Draft Guidance for Industry and Food and Drug Administration Staff

The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.
Document issued on: December 27, 2011

You should submit comments and suggestions regarding this draft document within 120 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to http://www.regulations.gov. Identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions for the Center for Devices and Radiological Health regarding this document contact the Premarket Notification (510(k)) Section at 301-796-5640.

For questions for the Center for Biologics Evaluation and Research regarding this document, contact the Office of Communication, Outreach and Development at 1-800-335-4709 or 301-827-1800.

When final, this document will supersede, Guidance on the CDRH Premarket Notification Review Program, 510(k) Memorandum K86-3, dated June 30, 1986 and The New 510(k) Paradigm - Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications, dated March 20, 1998.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Center for Biologics Evaluation and Research

Preface

Additional Copies

Additional copies are available from the Internet at. You may also send an e-mail request to dsmica@fda.hhs.gov to receive an electronic copy of the guidance or send a fax request to 301-827-8149 to receive a hard copy. Please use the document number (1766) to identify the guidance you are requesting.

OR

Office of Communication, Training and Manufacturers Assistance, HFM-40
Center for Biologics Evaluation and Research
Food and Drug Administration
1401 Rockville Pike, Suite 200N
Rockville, MD 20852-1448
E-mail: ocod@fda.hhs.gov
Phone: 800-835-4709 or 301-827-1800
Internet:
http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/default.htm

Table of Contents

Draft Guidance for Industry and Food and Drug Administration Staff

The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. Introduction

FDA developed this draft document to provide guidance to industry and FDA staff about current review practices for premarket notification (510(k)) submissions. The intent of this guidance is to identify, explain, and clarify each of the critical decision points in the decision-making process FDA uses to determine substantial equivalence. This draft guidance is not intended to implement significant policy changes to the current 510(k) review process. Rather, the intent of this guidance is to enhance the predictability, consistency, and transparency of the 510(k) program by describing in greater detail the regulatory framework, policies, and practices underlying FDA's 510(k) review. This guidance also updates FDA's policies with respect to the Special 510(k) program.

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 guidances means that something is suggested or recommended, but not required.

II. Background

A. The Medical Device Amendments and Device Classification

The Medical Device Amendments (MDA) (Pub. L. 94-295) to the Federal Food, Drug, and Cosmetic (FD&C) Act were enacted on May 28, 1976. The MDA directed FDA to issue regulations that classify all devices that were in commercial distribution at that time into one of three regulatory

control categories: Class I, II, or III, depending upon the degree of regulation necessary to provide reasonable assurance of their safety and effectiveness. The class into which a device is placed determines the requirements that a medical device manufacturer must meet prior to distributing a device in interstate commerce. According to section 513(a)(1) of the FD&C Act (21 U.S.C. § 360c(a)(1)), the three device classes are defined as follows:

- **Class I**: Devices are subject to a comprehensive set of regulatory authorities called general controls that are applicable to all classes of devices.[1]

- **Class II**: Devices for which general controls, by themselves, are insufficient to provide reasonable assurance of the safety and effectiveness of the device, and for which there is sufficient information to establish special controls to provide such assurance.[2]

- **Class III**: Devices for which general controls, by themselves, are insufficient and for which there is insufficient information to establish special controls to provide reasonable assurance of the safety and effectiveness of the device. Class III devices typically require premarket approval.[3]

Premarket notification is the process by which a new device[4], i.e., a post-Amendments device, is classified into one of these three device classes. A manufacturer who intends to market in the United States a Class I, II, or III device intended for human use, for which a Premarket Approval application (PMA) is not required, must submit to FDA a premarket notification submission (often referred to as a 510(k)), unless the device is exempt from the 510(k) requirements of the FD&C Act and does not exceed the limitations of exemptions for each of the device classification regulations (Section .9 of 21 CFR Parts 862 through 892, e.g., 21 CFR 862.9, 21 CFR 864.9, etc.). Under section 510(k) of the FD&C Act, a manufacturer must submit a 510(k) to FDA at least 90 days before introducing, or delivering for introduction, a device into interstate commerce for commercial distribution so the Agency can determine whether or not the device meets the criteria for market clearance (sections 510(k) and (n) of the FD&C Act (21 U.S.C. §§ 360(k) & (n))). The Agency bases its decision on

[1] General controls apply to all classes of medical devices and provide FDA with the means of regulating devices to assure their safety and effectiveness. General controls include but are not limited to provisions that relate to establishment registration and device listing; premarket notification, although most class I devices are exempt by regulation from this requirement; prohibitions against adulteration and misbranding; records and reports; and good manufacturing practices. Section 513(a)(1)(A) of the FD&C Act (21 U.S.C. § 360c(a)(1)(A)).

[2] The original definition of a class II device in the Medical Device Amendments of 1976 (Pub. L. 94-295) identified performance standards rather than special controls as the mechanism by which FDA could establish reasonable assurance of safety and effectiveness. The Safe Medical Devices Act of 1990 (Pub. L. 101-629) added "special controls," which can include the promulgation of performance standards as well as postmarket surveillance, patient registries, development and dissemination of guidance documents (including guidance for the submission of clinical data in premarket notification submissions), and other appropriate actions as FDA deems necessary to provide such assurance. Section 513(a)(1)(B) of the FD&C Act (21 U.S.C. § 360c(a)(1)(B)).

[3] Certain types of devices classified into class III that were in commercial distribution in the United States before May 28, 1976, and those determined to be substantially equivalent to such devices, may be cleared through the 510(k) process until FDA publishes regulations requiring them to go through the PMA process or reclassifies them into a lower class. Section 515(b)(1) of the FD&C Act (21 U.S.C. § 360e(b)(1)).

[4] For the purpose of this guidance document, a "new device" means a device within the meaning of section 201(h) of the FD&C Act that is not legally marketed. It can be either a completely new device or a modification of a legally marketed device that would require a new 510(k).

whether the device is substantially equivalent (SE) to a legally marketed predicate device (section 513(i) of the FD&C Act (21 U.S.C. § 360c(i))).

B. The 510(k) Classification Process

According to section 513(f) of the FD&C Act, a new (i.e., post-Amendments) device is automatically in Class III and must undergo premarket approval or reclassification before it can be marketed, unless it is a type of device that was in commercial distribution prior to May 28, 1976, and is substantially equivalent (SE) to another such device; or, it is within a type of device introduced after May 28, 1976, that has been reclassified into Class I or II and is SE to another device within such classification.

When FDA determines under section 510(k) of the FD&C Act that a new device is SE to a legally marketed (predicate) device, the new device is classified into the same class and subject to the same requirements as the predicate device. (See **Section IV.C.**) A determination that a new device is not substantially equivalent (NSE) to a predicate device results in the new device being classified into Class III. Thus, 510(k) review is both the mechanism by which a manufacturer seeks marketing authorization for a new device and by which FDA classifies devices into their appropriate regulatory category. Because devices are classified according to the level of regulatory control necessary to provide a reasonable assurance of safety and effectiveness,[5] classification of a new device through the 510(k) process requires FDA to determine the issues of safety and effectiveness presented by the new device, and the regulatory controls necessary to address those issues.[6]

---

[5] The three device classes are described in section 513(a) of the FD&C Act (21 U.S.C. § 360c(a)):

> (1) There are established the following classes of devices intended for human use:
> (A) CLASS I, GENERAL CONTROLS.—
> (i) A device for which the controls . . . are sufficient to provide reasonable assurance of the safety and effectiveness of the device.
> (ii) A device for which insufficient information exists to determine that the controls referred to in clause (i) are sufficient to provide reasonable assurance of the safety and effectiveness of the device or to establish special controls to provide such assurance, but because it—
> (I) is not purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, and
> (II) does not present a potential unreasonable risk of illness or injury,
> is to be regulated by the controls referred to in clause (i).
> (B) CLASS II, SPECIAL CONTROLS.—A device which cannot be classified as a class I device because the general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness of the device, and for which there is sufficient information to establish special controls to provide such assurance . . .
> (C) CLASS III, PREMARKET APPROVAL.—A device which because—
> (i) it (I) cannot be classified as a class I device because insufficient information exists to determine that the application of general controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device, and (II) cannot be classified as a class II device because insufficient information exists to determine that the special controls described in subparagraph (B) would provide reasonable assurance of its safety and effectiveness, and
> (ii)(I) is purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, or
> (II) presents a potential unreasonable risk of illness or injury,
> is to be subject, in accordance with section 515, to Premarket approval to provide reasonable assurance of its safety and effectiveness.

[6] If FDA has established special controls applicable to the device, the 510(k) would need to adequately address the issues covered by the special controls for the device to be classified into Class II. *See* Section 513(a)(1)(B) of the FD&C Act (21 U.S.C. § 360c(a)(1)(B)).

C. Evolution of the 510(k) Program

Since its inception, the 510(k) program has undergone a number of statutory changes. Notably, the Safe Medical Devices Act of 1990 (Pub. L. 101-629) added section 513(i), which codified FDA review practice in applying the "substantial equivalence" review standard. In addition, FDA has modified its implementation of the program to adapt to changing circumstances and to accommodate the evolving medical device landscape. For example, the alternative options of a Special 510(k) or an Abbreviated 510(k) initially proposed in guidance[7] still exist today. The current 510(k) program reflects the current statutory framework and FDA's implementation of that framework through regulation, guidance, and administrative practice. A history of the 510(k) program has been summarized in other documents that FDA has published.[8]

This guidance document provides updated information to two existing guidance documents entitled "Guidance on the CDRH Premarket Notification Review Program, 510(k) Memorandum K86-3" (K86-3 Guidance), issued on June 30, 1986 and "The New 510(k) Paradigm - Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications" (1998 Guidance) issued on March 20, 1998. The K86-3 Guidance was written and issued as final guidance prior to the February 27, 1997 implementation of FDA's Good Guidance Practices (GGPs). Neither guidance document has been updated since its initial publication date. Upon its issuance as a final guidance document, this guidance will replace those documents.

III. Scope

This guidance provides recommendations to industry and FDA staff about the content of 510(k) submissions and the decision-making process for determining substantial equivalence of devices reviewed under the 510(k) program. The guidance has been organized to coincide with the critical decision points outlined in the proposed 510(k) Decision-Making Flowchart (See **Appendix A**), which has been updated to track section 513(i) of the FD&C Act and relevant regulations more closely. This document provides guidance on the following issues:

- the appropriate use of multiple predicates (See Section IV.C);
- the processes associated with determining whether a new device with new indications for use has a new intended use (See Section IV.D);
- the process for determining whether different technological characteristics raise different questions of safety and effectiveness (See Section IV.E);

[7] *See* The New 510(k) Paradigm – Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications (March 20, 1998). Available at http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080189.pdf.

