will the changed material directly or indirectly contact body tissues or fluids?* Yes.

C4 – *Does a risk assessment identify any new or increased biocompatibility risks?* Yes. The new material B has a different chemical formulation than the original material A. The risk assessment identifies that the new formulation presents a new biocompatibility risk.

C4.1 – *Has the manufacturer used the same material in a similar legally marketed device?* No. The manufacturer has used the same material in another cleared catheter, but the processing of the material is different, which may affect biocompatibility. The use of material B in the other catheter does not address the biocompatibility concerns identified in the risk assessment covered in C4.

Decision: New 510(k).

25.

a. Change: A manufacturer decides to change the material of a catheter from material A to material B. Material B is used in another of the manufacturer's own cleared catheters with similar type and duration of patient contact. Material A is sterilized by gamma irradiation, and material B is sterilized by ethylene oxide.

Relevant questions:

C2 – *Is this a change in material type, material formulation, chemical composition, or the material's processing?* Yes.

C3 – *Will the changed material directly or indirectly contact body tissues or fluids?* Yes.

C4 – *Does a risk assessment identify any new or increased biocompatibility risks?* Yes. Material B has a different chemical formulation than material A. The risk assessment identifies that the new formulation presents a new biocompatibility risk.

C4.1 – *Has the manufacturer used the same material in a similar legally marketed device?* No. The manufacturer has used material B in another cleared catheter, but the processing of the material is different, which may affect biocompatibility. The use of material B in the other catheter does not address the biocompatibility concerns identified in the risk assessment covered in C4.

Decision: New 510(k).

b. Change: A manufacturer decides to change the material of a catheter from material A to material B. Material B is used in another of the manufacturer's own cleared catheters, which has the same type and duration of patient contact, as well as the same performance specifications. Both materials A and B are molded and are sterilized by ethylene oxide.

Relevant questions:

C2 – *Is this a change in material type, material formulation, chemical composition, or the material's processing?* Yes.

C3 – *Will the changed material directly or indirectly contact body tissues or fluids?* Yes.

C4 – *Does a risk assessment identify any new or increased biocompatibility risks?* Yes. Material B has a different chemical formulation than material A. The risk assessment identifies that the new formulation presents a new biocompatibility risk.

C4.1 – *Has the manufacturer used the same material in a similar legally marketed device?* Yes. The manufacturer has used material B in another cleared catheter, and the processing is the same. In addition, the size and geometry of the new device would not affect curing of the polymer or result in more material in the new device, and there are no differences in how material B is joined to other components of the catheter (e.g., type of adhesive, or conditions of heat welding) that could result in different interactive chemistries.
C5 – *Could the change affect the device's performance specifications?* No. The manufacturer has used the same material B in another model of catheter with the same performance specifications, which is processed in the same manner.
Decision: Documentation.

c. Change: A manufacturer decides to change the material of a catheter from material A to material B. Material B is used in another of the manufacturer's own cleared catheters, which has the same type and duration of patient contact, but different performance specifications. Both materials A and B are molded and are sterilized by ethylene oxide.
Relevant questions:
C2 – *Is this a change in material type, material formulation, chemical composition, or the material's processing?* Yes.
C3 – *Will the changed material directly or indirectly contact body tissues or fluids?* Yes.
C4 – *Does a risk assessment identify any new or increased biocompatibility risks?* Yes. Material B has a different chemical formulation. The risk assessment identifies that the new formulation presents a new biocompatibility risk.
C4.1 – *Has the manufacturer used the same material in a similar legally marketed device?* Yes. The manufacturer has used material B in another cleared catheter, and the processing is the same. In addition, the size and geometry of the new device would not affect curing of the polymer or result in more material in the new device, and there are no differences in how material B is joined to other components of the catheter (e.g., type of adhesive, or conditions of heat welding) that could result in different interactive chemistries.
C5 – *Could the change affect the device's performance specifications?* Yes. The manufacturer used the same material B in another model of catheter; however, the performance specifications were different. The new material could potentially affect the device's performance, so the manufacturer is directed to B5.
B5 – *Is it any other change in design (e.g., dimensions, performance specifications, wireless communication, components or accessories, or the patient/user interface)?* Yes.
B5.1 – *Does the change significantly affect the use of the device?* No. The new material does not significantly affect the use of this device.
B5.2 – *Does a risk assessment of the changed device identify any new risks or significantly modified existing risks?*
If the new material has significantly different physical properties than the material in the previously cleared device, the risk profile of the device could be significantly affected in terms of risk score, risk acceptability, etc., and submission of a new 510(k) may be required. However, for the purposes of this example, the new material is not expected to have significantly different physical properties, so a 510(k) would not be required.
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.