[8] *See* CDRH Preliminary Internal Evaluations – Volume I: 510(k) Working Group Preliminary Report and Recommendations. Available at http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDRH/CDRHReports/UCM220784.pdf. *See also* CDRH Preliminary Internal Evaluations – Volume II: Task Force on the Utilization of Science in Regulatory Decision Making Preliminary Report and Recommendations. Available at http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDRH/CDRHReports/UCM220783.pdf. *See also* 510(k) and Science Report Recommendations: Summary and Overview of Comments and Next Steps. Available at http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDRH/CDRHReports/UCM239449.pdf

- when performance data, with special emphasis on clinical performance data, may be necessary to support an SE determination (See Section IV.F); and
- how to develop 510(k) Summaries to promote greater transparency in the 510(k) decision-making process (See Section IV.G).

In addition, this guidance addresses two alternative approaches to the Traditional 510(k) submission process: the Special 510(k) and the Abbreviated 510(k) programs. This revision to the 1998 Guidance is intended to update industry and FDA staff on the Agency's current thinking, including recommendations intended to clarify and strengthen the factors to consider when deciding whether to submit a Special 510(k), and to clarify when the use of an Abbreviated 510(k) submission may be appropriate. FDA may convert either a Special 510(k) or an Abbreviated 510(k) into a Traditional 510(k) if it finds that the submission does not meet the factors for review under the relevant program, for example, the Special 510(k) submission contains modifications that may affect the intended use or alter the fundamental scientific technology of the device (see **Section V**).

The overarching principles in this guidance are applicable to devices that are subject to 510(k) review by CDRH, including the Office of Device Evaluation (ODE) and the Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD), as well as devices that are subject to 510(k) review by the Center for Biologics Evaluation and Research (CBER). This guidance is not intended to supplant existing device-specific guidance, but may cover broader areas not addressed in device-specific guidance documents. If you have questions about how this guidance and a device-specific guidance apply to a particular issue, please contact FDA to discuss. In addition, this guidance does not address review issues unique to combination products.

IV. The 510(k) Decision-Making Process

A 510(k) is a premarket submission made to FDA to demonstrate that the new device to be marketed is "substantially equivalent" to a device that is legally marketed in the United States (21 U.S.C. §§ 360(n), 360c(f)(1) & 360c(i); 21 CFR 807.92(a)(3)) and which is not subject to PMA. Manufacturers must compare their new device to one or more similar legally marketed devices to support its substantial equivalence.

The most commonly used method of demonstrating substantial equivalence is through the submission and FDA review and clearance of a Traditional 510(k). Under 21 CFR 807.87, FDA established basic content requirements for 510(k)s to be submitted by device manufacturers in support of substantial equivalence.[9]

[9] Although these basic content requirements apply to all 510(k)s, the type of data and information necessary to establish substantial equivalence varies by the type of device and the differences between the new device and the predicate device. FDA has issued many device-specific guidance documents that clarify data requirements for 510(k)s for particular device types. If a manufacturer is unsure of what information to include within a 510(k) submission, the manufacturer may contact FDA and submit a pre-IDE submission to seek additional feedback to ensure submissions contain appropriate data elements.

The Agency has provided a general framework on how to format an original submission for a Traditional 510(k) within guidance. *See* Format for Traditional and Abbreviated 510(k)s. Available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm084365.htm. The definitions of a Traditional, Special, and Abbreviated 510(k) are provided in this guidance.

A new device does not need to be identical to the predicate device for it to be found substantially equivalent to the predicate device. In FDA's experience, it is rare for a new device to be identical to a predicate device. Given the diversity of technologies evaluated under this review standard, this guidance adopts a flexible approach to determining "substantial equivalence" to accommodate evolving technology while maintaining predictability and consistency to promote confidence among device developers, practitioners, and patients.

A. The 510(k) Review Standard

1. The Statutory Standard

The 510(k) review standard (substantial equivalence of a new device to a legally marketed (predicate) device) differs from the PMA review standard (reasonable assurance of safety and effectiveness) in that the 510(k) review standard is comparative whereas the PMA standard relies on an independent demonstration of safety and effectiveness. Nonetheless, the principles of safety and effectiveness underlie the substantial equivalence determination in every 510(k) review. The standard for a determination of substantial equivalence in a 510(k) review is set out in section 513(i) of the FD&C Act, which provides:

> Substantial Equivalence
>
> (i)(1)(A) For purposes of determinations of substantial equivalence under subsection (f) and section 520(l), the term "substantially equivalent" or "substantial equivalence" means, with respect to a device being compared to a predicate device, that the device has the same intended use as the predicate device and that the Secretary by order has found that the device
>
> (i) has the same technological characteristics as the predicate device, or
>
> (ii)(I) has different technological characteristics and the information submitted that the device is substantially equivalent to the predicate device contains information, including appropriate clinical or scientific data if deemed necessary by the Secretary or a person accredited under section 523, that demonstrates that the device is as safe and effective as a legally marketed device, and (II) does not raise different questions of safety and effectiveness than the predicate device.
>
> (B) For purposes of subparagraph (A), the term "different technological characteristics" means, with respect to a device being compared to a predicate device, that there is a

---

To streamline the review process, sponsors are referred to that guidance regarding the elements that should be included within a Traditional 510(k) submission. This draft guidance also provides further discussion regarding Special and Abbreviated 510(k) submissions in **Sections V.A. and V.B.**

Please note that the use of the Standards Data Report for 510(k)s, Form 3654 (see **Appendix G**), recognized consensus standards, and device-specific guidance documents is not limited to Abbreviated 510(k) submissions. Appropriate reliance on these documents can facilitate the review of all 510(k) submissions and can help to make the review process more consistent. Medical device manufacturers should consider citing standards and device-specific guidance documents wherever appropriate, regardless of the type of 510(k) submission.

> significant change in the materials, design, energy source, or other features of the device from those of the predicate device.

Safety and effectiveness factor into both parts of this review standard. First, FDA must find that the intended use of the device and its predicate are "the same." As discussed in the Intended Use Section of this guidance, differences in the indications for use, such as the population for which a device is intended or the disease a device is intended to treat do not necessarily result in a new intended use. Such differences result in a new intended use when they affect (or may affect) the safety and/or effectiveness of the new device as compared to the predicate device and the differences cannot be adequately evaluated under the comparative standard of substantial equivalence. (See **Section IV.D.**)

Second, when comparing a new device to a predicate device, FDA must find that the two devices have "the same technological characteristics," or that any differences in technological characteristics do not raise different questions of safety and effectiveness and that the device is as safe and effective as a legally marketed device. "Different technological characteristics" is defined in section 513(i)(1)(B) of the FD&C Act as "a significant change in the materials, design, energy source, or other features of the device from those of the predicate device."

Although the 510(k) process involves a comparison of a new device to a predicate device rather than an independent demonstration of the new device's safety and effectiveness, as is required for approval of a PMA, in both cases FDA's review decision reflects a determination of the level of control necessary to provide a "reasonable assurance of safety and effectiveness."[10] The evidentiary standard, however, is different. In the 510(k) context, FDA generally relies, in part, on FDA's prior determination that a reasonable assurance of safety and effectiveness exists for the predicate device. Demonstrating basic similarities between a new device and a predicate device typically requires manufacturers to provide descriptive information such as a comparison of specifications, materials, and technology. In contrast, FDA generally evaluates differences between the new device and the predicate device to determine their effect on safety and effectiveness. It follows that the evidence necessary to show substantial equivalence will increase as differences between the new device and the predicate device increase, if those differences affect, or may affect, safety or effectiveness.

2. The Least Burdensome Principle

The FDA Modernization Act of 1997 (FDAMA) added two provisions commonly known as "the least burdensome provisions" to the FD&C Act. The provision relating to substantial equivalence, section 513(i)(1)(D), provides:

> Whenever the Secretary requests information to demonstrate that devices with differing technological characteristics are substantially equivalent, the Secretary shall only request information that is necessary to making substantial equivalence determinations. In making

[10] Under section 513(a)(2) of the FD&C Act, the safety and effectiveness of a device are to be determined:

> (A) with respect to the persons for whose use the device is represented or intended,
> (B) with respect to the conditions of use prescribed, recommended, or suggested in the labeling of the device, and
> (C) weighing any probable benefit to health from the use of the device against any probable risk of injury or illness from such use.

> such requests, the Secretary shall consider the least burdensome means of demonstrating substantial equivalence and request information accordingly.

Although the statutory provision refers only to information requests related to determining the substantial equivalence of technological characteristics of a device and its predicate, the underlying principle that information requests should relate to the review standard is a basic principle of good regulatory practice with broad applicability to the 510(k) decision-making process.

FDA has issued guidance[11] explaining how it intends to apply the least burdensome provisions ("the Least Burdensome Guidance"). The Least Burdensome Guidance interprets least burdensome as "a successful means of addressing a premarket issue that involves the most appropriate investment of time, effort, and resources on the part of industry and FDA," and specifies that the least burdensome provisions do not affect the statutory premarket review standards for devices. The recommendations discussed in this guidance for demonstrating substantial equivalence are consistent with the principles discussed in the Least Burdensome Guidance, but applies them by discussing the considerations that may affect the type of information necessary to demonstrate substantial equivalence at different decision points in review of a 510(k).

3. Categories of NSE Determinations

Generally, NSE determinations fall into two categories: (1) those that reflect FDA's affirmative determination that the device is a Class III device and cannot be reviewed in a 510(k) submission, and (2) those that reflect inadequacies in the evidence that preclude a finding of substantial equivalence.

The first category of NSE determinations includes a variety of different decisions, such as a finding of a lack of a predicate device, a new intended use, or different technological characteristics that raise different questions of safety or effectiveness when the new device is compared to the cited predicate device that as a matter of law result in an NSE determination. When FDA issues an NSE letter for a reason in this first category, the letter will typically not identify performance-based deficiencies. Consequently, the device is automatically classified into Class III and will require PMA approval or, if eligible, granting of a *De Novo* petition[12] before marketing. If FDA believes that the device found NSE may be eligible for the *De Novo* petition program, the NSE letter will typically indicate FDA's recommendation.

---

[11] *See* Final Guidance for FDA and Industry "The Least Burdensome Provisions of the FDA Modernization Act of 1997: Concept and Principles," issued on October 4, 2002. Available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm085994.htm.
See also Final Guidance for Industry and FDA Staff "Suggested Format for Developing and Responding to Deficiencies in Accordance with the Least Burdensome Provisions of FDAMA," issued on November 2, 2000. Available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073679.htm

[12] *See* Guidance for Industry and CDRH Staff "New Section 513(f)(2) - Evaluation of Automatic Class III Designation, Guidance for Industry and CDRH Staff," issued on February 19, 1998. Available at http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080197.pdf.
See also "Draft Guidance: De Novo Classification Process (Evaluation of Automatic Class III Designation)" issued on October 3, 2011. Once final, this guidance will represent the Agency's current thinking on this topic.