26. Change: The manufacturer of a dental implant changes the surface of a titanium dental implant from an untreated surface to one that is acid-etched. The surface is in direct contact with the patient's bone. The manufacturer has not previously used the acid-etching process, and a cleaning process is necessary to remove acid from the device surface.
Relevant questions:
C2 – *Is this a change in material type, material formulation, chemical composition, or the material's processing?* Yes. The material processing of the device has been changed.
C3 – *Will the changed material directly or indirectly contact body tissues or fluids?* Yes.
C4 – *Does a risk assessment identify any new or increased biocompatibility risks?* Yes. The risk analysis identified that the residue from the acid-etching process is a new chemical on the device and introduces a new biocompatibility risk, which may affect the biocompatibility of the device.
C4.1 – *Has the manufacturer used the same material in a similar legally marketed device?* No. The manufacturer has not previously used the acid-etching process.
Decision: New 510(k).
Note: This change could also be evaluated as a design change. See Example 22.

27. Change: The manufacturer of an implantable device applies a temporary tape to the device for identification of manufacturing steps. The tape has been demonstrated in peer-reviewed literature to not leave adhesive on the surface of the device.
Relevant questions:
C2 – *Is this a change in material type, material formulation, chemical composition, or the material's processing?* Yes. The material processing of the device has been changed.
C3 – *Will the changed material directly or indirectly contact body tissues or fluids?* Yes.
C4 – *Does a risk assessment identify any new or increased biocompatibility risks?* No. A risk assessment was performed and identified that the tape has been previously demonstrated to not leave adhesive on the surface of the device.
C5 – *Could the change affect the device's performance specifications?* No. The tape is temporary for manufacturing purposes, and is removed before clinical use of the device. Since the tape has been demonstrated to not leave adhesive on the surface of the device, it would not be expected to affect the device's performance.
Decision: Documentation.

IVD technology, engineering, performance, and materials change examples

28. Change: The manufacturer of a molecular assay received clearance for a quantitative real-time PCR assay that included extraction kit reagents. The kit is therefore labeled for use with a set of extraction reagents. The manufacturer makes changes to the column substrate for the extraction method.
Relevant questions:
D1– *Does the change alter the operating principle of the IVD?* No. The change in column substrate would not alter the operating principle.

D3 – *Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks?* Yes. The manufacturer's risk-based assessment indicates that changing the column substrate could significantly change the analytical and clinical performance of the modified test compared to the previously cleared version of this device indicating new or significantly modified existing risks.
Decision: New 510(k).

29. **Change:** The manufacturer of a bilirubin test system makes a change to the reagent, modifying from a liquid form to a lyophilized form of the reagent. The formulation and concentration of the reagent remain unchanged.
Relevant questions:
D1 – *Does the change alter the operating principle of the IVD?* No. This change in reagent would not alter the operating principle.
D3 – *Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks?* No. The manufacturer's risk-based assessment indicates that the performance of the modified IVD could not significantly change from the previously cleared performance claims and that the modified IVD presents no new or significantly modified existing risks, since the change in reagent state does not change the concentration or formulation of the reagent.
D4 – *Do design verification and/or validation activities produce any unexpected issues of safety or effectiveness?* No. Standard methods and performance criteria that have been established for evaluation of the device are used to verify and validate the modification and results of the verification and validation do not indicate new issues of safety or effectiveness. In assessing the impact of the new reagent formulation, the manufacturer uses the same protocols and criteria described in the original 510(k).
Decision: Documentation.