The second category of NSE determinations is for those devices for which FDA has not affirmed that the new device has a different intended use or that the different technological characteristics raise different questions of safety or effectiveness when compared to the cited predicate device, but rather that the information provided in the submission is insufficient to demonstrate substantial equivalence to the predicate device. In this situation, FDA generally first identifies the specific additional information – typically related to performance testing – that needs to be provided so that FDA may complete its evaluation of substantial equivalence. Upon receipt of FDA's request for additional information (either through a formal letter, email, phone call or fax), the manufacturer has the opportunity to respond to FDA's request. If the manufacturer does not provide the requested information or an adequate justification, or if the responses are insufficient, FDA will find the new device NSE. FDA will work with the manufacturer to try to resolve identified deficiencies but expects manufacturers to work with FDA staff in good faith and in a timely manner. If the manufacturer does not respond at all to FDA's request for additional information, the submission will be subsequently withdrawn by FDA within the timeframe specified by regulation and guidance.[13] In either case, the manufacturer may submit a new 510(k) with additional information that addresses the outstanding deficiencies communicated by FDA based on review of the prior 510(k). If a new 510(k) is submitted to address deficiencies raised in this type of NSE letter, FDA recommends that the new 510(k) clearly identify how the outstanding issues have been addressed and clearly identify whether the information submitted in the new 510(k) was previously submitted in the prior 510(k) that FDA reviewed or constitutes new information. Citation of the prior 510(k) number is strongly recommended.

B. The Flowchart

The 510(k) Substantial Equivalence Decision-Making Process Flowchart (referred to as the Flowchart) was originally presented in the K86-3 Guidance and has served as the overarching "framework" for 510(k) decision-making for decades. This Flowchart has provided a concise summary of the 510(k) decision-making process and serves as a common frame of reference for scientific and regulatory discussions related to the 510(k) process. However, this Flowchart has not been updated since 1986 and, consequently, does not incorporate certain terminology set out in subsequent amendments to the FD&C Act. Furthermore, the Flowchart's visual structure may be more complex than necessary. To specifically address these issues, FDA has proposed a modified Flowchart in this guidance that more closely tracks section 513(i) of the FD&C Act and relevant regulations and visually simplifies the decision-making algorithm.

[13] *See* 21 CFR 807.87(l). We typically inform manufacturers that if the information, or a request for an extension of time, is not received within 30 days, we will consider the 510(k) to be withdrawn and the submission will be deleted from our system. If the manufacturer provides the requested information after 30 days, it will be considered and processed as a new 510(k) (21 CFR 807.87(l)); therefore, all information previously submitted would have to be resubmitted so that the new 510(k) is complete. Further guidance on 510(k) actions is available in our guidance document entitled, "FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Performance Assessment" at http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM089738.pdf. If the manufacturer does submit a written request for an extension, FDA will permit the 510(k) to remain on hold for up to a maximum of 180 days from the date of the additional information request. However, FDA may grant additional time if the agency has made a decision to ask for new information for that type of device, such as because of a newly identified serious risk, and has not previously informed manufacturers.

It should be noted that the Proposed 510(k) Decision-Making Flowchart (see **Appendix A**) is meant to be used in conjunction with this guidance document and not as a "stand-alone" document without appropriate references to the context of each critical decision point.

C. Predicate Device(s)

As discussed in Section IV.A, the 510(k) review standard is substantial equivalence of a new device to a device legally marketed in the U.S. A legally marketed device, as described in 21 CFR 807.92(a)(3), is a device that (i) was legally marketed prior to May 28, 1976 (preamendments device[14]), for which a PMA is not required; ***or*** (ii) has been reclassified from Class III to Class II or I; ***or*** (iii) has been found SE through the 510(k) process. The legally marketed device for purposes of determining substantial equivalence is commonly referred to as the "predicate device."

Section 513(i) of the FD&C Act states that for a new device to be considered substantially equivalent to a predicate device, the new device must have the same intended use as the (primary) predicate device **and** the same technological characteristics or different technological characteristics that do not raise different questions of safety and effectiveness than the (primary) predicate device. Thus, as a general matter, to find a device substantially equivalent, FDA must be able to address Decision Points 1 through 4 in the Flowchart using one (primary) predicate device identified by the manufacturer. FDA may use one or more additional devices proposed by the manufacturer in certain instances to help support substantial equivalence, as described below.

1. Multiple Predicates

In certain circumstances, a manufacturer may use multiple predicate devices[15] to help demonstrate substantial equivalence. If the manufacturer intends to use multiple predicates to address Decision Points 2-4 on the Flowchart, each predicate device must have the same intended use as the new device, and any difference in technological characteristics from the predicate devices must not raise different questions of safety and effectiveness. This concept is illustrated in Multiple Predicates Scenarios 1 and 2. We recommend that you read these Scenarios side-by-side with the Flowchart in Appendix A so that you can follow the decision-making process.

Multiple Predicates Scenario 1: In this scenario, the manufacturer references multiple predicate devices to answer "yes" at Decision Point 2 in the Flowchart and establish that the intended use of the new device is the same as the predicate devices.[16] In this scenario, a new device commonly claims to

[14] *See* Preamendment Status. Available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/ComplianceActivities/ucm072746.htm

[15] *See* 510(k) and Science Report Recommendations: Summary and Overview of Comments and Next Steps. Available at http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDRH/CDRHReports/UCM239449.pdf. The use of a "split predicate," which refers to a situation in which a manufacturer is attempting to "split" the 510(k) decision making process by demonstrating that a new device has the same "intended use" as one marketed device while comparing the new device's "technological characteristics" with a second marketed device that has a different intended use is inconsistent with the 510(k) regulatory standard.

[16] It is important to note that if multiple predicates are used to support same intended use, any difference in technological characteristics between the new device and the cited predicate devices must not raise different questions of safety and effectiveness. Section 513(i) of the FD&C Act (21 U.S.C. § 360c(i)).

treat or diagnose multiple diseases or symptoms that all fall within the same overall intended use as the predicate devices.

Illustrative Example: A manufacturer submits a 510(k) for a plate indicated for fixation of both diaphyseal (the shaft of a long bone) and epiphyseal (the ends of a long bone) fractures, i.e., the plate can be used to set a long bone, such as the femur or thigh bone, that is broken in the middle or at the ends. The manufacturer cites a predicate device that is a plate indicated for middle bone fractures only and another predicate device that is indicated specifically for bone tip fractures only in order to support a "yes" answer at Decision Point 2 in the Flowchart. While the indications for use of each predicate device are different, both devices have the *same* intended use, namely, fracture fixation.[17] Thus, although the manufacturer could have used a single predicate device to achieve a "yes" answer at Decision Point 2 of the Flowchart, in cases where a manufacturer intends to market a device for more than one indication and a different predicate exists to support each specific indication, the manufacturer may cite more than one relevant predicate device to support an SE determination. In this case, using two appropriate predicates clearly identified by the manufacturer helped to facilitate clearance of the new device, which was indicated to treat both types of fractures treated by the predicates.

Multiple Predicates Scenario 2: In this scenario, multiple predicate devices are used to support substantial equivalence of a new device when the technologies and uses of different predicate devices are combined together into one device. This approach is generally applicable to well-understood technologies and permits FDA to reach an SE determination for a new device that combines the intended uses and the technological characteristics of more than one legally marketed predicate device.

In this case, FDA will determine whether the new device creates a new intended use or raises different questions of safety and effectiveness as a result of combining the different technologies. If the answer to either is "yes," the new device would be found NSE. For example, if a device combination introduces an added risk to a patient (when compared to each individual predicate device), or creates new or unstudied device capabilities, it may present a different question of safety and effectiveness and be found NSE.

Illustrative Example: A manufacturer submits a 510(k) for a urinary catheter that also measures temperature. The manufacturer cites one predicate device that is a urinary catheter that does not measure temperature and another predicate device that is a thermometer, which measures temperature. The new device combines both the intended use and technological characteristics of the urinary catheter with the intended use and technological characteristics of the thermometer. No new intended uses or different questions of safety and effectiveness are created by such a device combination, and with appropriate performance data the new device can be found SE.

2. Reference Devices

[17] *See* Guidance for Industry: General/Specific Intended Use. Available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073944.htm. In the scenario above, going from the general to specific indication may necessitate new performance testing, but it doesn't change the overall intended use of the device. These types of situations will need to be assessed on a case-by-case basis and in some scenarios, a general to specific indication may actually alter the overall intended use of the device technology in which case the multiple predicate concept may not be applicable.

In certain circumstances, where appropriate, a manufacturer may refer to legally marketed devices that have a different intended use or different technological characteristics that raise different questions of safety and effectiveness, to address specific scientific questions for a new device. If a manufacturer successfully navigates through Decision Point 4 on the Flowchart using a primary predicate device, other legally marketed devices, which FDA calls "reference devices," may be used to address certain performance characteristics of the new device. If a manufacturer intends to use a reference device, the manufacturer should provide a scientific rationale that justifies its use. A reference device is not considered to be a predicate device. This concept is illustrated in the Reference Device Scenario below. We recommend that you read this Scenario side-by-side with the Flowchart in Appendix A so that you can follow the decision-making process.

Reference Device Scenario: In this scenario, the scientific methods used to evaluate a legally marketed device with an intended use that differs from that of the new device are used to support the evaluation of certain characteristics of the new device. This scenario is very complicated; accordingly, FDA will need to rely on its scientific and regulatory expertise to determine when this scenario may be applied. Nevertheless, FDA believes that, in select cases, it is appropriate to use reference devices to support an SE determination.

Illustrative Example: A manufacturer submits a 510(k) for a total knee implant with coating X (the new device). Other coated knee implants with the same intended use with coatings A, B, and C are legally marketed. In addition, a total hip implant with coating X is legally marketed. The manufacturer cites the legally marketed knee implant with coating A as the predicate device. FDA determines that the new device has an appropriate predicate device (thus, answering "yes" at Decision Point 1) and the new device has the same intended use as the predicate device (thus, answering "yes" at Decision Point 2 in the Flowchart).[18] However, FDA determines that the new device does not have the same technological characteristics as the predicate device (thus, answering "no" at Decision Point 3 in the Flowchart), because the new device (knee implant with coating X) has a chemical profile different from the chemical profile of the cited predicate device (knee implant with coating A). There are no other technological differences between the new device and the cited predicate device (knee implant with coating A). FDA determines that the new device does not raise different questions of safety and effectiveness. In this case, FDA determines that the safety and effectiveness questions regarding the coating material are whether it is biocompatible and whether it impacts the fixation of the implant and these questions apply to both the new device and predicate device (thus, answering "no" at Decision Point 4 in the Flowchart).

After Decision Point 4 in the Flowchart, if appropriate, the manufacturer may refer to the reference device (the hip implant with coating X in this situation) to support the appropriate scientific methods for the characterization of coating X on the new knee implant device. In this particular example, the manufacturer provided an adequate scientific rationale to support that the methods used to characterize the biocompatibility and characteristics of the coating (e.g.,

[18] The answer at Decision Point 2 may possibly be "no" if the predicate device is uncoated. Introducing a coated arthroplasty device into an anatomical location which previously only had non-coated devices would likely create a new intended use due to the different fixation methods.

strength, abrasion, etc.) on the hip implant are applicable to the knee implant.[19] The reference device (hip implant with coating X) is used in this case solely to assist with the characterization of the coating on the new device (knee implant with coating X).

3. Identification and Documentation of the Predicate(s)

Although manufacturers may cite more than one predicate device in a 510(k), FDA recommends that the manufacturer identify the primary predicate device to which a substantial equivalence claim is being made.[20] Further, as part of the decision-making process, FDA should clearly cite the predicate device relied upon in determining substantial equivalence for the new device in its review documentation. If multiple predicates or reference devices are used in accordance with this guidance, the manufacturer should identify each device and explain why more than one predicate or a reference device is necessary and appropriate to support substantial equivalence. Manufacturers should choose the most appropriate predicate for their new device. This information also should be accurately cited in the 510(k) Summary (see **Appendix B**).

D. Intended Use

Under section 513(i) of the FD&C Act, FDA may only determine that a device is substantially equivalent to a predicate device if it has the same intended use.[21] (Refer to the 510(k) Decision-Making Flowchart in **Appendix A**). A finding of a new intended use for a device found NSE is relatively rare. Approximately 10% of all NSE decisions are due to a new intended use.[22] This type of NSE determination generally reflects a finding that a change in the *indications for use* of a device creates a new *intended use*. This section of the guidance provides further clarification about the terms "intended use" and "indications for use," describes how FDA determines what the intended use of a device is, and provides examples of changes in indications for use that may constitute a new intended use making the device ineligible for review under the 510(k) program.

1. Explanation of Intended Use and Indications for Use

[19] The applicability of the scientific methodology used to characterize certain aspects of a legally marketed device will depend upon the specific scenario. In this example, it is determined that the duration of contact, which impacts the biocompatibility testing, and the mechanical testing conducted to fully characterize the coating on the hip implant are directly relevant and informative for the same coating applied to the knee implant. However, if the manufacturer wanted to rely on the scientific methodology for a coating used in a different type of implant (e.g., cardiovascular), it may not be appropriate to exercise this approach.

[20] Although devices recently cleared under the 510(k) program are often selected as the predicate device to which substantial equivalence is claimed, any legally marketed Class II or Class I device may be used as a predicate device. However, section 513(i)(2) of the FD&C Act provides that a predicate device may not have been removed from the market at the initiative of the Commissioner of Food and Drugs or been determined to be misbranded or adulterated by a judicial order. *See also* 21 CFR 807.100.

[21] This guidance is not intended to supplant either of the following guidance documents: Determination of Intended Use for 510(k) Devices; Guidance for CDRH Staff (Update to K98-1). Available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm082162.htm
Or Guidance for Industry: General/Specific Intended Use. Available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073944.htm

[22] Refer to "Initial Results of 510(k) Audit: Analysis of Not Substantially Equivalent (NSE) Determinations." Available at http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHReports/ucm259173.htm

For purposes of substantial equivalence, the term **intended use** means the general purpose of the device – or what the device does – and encompasses the indications for use. The term **indications for use** 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.[23] The intended use of a device is one criterion that determines whether a device can be cleared for marketing through the 510(k) process or must be evaluated in a PMA application or, if appropriate, a *De Novo* petition. The indications for use statement in a 510(k) is one factor used to determine a device's intended use.

A finding of substantial equivalence means that the indications for use of the new device fall within the intended use of the predicate device and, therefore, the two devices have the same intended use. For devices with general indications for use that do not specify a disease, condition, or population (or an anatomical site from which a disease state or population may be inferred), the indications for use and intended use are the same. Such indications for use are referred to as "tool type" indications for use. Examples of devices with "tool type" indications for use include devices such as scalpels, which are often indicated for cutting tissue, or imaging devices, which are often indicated for taking images of the body. A scalpel indicated for removing a particular type of cancerous cell, however, has indications for use specific to the identified disease, condition, or population and therefore are not "tool type" indications for use.

2. Determining Intended Use

Section 513(i)(1)(E)(i) provides that the FDA's determination of intended use of a device "shall be based on the proposed labeling" submitted in a 510(k). When a review of the indications for use and all other information in the proposed labeling submitted with a 510(k) supports an intended use that is the same as that of the predicate device, FDA will determine that the new device and predicate device have the same intended use.[24]

When a review of the labeling submitted with a 510(k) shows that the indications for use of a new device and predicate device differ, FDA must evaluate whether the new[25] indications for use fall within the same intended use as that of the predicate device. As described in Section IV.A, because the substantial equivalence determination is grounded in safety and effectiveness, this determination depends upon the safety and effectiveness of the new device for the new indication relative to the safety and effectiveness of the predicate device.

Once FDA has determined the indications for use of the new device upon review of the proposed labeling, FDA may rely upon information regarding the safety and effectiveness of the new indications for use that does not appear in the proposed labeling submitted with the 510(k). For

[23] The term indications for use is defined in the PMA regulation at 21 CFR 814.20(b)(3)(i). We have a long-standing policy of applying the definition in the same way in the 510(k) context.

[24] This guidance does not address FDA's authority to consider information outside the labeling in reviewing a 510(k) and issue an "SE with limitations" under section 513(i)(1)(E)(i) because of a "reasonable likelihood" of an off-label use that "could cause harm." For guidance on Substantial Equivalence with limitations," please see the guidance document, Determination of Intended Use for 510(k) Devices; Guidance for CDRH Staff (Update to K98-1) at

http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm082162.htm.

[25] For purposes of Section IV.D.2, the term "new" refers to an indication that is new or differs from that of the predicate device.

example, FDA may rely upon publicly-available scientific information or Agency knowledge about how a disease progresses to determine whether indications for use to treat a certain disease or anatomical site constitute a new intended use.

3. Determining When Indications for Use Result in a New Intended Use

Not every change in indications for use that may affect safety or effectiveness will result in a finding of a new intended use. Only a change in the indications for use that raises different questions of safety and effectiveness and precludes a meaningful comparison with the predicate device constitutes a new intended use. FDA may find changes in indications for use of a device to constitute a new intended use when the changes raise a safety or effectiveness issue that was not raised by the predicate device or when the changes have the potential to significantly increase a safety or effectiveness concern raised by the predicate device.[26] In the first case, reliance on a predicate device is inadequate because the safety or effectiveness issue was not considered in reviewing the 510(k) for the predicate device. In the second case, although the safety or effectiveness issue may have been considered in the 510(k) for the predicate device, the finding of substantial equivalence for the predicate device cannot be generalized to the new indications for use because of a probable, significant change in the incidence or severity of the issue. In both cases, the predicate device is not an adequate "proxy" for an independent determination of safety and effectiveness.

> Illustrative Example: A new device's instructions for use describe using a general surgery device in a body cavity, but the predicate device is used only to treat external injuries. A comparison to the predicate device may not be adequate to address the risk of infection posed by internal use of the device. Because of the need for an independent assessment of an issue that was not evaluated or was of significantly less concern during FDA's review of the 510(k) for the predicate device, FDA may determine that the indication for use of the new device does not fall within the intended use of the predicate device and a PMA application or, if appropriate, a *De Novo* petition, is required.

4. Changes in Indications for Use that May Result in a New Intended Use

All new indications for use should be evaluated to determine whether they reflect a new intended use. Certain types of changes, however, warrant particular attention in evaluating whether the new indications for use result in a new intended use because they are likely to affect safety or effectiveness:

- a change from a functional/performance indication to a treatment or aesthetic indication;
- a change from a diagnostic indication to a screening indication, or vice versa;
- a change in the anatomical structure of use;
- a change in the patient population (e.g., adult versus pediatric; different disease populations);
- a change in the clinical context or setting (e.g., periodic monitoring versus continuous monitoring; hospital versus home use).

[26] *See* 21 CFR 807.92(a)(5).

E. Technological Characteristics

After FDA has determined that a valid predicate device exists for a new device and that both devices have the same intended use, FDA will move to Decision Points 3 and 4 of the Flowchart (see Appendix A). In these steps of the 510(k) review process, FDA compares the technological characteristics of the new device and the predicate device to determine whether differences exist, and whether any differences in technology raise different questions of safety and effectiveness. Although devices reviewed under the 510(k) program commonly have technological differences from their predicate devices, FDA rarely makes a finding of NSE at Decision Point 4.[27]

1. Step 1 – Identification of Technological Characteristics of the New and Predicate Device

For FDA to evaluate whether differences exist between the technological characteristics of the new device and the predicate device(s), the manufacturer should clearly identify the technological characteristics of each device individually. Technological characteristics include materials, design, energy source, and other device features.[28]

To facilitate FDA's review of a device's technological characteristics, the device description in a 510(k) [29] should include all information necessary to fully and clearly explain the new device's technological characteristics. This information will be evaluated by FDA to determine whether the technology of the new device is different and, if so, whether it raises different questions of safety and effectiveness as compared to the predicate(s). Examples of key characteristics that should be provided as part of a 510(k) submission include, but are not limited to, the following features:

- An overall description of the device design. A complete description of the device may be facilitated by the submission of engineering drawings or other figures. If the device consists of multiple components, a diagram identifying how the different components of the device system work together may be beneficial. The device description should also include a discussion of the physical specifications, dimensions and mechanical tolerances of the new device.[30] Each aspect of the new device should have a clear purpose within the context of the overall design and intended use. In cases where this is not apparent, it is important for the

[27] Refer to "Initial Results of 510(k) Audit: Analysis of Not Substantially Equivalent (NSE) Determinations." Available at http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHReports/ucm259173.htm

[28] Section 513(i)(1)(B) of the FD&C Act and 21 CFR 807.100(b)(2)(ii)(A).

[29] FDA's regulations require manufacturers to include in their 510(k)s "[a] description of the device that is the subject of the premarket notification submission, such as might be found in the labeling or promotional material for the device, including an explanation of how the device functions, the scientific concepts that form the basis for the device, and the significant physical and performance characteristics of the device, such as device design, material used, and physical properties." 21 CFR 807.92(a)(4).

[30] The original Flowchart from the K86-3 Guidance included a decision point related to whether or not "descriptive characteristics" were precise enough to ensure equivalence. However, the term "descriptive characteristics" does not appear in the statute or regulations. The Proposed 510(k) Decision-Making Flowchart described in **Appendix A** specifically addresses this area to reflect the statute more closely and minimize confusion.

510(k) submission to provide a discussion of how a particular device design or component contributes to the overall use and function of the new device.