30. **Change:** The manufacturer makes a change in the traceability of an IVD calibrator of a test system.
Relevant questions:
D1- *Does the change alter the operating principle of the IVD?* No. A change in the traceability of an IVD calibrator would not alter the operating principle of the test system.
D3 – *Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks?* Yes. The manufacturer's risk-based assessment indicates that a change in the traceable reference standard for the assay calibrators could significantly change the clinical performance of the modified IVD test system from the previously cleared performance claims indicating new or significantly modified existing risks.
Decision: New 510(k).

31. **Change:** A manufacturer makes a change in the buffer solution of an IVD as a result of a change in vendor. The replacement buffer solution is equivalent to the previous buffer solution.
Relevant questions:
D1 – *Does the change alter the operating principle of the IVD?* No. The change in buffer solution would not alter the operating principle of the IVD.
D3 – *Does a risk-based assessment of the changed device identify any new risks or significantly existing modified risks?* No. The manufacturer's risk-based assessment

indicates that the new buffer solution is equivalent to the previous buffer solution and indicates that the performance of the modified IVD could not significantly change from the previously cleared performance claims of the modified IVD and that the modified IVD does not present new or significantly modified existing risks.
D4 – *Do design verification and/or validation activities produce any unexpected issues of safety or effectiveness?* No. Standard methods and performance criteria that have been established for evaluation of the device are used to verify and validate the change and results of the verification and validation studies do not indicate new issues of safety or effectiveness.
Decision: Documentation.

32. **Change:** An IVD manufacturer makes a material change to their reagent and the manufacturer's risk-based assessment indicates that the change in material could result in significantly changing the analytical performance from the previously cleared performance claims due to a potential change in the cut-off.
Relevant Questions:
D1 – *Does the change alter the operating principle of the IVD*? No. The change in material is not one that alters the operating principle of the IVD.
D3 – *Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks*? Yes. The manufacturer's risk-based assessment indicates that a change in the material of the reagent would result in a change in analytical cut-off that could significantly change the performance of the modified test compared to the previously cleared performance claims. In particular, this change in cut-off would be a change that is clinically significant in terms of clinical decision making since patients with samples around the cut-off could now receive a different diagnosis and treatment.
Decision: New 510(k).

Appendix B: Documentation

Whenever a manufacturer changes its device, it must take certain actions to comply with the QS regulation, 21 CFR Part 820, unless a regulatory exemption exists. The QS regulation requires that design changes and production and process changes be documented prior to implementation. 21 CFR 820.30(i) and 820.70(b). If a manufacturer determines that the device change(s) does not require submission of a new 510(k), it should document the decision-making process and the basis for that conclusion. The documentation should be prepared in a way that an FDA investigator or other third party can understand what the change is and the rationale underlying the manufacturer's conclusion that submission of a new 510(k) is not required.

The QS regulation also requires that manufacturers establish and maintain procedures to control all documents that are required by the QS regulation. 21 CFR 820.40. Manufacturers may specify the type and level of documentation needed to evaluate changes that may or may not require submission of a new 510(k), as well as the methods of review and approval of such decisions. Manufacturers may also develop standard operating procedures (SOPs) and other documents that allow for different levels of documentation, depending on the nature of the change that must be evaluated.

FDA notes that only highlighting the flowcharts in this guidance document, or simply answering "yes" or "no" to each question without further details or justification, is not sufficient documentation. The manufacturer should provide an appropriately robust justification of a decision that submission of a new 510(k) is not required.

Documentation should include the following:

- Product name
- Date of change assessment
- Description of the device
- Description of the change(s)
- Reason why the change(s) is being made
- Applicable regulatory history, including the 510(k) number of the most recently cleared version of the device
- Comparison of the modified device to the most recently cleared version of the device (consider including a table)
- Applicable elements of this guidance, including the applicable questions from the body of the document
- Analysis and assessment of the elements on this list and a conclusion of whether submission of a new 510(k) is required
- Reference to related documents, particularly those that support the decision whether or not submission of a new 510(k) is required (e.g., risk analysis)
- Signature(s)

It may be helpful to document the assessment of each change in a way that corresponds to the decision-making framework discussed in this guidance document. If a manufacturer decides to do so, the documentation should list each relevant question, the answer to each of those

questions, and the information and analysis that support the answer. The justification may be in the form of a detailed response, a relevant attachment, or other robust method that provides the rationale. Risk analyses will be particularly helpful in supporting the manufacturer's assessment. As a reminder, when making the decision on whether to submit a new 510(k), the manufacturer's basis for comparison of any changed device should be the original device, i.e., the device described in their most recently cleared 510(k) for the device, their legally marketed preamendments device, or their device that was granted marketing authorization via the De Novo classification process.