- Materials. For many devices, a full identification of the detailed chemical formulation used in the materials of construction, especially for those materials that come into contact with the patient, should be provided.[31] Any additives, including color additives, coatings, or other surface modifications should also be fully identified. For some devices, the processing of the material (e.g., forged vs. cast) or the state of the material (e.g., amorphous vs. crystalline) may also significantly contribute to or affect the overall safety or function of the device, and so should be included as part of the device description.

- Energy sources. This not only includes energy delivery to the device, including the use of batteries, but also energy delivery that is part of the functional aspect of the device (e.g., laser, radiofrequency, ultrasound, etc.) and that affects the patient and/or the health care professional using the device. Where applicable, a discussion of this characteristic should be provided.

- Other technological features. These include, but are not limited to, software/hardware features, density, porosity, degradation characteristics, nature of reagents (recombinant, plasma derived, etc.), principle of the assay method, manufacturing-related aspects, etc., that are not explicitly included as part of the materials, design or energy source characteristics. These technological features should be included as part of the device description in the 510(k) submission.

A 510(k) submission should also contain information about the technological characteristics of the predicate device.[32] In cases where the predicate device and the new device are owned by the same manufacturer, the manufacturer should provide the full documentation of the predicate's technological characteristics to permit a substantive comparison with the new device. In cases where the predicate device and the new device are owned by different manufacturers, or where access to the predicate device's detailed technological characteristics is limited, the manufacturer of the new device should provide information necessary and sufficient to fully and clearly identify and describe the technological characteristics of the predicate device.

2. Step 2 – Identification of Differences in Technological Characteristics Between the New and Predicate Device

Once the technological characteristics of the new and predicate device(s) have been fully identified, the next step involves a comparison of these characteristics to identify any differences. This may involve a line-by-line comparison of detailed specifications as well as a comparison of the system-level technological characteristics of the devices. FDA relies upon information provided about the

[31] Note that the FDA does not clear/approve materials. For additional considerations, refer to the FDA guidance, "Use of International Standard ISO-10993, 'Biological Evaluation of Medical Devices Part 1: Evaluation and Testing' (Replaces #G87-1 #8294) (blue book memo)." Available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080735.htm.

[32] *See* 21 CFR 807.92(a)(3), (6).

predicate device and the new device to determine whether the new device has different technological characteristics (Decision Point 3) in comparison to the predicate(s).

At this point, FDA will assess whether the similarities/differences in technological characteristics between the new and predicate device(s) have been appropriately identified. FDA highly recommends that the manufacturer summarize this information in tabular format to facilitate this step of review.

3. Step 3 – Determination of Whether the Differences in Technological Characteristics Raise Different Questions of Safety and Effectiveness

If FDA determines that there are differences in the technological characteristics of the new device and the predicate device, FDA reviews and evaluates all relevant information bearing on any such differences in technological characteristics to determine whether they raise different questions of safety and effectiveness for the new device as compared to the predicate device (Decision Point 4 on the Flowchart).[33] A "different question of safety or effectiveness" is a question raised by the technological characteristics of the new device that was not applicable in the 510(k) for the predicate device, and poses an important safety or effectiveness concern for the new device.

Some examples are provided below to illustrate cases where the response to this general question was "yes," i.e., the new device was determined to raise different safety and effectiveness questions in comparison to the predicate device, and the new device was found NSE.

Illustrative Example 1
Predicate: A polymer-based implant (i.e., plastic or rubber)
New Device: An implant derived from a recombinantly-produced polymer source (i.e., a material that is made to mimic skin)
Intended Use: Same
Different questions of safety and effectiveness? Yes
Why: In this example, because the devices are made of significantly different materials and processes (i.e., native polymer versus recombinantly-produced synthetic tissue), there are different questions of safety and effectiveness. These include whether the synthetic tissue might chemically interact with the cells of the body and interfere with their natural reparative processes. Because these types of questions were not necessary to take into account for the predicate device, the new device would be found NSE.

Illustrative Example 2
Predicate: A mechanical device used for embryo dissection
New Device: An electrical device used for embryo dissection
Intended Use: Same
Different questions of safety and effectiveness? Yes
Why: In this example, changing the process from a mechanical process to an electrical energy source (e.g., laser) changes the way the device operates and raises different safety concerns regarding how the heating aspect of the electrical mechanism affects the embryo.

[33] Manufacturers should be prepared to provide appropriate performance data to address any differences, even ones that appear to be minimal, that could affect safety and effectiveness to demonstrate that the new device is as safe and effective as the predicate device.

Because these types of questions were not necessary to take into account for the predicate device, the new device would be found NSE.

Illustrative Example 3
Predicate: A surgical ablation clamp that is used in open cardiac surgical procedures. The cardiac surgeon can clearly see the tissue on which energy is being delivered and can directly see the change in the tissue throughout the procedure.
New Device: A percutaneous cardiac ablation catheter that is used during a closed cardiac electrophysiology procedure, i.e., a device that is inserted in a blood vessel and where the catheter tip is placed in the heart. The catheter is used by a cardiac electrophysiologist who relies on indirect visualization methods (e.g., electrocardiography) to see the tissue he/she is ablating and the change in the tissue throughout the procedure.
Intended Use: Same
Different questions of safety and effectiveness? Yes
Why: In this example, the specialist conducting the procedure with the new device is different from the predicate device. Moreover, the specialist using the new device relies on different visualization methods and endpoints, which involve different questions to determine the safety and effectiveness of the device. Because these types of questions were not necessary to take into account for the predicate device, the new device would be found NSE.

In the event the answer to Decision Point 4 is "No" and the differences between the new device and the predicate device do not raise different questions of safety and effectiveness, then the scientific review of the performance data will proceed. However, if the answer to Decision Point 4 is "Yes" and the differences between the new device and predicate device raise different questions of safety and effectiveness, then the new device will be found NSE. Upon receipt of this type of NSE letter, the manufacturer may submit a PMA application or, if appropriate, a *De Novo* petition.

F. Requests for Performance Data

Although FDA may rely upon descriptive information alone to address the critical questions in the Flowchart (Decision Points 1 through 4), performance data are typically needed to demonstrate the substantial equivalence of a new device to a predicate device. In addition, information on device performance described in labeling or other sections of the 510(k) should be supported with appropriate performance data. The type and quantity of performance data necessary to support a determination of substantial equivalence depend upon the device. Performance data may be needed to address a variety of safety and effectiveness issues and may be generated from different types of tests and studies, such as:

- mechanical, electrical, and biological engineering performance, such as fatigue, wear, tensile strength, compression, flowrate, burst pressure;
- biocompatibility;
- electromagnetic compatibility (EMC);
- sterility;
- stability/shelf life data;
- software validation;
- laboratory;

- other forms of non-clinical, including device-specific;
- animal/cadaver[34]; and
- clinical.

FDA's data requests typically follow a stepwise analytical process to ensure the information requested reflects the least burdensome approach to establishing substantial equivalence.[35] First, FDA considers whether descriptive information about the technological characteristics, such as the materials, design, or specifications, of the new device is sufficient. Very few 510(k) submissions rely solely on descriptive information about materials, design, specifications, and other technological characteristics (see 21 CFR 807.87(f) and (g)). When this information is not sufficient to support a substantial equivalence determination, FDA then considers whether non-clinical performance testing data would be sufficient. Non-clinical performance testing includes a wide variety of test modalities that will be dependent upon the specifics of the actual device. Although FDA considers animal data as part of the non-clinical performance testing data, animal data are typically requested when other forms of non-clinical data are not sufficient to demonstrate substantial equivalence.

When non-clinical performance testing data are insufficient, or available scientific methods are not acceptable, e.g., the scientific methods are deemed unacceptable because they are not clinically validated or are not supported by a valid scientific rationale, FDA may request clinical performance data to support a substantial equivalence determination. FDA currently requests clinical data for less than 10 percent of 510(k) submissions. In some instances, clinical data may be a less burdensome means of demonstrating substantial equivalence than other means of performance testing. Clinical data provided in support of any marketing application, including a 510(k) when those data are relevant to a substantial equivalence determination, should fit the definition of valid scientific evidence in 21 CFR 860.7(c)(2)[36] and comply with the Investigational Device Exemptions (IDE) regulations.[37]

---

[34] Nonclinical laboratory studies that support the safety of medical devices must be conducted in compliance with 21 CFR Part 58, Good Laboratory Practice (GLP) for Nonclinical Laboratory Studies, as applicable, to ensure the quality, reliability, and integrity of study data. Any nonclinical laboratory studies submitted as part of a 510(k) should include a statement that all nonclinical laboratory studies were conducted in compliance with 21 CFR Part 58, or if not in compliance, then a statement of the reason for noncompliance should be provided.

[35] FDA follows the "least burdensome" provisions. *See* Final Guidance for FDA and Industry "The Least Burdensome Provisions of the FDA Modernization Act of 1997: Concept and Principles," issued on October 4, 2002. Available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm085994.htm

[36] 21 CFR 860.7(c)(2): Valid scientific evidence is evidence from well-controlled investigations, partially controlled studies, studies and objective trials without matched controls, well-documented case histories conducted by qualified experts, and reports of significant human experience with a marketed device, from which it can fairly and responsibly be concluded by qualified experts that there is reasonable assurance of the safety and effectiveness of a device under its conditions of use. The evidence required may vary according to the characteristics of the device, its conditions of use, the existence and adequacy of warnings and other restrictions, and the extent of experience with its use. Isolated case reports, random experience, reports lacking sufficient details to permit scientific evaluation, and unsubstantiated opinions are not regarded as valid scientific evidence to show safety or effectiveness. Such information may be considered, however, in identifying a device the safety and effectiveness of which is questionable.

[37] In the U.S., clinical studies/investigations (*see* 21 CFR 812.3(h)) involving one or more human subjects to determine the safety or effectiveness of a device must be conducted in accordance with the Investigational Device Exemptions (IDE) regulations, 21 CFR Part 812, as applicable. In addition, such studies/investigations must comply with the regulations governing institutional review boards (21 CFR Part 56) and informed consent (21 CFR Part 50).

In many cases, the clinical data necessary to support a 510(k) involve a relatively small number of patients and may involve a simpler study design than is necessary to support a premarket approval (PMA) application. FDA considers any data involving human subjects to be clinical data.

Although not an exhaustive list of instances in which FDA may request clinical data to demonstrate substantial equivalence, the following scenarios illustrate the most common situations in which clinical data may be requested. As explained in the Scope Section (see **Section III**), the information in this guidance and the examples below do not take the place of any device-specific guidance.

Note: the examples provided below distinguish between examples that are only applicable to diagnostic, including *in vitro* diagnostic (IVD) devices and therapeutic devices. This is because there are significant differences in the clinical data requirements for these two types of devices.