Changes to a medical device or its processes vary in complexity. Some types of changes are straightforward and will generally result in a decision that submission of a new 510(k) is not required. To that end, a manufacturer may establish a documentation process that accommodates different levels of documentation depending on the complexity of the change. Simple changes would have simple documentation and may not necessarily go through each question in detail; more complex changes should have more detailed documentation. Examples of types of changes that can typically be documented with simple documentation include:

- Change of company labels to update to new company name, e.g., following acquisitions or address changes
- Labeling layout changes where content is not changed, for instance, due to a corporate rebranding initiative
- Addition of a unique device identifier (UDI) to labeling
- Raw material supplier changes that only modify the reference number or brand name of raw materials and do not change the raw material itself

It is important that the manufacturer include, as part of the documentation process, a means to re-evaluate the change should initial assumptions subsequently not be met. In those situations, an update to the existing assessment, or a new assessment, should be documented.

The examples below are provided to illustrate one possible approach to documentation; other approaches may also be appropriate. Manufacturers are encouraged to use an approach that works for their specific purposes, taking into account the considerations discussed above. The first example below is a simple change that does not necessitate detailed analysis. The second example is a more complex change for which additional analysis and reference to supporting documentation are warranted. Note that these are generalized examples to demonstrate documentation principles and do not necessarily account for every possible detail, risk, or consideration.

Regulatory Change Assessment
(Example 1)

Product Name: Device ABC

Date of Assessment: 10/25/16

Device Description: ABC is intended to treat headaches. Device consists of plates and screws. See design specifications at Document 15-XXXX.

Description of Change(s): ABC was recently acquired from Corporation X. Labeling will be updated to be consistent with our standard labeling. Specifically, the company logo, name, contact information, and labeling layout will be updated.

Reason for Change(s): To make ABC's labeling consistent with our standard labeling.

Applicable Regulatory History (including 510(k) #s and comparison of modified device to most recently cleared version):
Device originally cleared in K10xxxx, cleared with updated plates in K12xxxx, cleared with updated screws in K14xxxx. Only changes between K14xxxx version and modified device are company logo, name, contact information, and labeling layout.

Completed Checklist Attached:

☐Yes

☒No (include rationale if selected)

The changes proposed are to the labeling, but do not change the content of the labeling aside from company name and contact information, which does not change the indications for use statement, is not a change to the contraindications or warnings, and could not affect the directions for use. Therefore the labeling change could not significantly affect safety or effectiveness. FDA's Deciding When to Submit a 510(k) for a Change to an Existing Device guidance states at A4 that "Many labeling changes result from attempts to clarify labeling. Manufacturers should consider whether the change is intended to or could affect how the device is used in practice." Because this change does not change the indications for usestatement , is not a change to the contraindications or warnings, and could not affect how the device is used, submission of a new 510(k) is not required.

Recommended Regulatory Action:

☐Submit 510(k)

☒Letter to file

Supporting Documents:

Design Specifications: 15-XXXX
Risk-Based Assessment: N/A

Signatures: xxxx

Regulatory Change Assessment (Example 2)

Product Name: Cardiopulmonary Bypass (CPB) Cannula

Date of Assessment: 1/17/20

Device Description: Cardiopulmonary Bypass Cannula is intended to cannulate the vessels, perfuse the coronary arteries, and interconnect the catheters and cannulas with an oxygenator. The current design uses a 304 stainless steel guidewire with a coating composed of material X; the tips of the guidewire are partially uncoated. See design specifications at Document 18-XXXX.

Description of Change(s): The change is to remove the coating from the guidewire. Previously, the tips were uncoated, but now the entire guidewire will be uncoated. This change applies to models 1 and 2. These models were originally cleared in K10xxxx. The uncoated guidewire will continue to be made of 304 stainless steel. The replacement and current guidewires are identical in design, performance, and materials, with the exception of the coating.

The current guidewire was chosen originally because it was from our current guidewire supplier (which supplies guidewires for other cannulas we manufacture), met the dimensional specifications, and was cost-effective. The coating on the original cannula was not a specific design feature that was required for the design, although it may contribute to longevity of the guidewire and enhances lubricity.

The proposed change will remove the coating, which will expose the stainless steel along the entire length of the guidewire. This change does not introduce any new blood-contacting materials as the current guidewire tip is uncoated, and was tested for biocompatibility in the most recently cleared 510(k). We previously marketed a cannula with an uncoated 304 stainless steel guidewire, cleared in K08xxxx (see DHF XXXX).

Removing the coating from the guidewire will also result in a small change to the diameter of the guidewire due to the lack of the coating.

We have confirmed that the Type 304 material used for the uncoated guidewire is from the same supplier as we have used previously (see Communication 11/7/19-XXXX from supplier), and there have been no issues with rusting (which could introduce embolic particles during device use). In addition, we have confirmed that there are no manufacturing residuals on the surface of the Type 304 stainless steel guidewire that would be available to the patient now that the guidewire is no longer coated (see Memo 19-XXXX).

Reason for Change(s): The coated guidewire has been discontinued by the supplier.

Applicable Regulatory History (including 510(k) #s and comparison of modified device to most recently cleared version):
CPB Cannula was originally cleared in K10xxxx. The labeling layout was changed in 2012 (see Regulatory Change Assessment 12-XXXX). The differences between the K10xxxx version and

the modified device therefore include an updated labeling layout and the removal of the guidewire coating.

Completed Checklist Attached:

☒Yes

☐No (include rationale if selected)

Recommended Regulatory Action:

☐Submit 510(k)

☒Letter to file

Supporting Documents:

Design Specifications: 18-XXXX
Risk-Based Assessment: 20-XXXX
Verification and Validation Summary: 20-YYYY

Signatures: xxxx

Main Flowchart Questions

Change made with intent to significantly improve the safety or effectiveness of the device?

☐Yes

☒No The change was made because the supplier discontinued the coating.

Labeling change?

☐Yes

☒No Labeling changes section N/A

Technology, engineering, or performance change?

☒Yes Coating will be removed which will change the design of the device and slightly decrease the diameter of the guidewire. This change will be evaluated to determine if this could affect the performance of the device.

☐No

Materials change?

☒Yes Removing the coating material from the device. This change will be evaluated to determine if processing could affect the biocompatibility of the device.

☐No

Labeling Questions

A1 – Is it a change in the indications for use statement?
☐Yes Go to A1.1
☐No Go to A2

A1.1 -- Is it a change from a device labeled for single use only to a device labeled as reusable?
☐Yes Submit 510(k)
☐No Go to A1.2

A1.2 -- Is it a change from prescription (Rx) to over the counter (OTC) use?
☐Yes Submit 510(k)
☐No Go to A1.3

A1.3 -- Is it a change to the device name or a change solely to improve readability or clarity?
☐Yes Document to file
☐No Go to A1.4

A1.4 -- Does the change describe a new disease, condition, or patient population that the device is intended for use in diagnosing, treating, preventing, curing or mitigating?
☐Yes Submit 510(k)
☐No Go to A1.5

A1.5 – Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks?
☐Yes Submit 510(k)
☐No Document to file

A2 – Does the change add or delete a contraindication?
☐Yes Submit 510(k) (If adding a contraindication, submit CBE 510(k))
☐No Go to A3

A3 – Is it a change in warnings or precautions?
☐Yes Go to A1.1
☐No Go to A4

A4 – Could the change affect the directions for use of the device?
☐Yes Go to A1.1
☐No Document to file

Technology, Engineering, and Performance Changes

B1 – Is the device an in vitro *diagnostic device?*
☐Yes Go to D1 (Technology, Engineering, Performance and Materials Changes for IVDs)
☒No Go to B2

B2 – Is it a control mechanism, operating principle, or energy type change?
☐Yes Submit 510(k)
☒No Go to B3