1. New or Modified Indications for Use – Same Intended Use

In rare instances, FDA may rely upon clinical data to determine that new or modified indications for use fall within the same intended use as a predicate device.

Illustrative Examples:

- The new device is an IVD that is indicated for over-the-counter use, whereas the predicate device is indicated for prescription use in the home or prescription use in a clinical setting. Clinical data demonstrating that the user can collect the sample, generate an accurate result, and adequately interpret the result may be necessary to characterize whether the new device has equivalent safety and effectiveness as the predicate device. For some devices, however, this change may result in a new intended use and an NSE determination.
- The new device is an IVD, which presents a new cutoff reflected in the indications for use that needs to be validated with a new clinical dataset.
- The manufacturer modifies the indications for use, explicitly or implicitly, by proposing a different surgical implantation method which also impacts the indications for use, e.g., a minimally invasive procedure in place of an open procedure, and the safety and effectiveness of the new device cannot be adequately replicated or otherwise characterized in a non-clinical performance (including animal) test environment to adequately support substantial equivalence to the predicate. Although on its face a minimally invasive procedure would appear to involve less serious risks than an open procedure, the minimally invasive procedure may be less effective or may present different but still serious risks.

2. Technological Differences

FDA may request clinical data for a 510(k) when the technological differences between the new device and predicate device are significant but do not support an immediate NSE determination due to different questions of safety and effectiveness. In these limited situations, clinical data may be needed to evaluate the safety and effectiveness of the new device as compared to the predicate device.

Illustrative Examples:

- A new device adds a unique technology that makes non-clinical testing insufficient. An example is a new IVD that measures microbial genetic material whereas the predicate device is based on microbial culture technology.
- Performance characteristics of the new device in comparison to the predicate are significantly different in non-clinical performance testing, e.g., the predicate is rigid whereas the new device is designed to be more flexible. Clinical data may be necessary to demonstrate the new device could perform equivalent to the predicate.
- Some devices that display data about the patient's anatomy or physiology, e.g., glucose meters, pulse oximeters, blood pressure cuffs, are supported by software. If there is a change in the software that relates to how the software analyzes the patient's anatomy or physiology, the software may need to be tested on actual patients to assure that it performs in a manner that is equivalent to the previous version. In this case, non-clinical data may not suffice.
- The technological characteristics of the new device do not permit the ability to solely rely on the clinical performance data of the predicate device. In such a case, the new device may need clinical data to demonstrate that its risks have been appropriately mitigated. An example is an IVD whose technological characteristics, such as analytical sensitivity or reproducibility, differ between the new device and predicate device.

3. Non-clinical Testing Methods are Limited or Inappropriate Because of the Indications for Use or Device Technology

FDA requests clinical data for a 510(k) submission to address issues that cannot be adequately addressed using non-clinical test methods because of the indications for use or device technology. For instance, for certain indications or technologies, FDA may request clinical data when non-clinical testing methods are not validated, are limited or are inappropriate, because of either their scope or their applicability, to demonstrate substantial equivalence.

Illustrative Examples:

- For some devices, the way they are used and the environment in which they are used affect the way they perform. For example, the non-clinical performance testing on the new device may be insufficient to support a substantial equivalence determination if the testing cannot replicate the way the device will be used or the way similar devices have been demonstrated to fail in a clinical setting. Although the non-clinical testing for these devices might be informative for many other aspects of the device, it may be necessary to supplement the non-clinical data with clinical performance data.
- If the non-clinical testing of a device raises unanswered safety concerns that cannot be mitigated, such a device may require clinical testing to assure that the safety questions are not greater than those raised by the predicate device.

New scientific information may affect FDA's expectations concerning the type and level of performance data included in a 510(k) submission. FDA may reduce performance testing requirements for device types with long histories of safe use and well understood mechanisms of action. On the other hand, a pattern of adverse events or published literature documenting poor clinical outcomes with a particular technology may lead FDA to reconsider its regulatory approach to premarket submissions for such technology. Should FDA change its scientific decision making with

regard to a particular device, FDA will consider its regulatory options (e.g., Notice to Industry letter, other types of guidance, advisory panel meeting, etc.), explaining such change and the basis for the decision to ensure transparency in the change in policy.

G. The 510(k) Summary

The 510(k) Summary is a document that provides a high-level discussion of the content of a 510(k) and must include all the elements identified in 21 CFR 807.92. A 510(k) Summary must be in sufficient detail to provide an understanding of the basis for a determination of substantial equivalence.

In an effort to improve the transparency and predictability of the 510(k) program and to ensure that the 510(k) Summary reflects the information provided in a 510(k) submission to support a substantial equivalence determination, FDA intends to verify the accuracy and completeness of the information included in a 510(k) Summary.

Although the 510(k) Summary is a document created by the manufacturer and is included in the 510(k), revisions to the 510(k) Summary may be necessary to accurately reflect the FDA's decision-making process. For example, manufacturers have in the past identified several 510(k)s as potential predicate devices, whereas FDA may have used only one of these devices as an appropriate predicate device in its substantial equivalence determination for the new device. In addition, it is possible during the course of FDA's review of the 510(k), that additional information or testing may be requested and submitted. Consequently, the manufacturer may be requested to update the 510(k) Summary to accurately include and convey the information identified in 21 CFR 807.92 and which was used to support the final decision-making process.

In **Appendix B**, FDA describes the requirements of the content to be included in a 510(k) Summary, in accordance with 21 CFR 807.92, and provides guidance on the information to be included in a 510(k) Summary to ensure compliance with 21 CFR 807.92 and consistency in the level of information conveyed and captured in the 510(k) Summaries which are available to the public on FDA's website.

V. Alternative Approaches to the Traditional 510(k) Submission

The two alternative types of 510(k) submissions identified in the guidance entitled "The New 510(k) Paradigm – Alternative Approaches to Demonstrating Substantial Equivalence in Premarket Notifications" issued in March 1998 were intended to streamline the process of submission and review for devices by using aspects of the Quality System (QS) regulation for Special 510(k) submissions, and by using recognized consensus standards and device-specific guidance for Abbreviated 510(k)s. Use of either alternative, however, does not limit FDA's ability to obtain any information authorized by the statute or regulations. Furthermore, a manufacturer's use of either of these alternative 510(k) submissions is optional.

A. Special 510(k) Program

The Special 510(k) Program is intended to facilitate the submission, review, and clearance of a modification to a manufacturer's device that is already cleared for distribution into interstate commerce via a 510(k) submission.[38] A modification to a marketed device may qualify for a Special 510(k) when all three of the following factors are met:

- the requested modification is made to a legally marketed device and submitted by the owner of that device;
- the indications for use[39] and fundamental scientific technology[40] of the proposed device are unchanged from the legally marketed device; and
- the manufacturer is in conformance with the Quality System (QS) regulation.[41]

Special 510(k)s are considered appropriate where, under certain circumstances, compliance with design controls are sufficient to permit a more streamlined submission. For certain modifications, a thorough and effective use of design controls should produce reliable results that can form, in addition to the other 510(k) content requirements specified in 21 CFR 807.87, a basis for a substantial equivalence determination. Under this alternative submission, a manufacturer who intends to modify its own legally marketed device must conduct a risk analysis and complete verification and validation activities that adequately demonstrate the design outputs of the modified device meet the design input requirements (21 CFR 820.30). The manufacturer should ensure the satisfactory completion of this process and determine that the other considerations described further in Parts 1-5 of this section and **Appendix D** have been addressed before submitting a Special 510(k). Under the QS regulation, data generated through the use of design control procedures must be maintained by the manufacturer and be available for FDA inspection (21 CFR 820.30[42] and 820.180). The content of a Special 510(k) submission should reference the cleared 510(k) number and declare conformity with design control requirements.

When a manufacturer considers submitting a Special 510(k), FDA recommends that the manufacturer take into account any relevant guidance documents, special controls, or recognized consensus standards that apply to the device type and that should be addressed by the design control

[38] Manufacturers of preamendments devices (i.e., devices that were in commercial distribution before May 28, 1976) may submit Special 510(k)s if the modifications to such devices qualify for review under the Special 510(k) program. When the legally marketed (unmodified) device is a preamendments device, the manufacturer should clearly state that the device is a preamendments device, is legally marketed, and has not been the subject of premarket notification clearance. (Please refer to the information provided by the Office of Compliance "Preamendment Status" available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/ComplianceActivities/ucm072746.htm for the procedures for demonstrating preamendments status. Manufacturers should maintain this information.)

[39] Please refer to the following for additional guidance, "Deciding When to Submit a 510(k) for a Change to an Existing Device."

[40] The term fundamental scientific technology is used in the same manner as when used to define the limitations of exemptions from section 510(k) of the FD&C Act as found in each of the device classification regulations, 21 CFR Parts 862-892, e.g., 21 CFR 862.9, 864.9, and 866.9.

[41] This also implies that the manufacturer is in "good standing" with the Agency from the perspective of the Office of Compliance.

[42] Design controls are explicitly defined in 21 CFR 820.30 and include the following elements: design and development planning, design input, design output, design review, design verification, design validation, design transfer, design changes, and design history file.

processes.[43] For example, if a manufacturer is modifying a soft contact lens care product, then the manufacturer's design control inputs should include the special controls that FDA has established for that device type.[44] If a manufacturer modifies an *in vitro* diagnostic, the manufacturer's design inputs should include any recognized clinical and laboratory standards, such as those developed by the Clinical and Laboratory Standards Institute (CLSI).

CDRH and CBER generally process Special 510(k) submissions within 30 days of receipt per cycle by the respective Document Control Center (DCC). Modifications that affect the indications for use or alter the fundamental scientific technology of the device are not appropriate for review in a Special 510(k). For these types of changes, reliance on design controls is insufficient to support substantial equivalence and such changes generally raise safety and effectiveness issues that warrant a more intensive evaluation by FDA. FDA's policy since 1998 has been to require a Traditional 510(k) in these circumstances. In the event a manufacturer submits a Special 510(k) that CDRH or CBER does not consider to be eligible for review under the Special 510(k) program, the 510(k) submission will be converted to a Traditional 510(k). The conversion of a submission from a Special 510(k) to a Traditional 510(k) can result in a delay of an efficient review process as significant performance data will typically need to be provided by the manufacturer to ensure an appropriate review under the Traditional 510(k) program. Therefore, it is important for the manufacturer and FDA to ensure that Special 510(k) submissions are appropriate for the Special 510(k) program. Each modification should be evaluated in light of the considerations described below to optimize the chance that a Special 510(k) will be accepted for review.

1. Indications for Use

Special 510(k)s should identify prominently all changes in the proposed labeling that may result from a modification to the manufacturer's legally marketed device. Modifications to the indications for use of the device or any labeling change that affects the indications for use should not be submitted as a Special 510(k).[45] FDA recommends that all modifications in labeling for the new device in comparison to the predicate device be provided in a tabular format to facilitate an efficient FDA review of any changes within the labeling. In keeping with current practices, a Special 510(k) should state clearly that the indications for use of the modified device, as described in its labeling, have not changed as a result of the modification(s).