B3 – Is it a change in sterilization, cleaning, or disinfection?
☐Yes Go to B3.1
☒No Go to B4

B3.1 – Is it a change to an "established category B" or "novel" sterilization method, does the change lower the sterility assurance level, or is it a change to how the device is provided?
☐Yes Submit 510(k)
☐No Go to B3.2

B3.2 – Could the change significantly affect the performance or biocompatibility of the device?
☐Yes Submit 510(k)
☐No Document to file

B4 – Is there a change in packaging or expiration dating?
☐Yes Go to B4.1
☒No Go to B5

B4.1 – Is the same method or protocol, as described in a previously cleared 510(k), used to support the change?
☐Yes Document to file
☐No Submit 510(k)

B5 – Is it any other change in design (e.g., dimensions, performance specifications, wireless communication, components or accessories, or the patient/user interface)?
☒Yes Go to B5.1
There are two changes, one to the coating of the guidewire, one to the dimensions of the guidewire. Each will be considered below.

☐No Document to file

B5.1 – Does the change significantly affect the use of the device?
☐Yes Submit 510(k)
☒No Go to B5.2
The lack of the coating and the small dimensional change are not expected to 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?

☐Yes Submit 510(k)

☒No Go to B5.3

See full risk-based assessment in Document 20-XXXX.

Dimensional change: it is unlikely that the small reduction in guidewire diameter could affect safety or effectiveness. Decreasing the diameter of the guidewire would not be expected to hinder the interaction between the guidewire, introducer, and cannula, and it would not be expected to reduce the strength of the guidewire, as the coating did not improve the strength of the wire and the wire itself remains unchanged.

Removal of the coating: it is unlikely, but possible, that the removal of the coating could impact the way the guidewire interacts with the introducer and cannula. We have previously obtained clearance for cannulas with uncoated stainless steel guidewires, however, which did not have markedly different performance (see DHF XXXX). This suggests that the significance of this change is low.

We have determined there are no new or significantly modified risks due to this change.

B5.3 – Are clinical data necessary to evaluate safety or effectiveness for purposes of design validation?

☐Yes Submit 510(k)

☒No Go to B5.4

B5.4 – Do design verification and/or validation activities produce any unexpected issues of safety or effectiveness?

☐Yes Submit 510(k)

☒No Document to file

See verification and validation testing report in Document 20-YYYY, conducted after the risk-based assessment. Functional testing evaluated the interaction between the guidewire, introducer, and cannula to verify that the uncoated guidewire did not affect device performance. There were no unexpected issues of safety or effectiveness.

Materials Changes

C1 – Is the device an in vitro *diagnostic product (IVD)?*
☐Yes Go to D1 (Technology, Engineering, Performance and Materials Changes for IVDs)
☒No Go to C2

C2 – Is this a change in material type, material formulation, chemical composition, or the material's processing?
☒Yes Go to C3
The coating material X will be removed.

☐No Document to file

C3 – Will the changed material directly or indirectly contact body tissues or fluids?
☒Yes Go to C4
☐No Go to C5

C4 – Does a risk assessment identify any new or increased biocompatibility concerns?
☐Yes Go to C4.1
☒No Go to C5
The tips of the current guidewire are uncoated, so there is no new material here to create new biocompatibility concerns. The removal of the coating material is not expected to have a biocompatibility impact as the processing is unlikely to leave residuals that were previously masked by the coating. In addition, we have previously marketed cleared cannulas with uncoated stainless steel guidewires, which passed biocompatibility testing (see DHF XXXX). The source of the stainless steel used to manufacture these guidewires has not changed, and we have had no issues with rusting components, so embolic risk is not a concern.

C4.1 – Has the manufacturer used the same material in a similar legally marketed device?
☐Yes Go to C5
☐No Submit 510(k)

C5 – Could the change affect the device's performance specifications?
☒Yes Go to B5
See design change analysis above.

☐No Document to file

Technology, Engineering, Performance, and Materials Changes for *In Vitro* Diagnostic Devices

D1 – Does the change alter the operating principle of the IVD?
☐Yes Submit 510(k)
☐No Go to D2

D2 – Is the change identified in a device-specific final guidance or classification regulation?
☐Yes Submit 510(k)
☐No Go to D3

D3 – Does a risk-based assessment of the changed device identify any new risks or significantly modified existing risks?
☐Yes Submit 510(k)
☐No Go to D4

D4 – Do design verification and/or validation activities produce any unexpected issues of safety or effectiveness?
☐Yes Submit 510(k)
☐No Document to file

Appendix C: Significant Terminology

The following significant terminology is provided to clarify the meaning of medical device terms as used in this guidance document. Wherever possible, existing definitions or descriptors from the FD&C Act, medical device regulations, or FDA guidance documents have been used. In some cases, where regulatory definitions or descriptors are unavailable, we have relied on dictionary definitions of terms.

510(k) Holder: The person who possesses the 510(k) clearance for a device.

Contraindications: See "precautions, warnings and contraindications" below.

Control Mechanism: The manner by which the actions of a device are directed. An example of a change in control mechanism would be the replacement of an electromechanical control with a microprocessor control.

Dimensional Specifications: The physical size and shape of the device. Such specifications may include the length, width, thickness, or diameter of a device, as well as the location of a part or component of the device.

Directions for Use: The directions or instructions under which the user can use the device safely and for the purposes for which it is intended. Directions for use requirements applicable to prescription and over-the-counter devices appear throughout 21 CFR Part 801, and 21 CFR 809.10 for IVD devices.

Documentation: For the purpose of this guidance, documentation means recording the rationale behind the manufacturer's decision whether to submit a new 510(k) for changes in a device. Consideration of each decision point should be recorded, as well as the final conclusions reached. If testing or other engineering analysis is part of the process, the results of this activity should be recorded or referenced. A copy of this documentation should be maintained for future reference.

Energy Type, Character, or Source: The type of power input to or output from the device. Examples of a change in energy type or character would be a change from AC to battery power (input) or a change from ionizing radiation to ultrasound to measure a property of the body (output).

Environmental Specifications: The (range of) acceptable levels of environmental parameters or operating conditions under which the device will perform safely and effectively. Examples of changes in environmental specifications are expanding the acceptable temperature range in which the device will operate properly or hardening the device to significantly higher levels of electromagnetic interference.

Human Factors of Patient/User Interface: The human factors of the patient or user interface refer to the way in which the device and the patient or user interact. This includes the way in which the device presents alarms to the user, the layout of the control panel, the mode of presentation of information to the user or patient, and the way in which the device physically interacts with the

user and/or patient (e.g., the way in which a CPAP mask attaches to a patient's face, or the way a surgical instrument is designed to fit in a surgeon's hand).

Expiration Date: The date beyond which the product may cease to perform safely or effectively and beyond which the manufacturer states the product should not be used.

Harm: Physical injury or damage to the health of people.[10]

Hazard: Potential source of harm.

Intended Use: For purposes of substantial equivalence, the term "intended use" means the general purpose of the device or its function, and encompasses the indications for use.[11]

Indications for Use: The term indications for use, as defined in 21 CFR 814.20(b)(3)(i), describes the disease or condition the device will diagnose, treat, prevent, cure or mitigate, including a description of the patient population for which the device is intended.[12]

In Vitro Diagnostic Device: Those reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body.[13]

Label: The term "label" means a display of written, printed, or graphic matter upon the immediate container of any article.[14]

Labeling: The term "labeling" means all labels and other written, printed, or graphic matter (1) upon any article or its containers or wrappers, or (2) accompanying such article.[15] This can include, among other things, any user or maintenance manuals and, in some instances, promotional literature.

Manufacturer: For the purposes of this document, the term manufacturer includes any 510(k) holder, even if that person does not actually fabricate the existing device. The term also includes a person who manufactures a preamendments device of a type subject to premarket notification (510(k)), and a person who manufactures a device that was granted marketing authorization via the De Novo classification process.

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[10] Definition based on ISO 14971.
[11] See FDA's guidance *The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications (510(k))* https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/UCM284443.pdf See also 21 CFR 801.4.
[12] See FDA's guidance *The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications (510(k))* https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/UCM284443.pdf
[13] 21 CFR 809.3(a).
[14] Section 201(k) of the FD&C Act.
[15] Section 201(m) of the FD&C Act.