Finally, a manufacturer may file a Special 510(k) for a combination of indications for use when the modified device relies upon the manufacturer's own legally marketed devices and no new indications for use are added. All of the manufacturer's legally marketed devices should be identified and

---

[43] Note that if FDA has established special controls applicable to the device, the 510(k), whether Traditional, Special, or Abbreviated, would need to adequately address the issues covered by the special controls for the device to be classified into Class II. For information about special controls, standards, and guidance documents, please see the web page maintained by each Center, the CDRH web page, available at http://www.fda.gov/MedicalDevices/default.htm and the CBER web page, available at http://www.fda.gov/BiologicsBloodVaccines/default.htm. *See also* Blue Book Memo K95-1 entitled "510(k) Requirements During Firm-Initiated Recalls." Available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080297.htm.

[44] *See* Guidance for Industry − Premarket Notification (510(k)) Guidance Document for Contact Lens Care Products. Available at http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM080218.pdf

[45] We do not consider reasonable alterations in grammar, punctuation, and word order to be a change that affects the indications for use, as long as the change does not alter the meaning of the indications for use statement.

adequate information should be provided to demonstrate that the combined device/system is substantially equivalent to the sum of the legally marketed devices.

2. Effects on Fundamental Scientific Technology

Special 510(k)s should not be submitted for modifications that potentially alter the fundamental scientific technology of the device. These types of modifications generally include modifications to the device's operating principle(s) or mechanism of action, such as automation of a manual device or incorporation of a sensing or feedback circuit. The examples below illustrate certain types of changes that generally would not be appropriate for a Special 510(k).

- a change in a surgical instrument that uses a sharpened metal blade to one that cuts with a laser;
- a change in an in vitro diagnostic (IVD) device that uses immunoassay technology to one that uses nucleic acid hybridization or amplification technology;
- an incorporation of a sensing mechanism in a device to allow the device to function "on demand" rather than continuously;
- a change in material of the device to one that has not been used in the device type previously;
- a change that requires clinical data to validate the change;
- a change in software (e.g., from off-the shelf to proprietary software);
- a change from wired to wireless technology; or
- a change in the algorithm that adds a new diagnostic criterion and/or measurement parameter for a diagnostic device.

3. Performance Data

The Special 510(k) program relies on the manufacturer's conformance to the QS regulation, specifically 21 CFR 820.30. As such, performance data should not be submitted in a Special 510(k) for review. If performance data are submitted, FDA will convert the submission to a Traditional 510(k). It should be noted that a device-specific guidance may request test data in which case the extent of the requested data should be considered with regards to whether or not the device can be appropriately reviewed as part of the Special 510(k) program. Manufacturers should be aware that if test data or methods, especially those that do not comply with a recognized consensus standard, are essential to the review process, then a Special 510(k) is not the appropriate submission type.

Submissions that require clinical studies or animal data to support substantial equivalence are not appropriate for the Special 510(k) program because FDA's substantial equivalence determination depends to a great extent on the interpretation of actual test results rather than just an assessment of acceptance criteria for these types of performance data. However, in rare circumstances, if clinical or animal testing are conducted under design validation (21 CFR 820.30(g)), for example, to ensure that the modified device meets user requirements, or to demonstrate continued conformance with a

special control or recognized standard, then a Special 510(k) may be appropriate. For example, in the case of a non-invasive blood pressure device, the safety and effectiveness is demonstrated through conformance with AAMI/ANSI SP-10, an FDA-recognized standard that provides specific detail with respect to the patient population to be studied, test methods, and acceptance criteria. It is this level of detail explicitly included within the standard that permits FDA to review most modifications of these devices through a Special 510(k).

If you have any questions regarding whether your device modification is appropriate for the Special 510(k) program, we encourage you to contact the appropriate CDRH or CBER review branch or the CDRH 510(k) Staff for clarification.

4. Risk Assessment for Special 510(k)s

Risk assessment and the mitigation of risk are vital elements of design control requirements, which are applicable to Class II and III devices and to specific Class I devices, under the Quality System regulation.[46] Given the reliance of the Special 510(k) program on adherence to the design control requirements in 21 CFR 820.30, information regarding risk assessment is important to the review of Special 510(k) submissions and should be included in submissions for such devices.

The risk assessment should include details regarding the reasons for the submission, i.e., the reason for the manufacturer's modification(s) to its own legally marketed device as well as a history of changes made to the device between the previous and present submissions. FDA recommends inclusion of a risk assessment chart that describes, for each device modification under consideration, the verification and validation activities, with acceptance criteria and scientific justification for each activity and acceptance criteria. (An example of such a chart is provided in **Appendix E** of this document). Please note that the risk assessment information should pertain to the modifications contained in the present submission and cover all aspects of the possible effects on the safety and effectiveness of the modified device. We also recommend that manufacturers' risk assessment include all historic modifications that have been made since their last clearance for their relevant predicate device, including modifications that manufacturers determined did not require submission of a 510(k).

5. Additional Circumstances When a Special 510(k) May Not Be Appropriate

In addition to modifications that affect the indications for use or alter the fundamental scientific technology of the device, as discussed in **Sections V.A.1** and **V.A.2** above, FDA has also identified the following situations for which a Special 510(k) is not appropriate. In the event a Special 510(k) is submitted for any of the situations below, the submission will be converted to a Traditional 510(k).

a. Premarket submissions for a reprocessed single-use device (SUD) that require submission of validation data.[47]

[46] 21 CFR 820.30.

[47] *See* Guidance for Industry and FDA Staff - Medical Device User Fee and Modernization Act of 2002, Validation Data in Premarket Notification Submissions (510(k)s) for Reprocessed Single-Use Medical Devices. Available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071434.htm

b. Premarket submissions for a reusable dialyzer. A premarket review of the actual underlying test data that characterizes the effect of reuse on dialyzer performance is necessary to determine substantial equivalence.[48]

c. Premarket submissions for biliary, esophageal, or tracheal stents. A premarket review of the actual underlying data related to design and testing is necessary to ensure equivalence. Postmarket information has indicated that small changes in the stent itself or the delivery system can lead to unexpected adverse events.

d. Premarket submissions where the manufacturer is explicitly seeking to add language to the labeling related to the compatibility of the device when used in magnetic resonance imaging (MRI) systems.[49]

e. Any modification as a result of correction or removal undertaken to address a risk to health posed by the device.[50] FDA's review of the data or other information about the modification is necessary to ensure that all of the safety concerns associated with the recall have been addressed.[51]

f. Premarket submissions for devices that incorporate nanotechnology.[52]

g. Manufacturer is the subject of a current Warning Letter, and there are unresolved deficiencies with design control and other applicable provisions of the QS regulation. In these situations, corporate-wide deficiencies, particularly with design controls, undermine use of a Special 510(k) because this alternative is predicated on a manufacturer's compliance with design control provisions.

h. Combination products[53] should not be submitted for review under the Special 510(k) program.

---

[48] *See* Guidance for the Content of Premarket Notification for Conventional and High Permeability Hemodialyzers. Available at http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080166.pdf

[49] *See* Guidance for Industry: Guidance for the Submission of Premarket Notifications for Magnetic Resonance Diagnostic Devices. Available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073817.htm. *See also* Guidance for Industry and FDA Staff: Establishing Safety and Compatibility of Passive Implants in the Magnetic Resonance (MR) Environment. Available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm107705.htm.

[50] *See* 21 CFR 806.10. Under certain circumstances, however, FDA may accept a Special 510(k) for such modification. *See* FDA Blue Book Memo K95-1 entitled "510(k) Requirements During Firm-Initiated Recalls." Available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080297.htm.

[51] Data and information in a Traditional 510(k) regarding a modified device, where the modification is associated with corrections or removals as described in 21 CFR Part 806, medical device reports (MDRs) submitted under 21 CFR Part 803, corrective and preventive actions under the QS regulation (21 CFR 820.100), user complaints, or FDA warning letters or inspection findings (FDA Form 483), should include: a full description of the investigation of the cause or source of the problem; an explanation of how the proposed change to the device design, labeling and/or manufacturing process addresses the problem and mitigates harm; and any associated FDA Establishment Identifier (FEI) and MDR numbers, if applicable.

[52] Refer to "Draft Guidance: Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology." Available at: http://www.fda.gov/ScienceResearch/SpecialTopics/Nanotechnology/ucm257926.htm. Once final, this guidance will represent the Agency's thinking on this topic.

B. Abbreviated 510(k) Program

The Abbreviated 510(k) Program is intended to leverage established information regarding various aspects of the 510(k), such as device description, performance test methods, test acceptance criteria, etc., that exist in the public domain and that FDA has accepted. In particular, an Abbreviated 510(k) may be suitable for devices for which:

- a device-specific guidance document exists, including a special controls guidance document that narrows or standardizes the premarket review questions for the device;
- other types of special controls have been established for the device type that narrow or standardize the premarket review questions for a device; or
- FDA has recognized a device-specific standard applicable to the proposed device and that consensus standard comprehensively describes many different aspects of device design and performance (e.g., acceptance criteria). [54]

Manufacturers of such devices may document conformance with device-specific guidance, other special controls, or consensus standards in a "summary report" explaining how such conformance satisfies the requirements of 21 CFR 807.87. An Abbreviated 510(k) is subject to the same review timeframe as a Traditional 510(k).

1. Device-Specific Guidance and Special Controls

Conformance with special controls and/or device-specific guidance documents may be documented in a "summary report" outlining adherence to relevant guidance documents and/or special controls. A 510(k) that conforms to an FDA guidance document and/or special control(s) should be easier to prepare and review, thus facilitating the 510(k) review process.

2. Recognized [Consensus] Standards

The FDA Modernization Act of 1997 (FDAMA) (Pub. L. 105-115) amended section 514 of the FD&C Act to specifically authorize the Agency to recognize all or part of national and international standards through publication of a notice in the Federal Register (consensus standards program) (21

---

[53] Combination product includes: (1) a product comprised of two or more regulated components, i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity; (2) two or more separate products packaged together in a single package or as a unit and comprised of drug and device products, device and biological products, or biological and drug products; (3) a drug, device, or biological product packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug, device, or biological product where both are required to achieve the intended use, indication, or effect and where upon approval of the proposed product the labeling of the approved product would need to be changed, e.g., to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose; or (4) any investigational drug, device, or biological product packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect. 21 CFR 3.2(e).

[54] For a current list of FDA recognized standards, please refer to http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Standards/default.htm

U.S.C. § 360d). FDA may cite recognized standards in guidance documents or individual policy statements, or establish them as special controls that address specific risks associated with a type of device. The extent of the consensus standards program has grown in scope and applicability since its inception as part of FDAMA.