Material Formulation: The base formulation of a polymer, alloy, etc., plus any additives, colors, etc., used to establish a property or the stability of the material. This does not include processing aids, mold release agents, residual contaminants, or other manufacturing aids that are not intended to be a part of the material, but that could be present as impurities on the final device. An example of a change in material formulation would be a change from a series 300 stainless steel to a series 400 stainless steel. Another example of a change in material formulation would be the addition or subtraction of a chemical or compound to or from a polymer.

Material Supplier: The firm supplying the raw material to a finished device manufacturer.

Material Type: The generic name of the material from which the device is manufactured. An example of a material type change would be the change from natural latex rubber to synthetic rubber.

Method of Sterilization: The physical or chemical mechanism used to achieve sterility or to achieve a specific sterility assurance level (SAL).

Operating Principle: The mode of operation or mechanism of action through which a device fulfills (or achieves) its intended use. An example of a change in operating principle would be using a new algorithm to compress images in a picture archiving and communications system. For an IVD, an example would be a change from immunofluorescence to ELISA.

Packaging: Any wrapping, containers, etc., used to protect, to preserve the sterility of, or to group medical devices.

Performance Specifications: The performance characteristics of a device as listed in device labeling or in finished product release specifications. Some examples of performance specifications are measurement accuracy, output accuracy, energy output level, and stability criteria.

Preamendments Device: A device commercially distributed in the United States prior to May 28, 1976 that has not been significantly changed or modified since then, and for which premarket approval has not been required under section 515(b) of the FD&C Act.

Precautions, Warnings, and Contraindications:

- Precautions describe any special care to be exercised by a practitioner or patient for the safe and effective use of a device. This definition also includes limitations stated for IVDs.
- Warnings describe serious adverse reactions and potential safety hazards that can occur in the proper use or misuse of a device, along with consequent limitations in use and mitigating steps to take if they occur.

- Contraindications describe situations in which the device should not be used because the risk of use clearly outweighs any reasonably foreseeable benefits.[16]

Reprocessing: Validated processes used to render a medical device, which has been previously used or contaminated, fit for a subsequent single use. These processes are designed to remove soil and contaminants by cleaning and to inactivate microorganisms by disinfection or sterilization.[17]

Reusable Medical Device: A device intended for repeated use either on the same or different patients, with appropriate cleaning and other reprocessing between uses.

Reuse: Use of a device more than once on a single patient or on more than one patient. Actions necessary for reuse of a device may include instructions for assembly/disassembly, on-site sterilization or disinfection, etc. This definition does not include the refurbishing or repair of a device for redistribution or resale.

Risk: The combination of the probability of occurrence of harm and the severity of that harm. For the purposes of this guidance, may relate to either safety or effectiveness (e.g., risk of decreasing device effectiveness).

Shelf-life: The term or period during which a device remains suitable for its intended use. This period ends at the device's expiration date.

Single-use Device (SUD): A device that is intended for one use or on a single patient during a single procedure.

Software: The set of electronic instructions used to control the actions or output of a medical device, to provide input to or output from a medical device, or to provide the actions of a medical device. This definition includes software that is embedded within or permanently a component of a medical device, software that is an accessory to another medical device, or software that is intended to be used for one or more medical purposes that performs these purposes without being part of a hardware medical device.

Sterility Assurance Level (SAL): The probability of a single viable microorganism occurring on an item after sterilization.

Sterilization: A validated process used to render product free from viable microorganisms. NOTE: In a sterilization process, the nature of microbial inactivation is described as exponential and, thus, the survival of a microorganism on an individual item can be expressed in terms of

[16] ODE Bluebook Memorandum G91-1, Device Labeling Guidance (https://www.fda.gov/RegulatoryInformation/Guidances/ucm081368.htm).
[17] See FDA's guidance Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling (https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm253010.pdf) .

probability. While this probability can be reduced to a very low number, it can never be reduced to zero.[18]

User Interface: A device user interface includes all points of interaction between the product and the user, including elements such as displays, controls, packaging, product labels, and directions for use.

Warnings: See "precautions, warnings, and contraindications" above.

[18] See FDA's guidance Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling (https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm253010.pdf) .