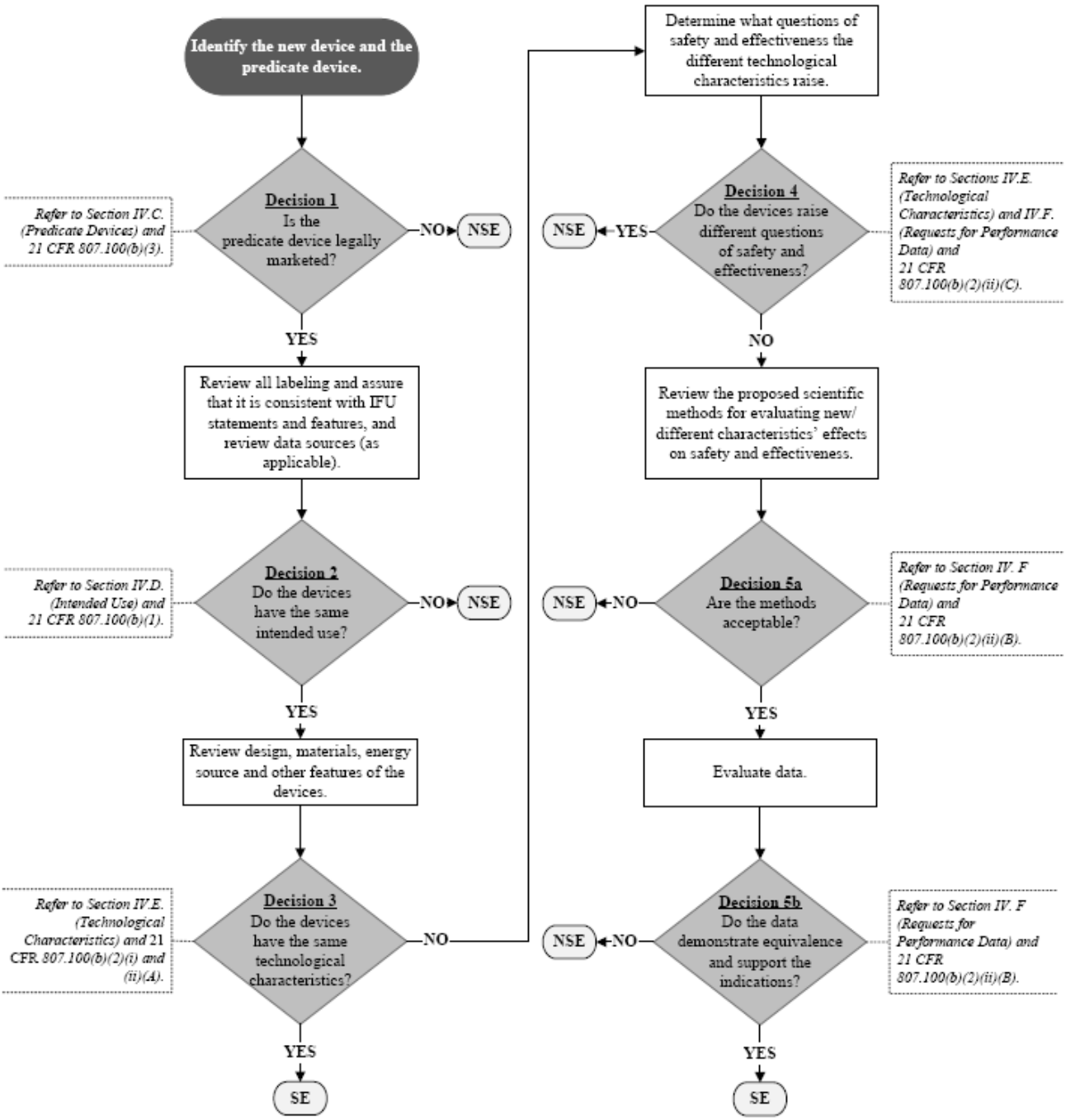
Most, if not all, 510(k)s cite at least one standard. The most commonly cited standards are "horizontal" standards that address, for example, sterilization, biocompatibility, and electrical safety. Given the ubiquitous nature of standards usage in 510(k)s, FDA does not identify all 510(k)s that cite one or more standards as "Abbreviated" 510(k)s. Such submissions would be a Traditional, Abbreviated, or Special 510(k) based on other factors. FDA considers 510(k)s to be eligible for the "Abbreviated 510(k)" program because of reliance on consensus standards when the submission cites a comprehensive device-specific consensus standard (i.e., one that encompasses many different aspects of device design and performance). FDA continues to support and encourage the development and use of all types of consensus standards for medical devices. While reliance on partial standards or limited aspects of recognized standards will not, alone, support inclusion in the revised Abbreviated 510(k) program, the use of standards improves the quality of submissions and increases the efficiency of Agency review of all premarket notifications.

3. Elements/Overview of an Abbreviated 510(k)

An Abbreviated 510(k) must include the required elements identified in 21 CFR 807.87. However, a manufacturer who submits an Abbreviated 510(k) that relies on a device-specific guidance document and/or special control(s) should include a summary report that describes how the guidance document and/or special control(s) were used during device development and testing. The summary report should include information regarding the manufacturer's efforts to conform to the guidance document and/or special control(s) and should outline any deviations. Manufacturers who submit an Abbreviated 510(k) that relies on a recognized standard with a declaration of conformity should provide the information described in **Appendix G** and also refer to FDA's guidance, "Recognition and Use of Consensus Standards." Manufacturers who submit an Abbreviated 510(k) that relies on a recognized standard(s) without a declaration of conformity should provide a statement regarding conformity to that standard(s) and also refer to the Agency's guidance, "Use of Standards in Substantial Equivalence Determinations."[55] While an Abbreviated 510(k) is subject to the same review timeframe as a Traditional 510(k), FDA believes that reliance on a manufacturer's summary report on the use of a device-specific guidance, special controls, and/or recognized consensus standards should help to facilitate the review process.

[55] *See* Guidance for Industry and for FDA Staff: Use of Standards in Substantial Equivalence Determinations. Available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073752.htm

Appendix A. Proposed 510(k) Decision-Making Flowchart



SE = "Substantially Equivalent"
NSE = "Not Substantially Equivalent"

This Flowchart is not intended to be used as a 'stand-alone' document and should only be considered in conjunction with the accompanying text in this guidance.

Appendix B. The 510(k) Summary Document Requirements

In Appendix B, FDA provides further clarification and guidance to facilitate compliance with the requirements set forth in 21 CFR 807.92 and consistency in the information conveyed in the 510(k) Summaries which are available to the public on FDA's website. As noted earlier in this guidance document, if during the course of review, additional testing or information are requested, the manufacturer should submit a revised 510(k) Summary to reflect the additional information. The following identifies the information that must be included in the 510(k) Summary under 21 CFR 807.92, information that we recommend be included in the 510(k) Summary, and other considerations.

- 807.92(a)(1): "The submitter's name, address, telephone number, a contact person, and the date the summary was prepared."
    - The "submitter" or manufacturer should be the holder of the 510(k), not a consultant or law firm.

- 807.92(a)(2): "The name of the device, including the trade or proprietary name if applicable, the common or usual name, and the classification name, if known."
    - FDA recommends that the manufacturer list all applicable names and model numbers, if known.
    - If the submission is bundled[56], the 510(k) Summary should list all applicable classification regulations and product codes.

- 807.92(a)(3): "An identification of the legally marketed device to which the submitter claims equivalence. A legally marketed device to which a new device may be compared for a determination regarding substantial equivalence is a device that was legally marketed prior to May 28, 1976, or a device which has been reclassified from class III to class II or I (the predicate), or a device which has been found to be substantially equivalent through the 510(k) premarket notification process."
    - FDA recommends that the manufacturer provide the 510(k) number of the device used as the predicate device in support of the current 510(k) submission.
    - If using an exempt device as a predicate, the manufacturer should list the classification regulation and the product code.
    - If using a device that has been reclassified from Class III to II as a predicate, where a 510(k) has not been submitted, please list the PMA number.
    - If the manufacturer lists an inappropriate predicate device, FDA will request that such information be removed and the 510(k) Summary updated accordingly by the manufacturer.

- 807.92(a)(4): "A description of the device that is the subject of the premarket notification submission, such as might be found in the labeling or promotional material for the device, including an explanation of how the device functions, the scientific concepts that form the basis for the device, and the significant physical and performance characteristics of the device, such as device design, material used, and physical properties."

[56] *See* Guidance for Industry and FDA Staff entitled "Bundling Multiple Devices or Multiple Indications in a Single Submission." Available at http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089732.pdf

The description of the device attributes should include the following details:

- Device Identification:
  - List all key device components included in the submission (e.g., catheter, cable wire, leads)
  - List all model numbers (if known) and briefly explain the differences among models

- Device Characteristics (address all that apply):
  - software
  - biologics
  - drugs
  - any patient-contacting materials
  - coatings
  - additives
  - single-use
  - sterile
  - sterilization method [specify]

- Environment of Use (address all that apply):
  - healthcare facility/hospital
  - home
  - ambulatory
  - other [specify]

- Brief Written Description of the Device:
  - Explanation of how the device works/principle of operation
  - Mechanism of action
  - Key device features
  - Energy source (if applicable)
  - Other critical device features

- Materials of Use
  - General type of material used (e.g., polysulfone, stainless steel)
  - If material complies with a FDA recognized consensus standard for medical use, include the applicable number (e.g., ASTM FXXXX-last 2 numbers of the year)
  - Duration and type of contact

- Key Performance Specifications/Characteristics of the Device

- 807.92(a)(5): "A statement of the intended use of the device that is the subject of the premarket notification submission, including a general description of the diseases or conditions that the device will diagnose, treat, prevent, cure, or mitigate, including a description, where appropriate, of the patient population for which the device is intended. If the indication statements are different from those of the legally marketed device identified in paragraph (a)(3) of this section, the 510(k) summary shall contain an explanation as to why

the differences are not critical to the intended therapeutic, diagnostic, prosthetic, or surgical use of the device, and why the differences do not affect the safety and effectiveness of the device when used as labeled."

- The 510(k) Summary should include the Indications for Use, which should be identical to that proposed on the Indications for Use Sheet and the labeling.
- If the Indications for Use are different from those of the predicate device, a brief explanation is required to address why the differences in the Indications do not affect the safety and effectiveness of the device and do not alter the intended therapeutic, diagnostic, prosthetic, or surgical use of the device.

- 807.92(a)(6): "If the device has the same technological characteristics (i.e., design, material, chemical composition, energy source) as the predicate device identified in paragraph (a)(3) of this section, a summary of the technological characteristics of the new device in comparison to those of the predicate device. If the device has different technological characteristics from the predicate device, a summary of how the technological characteristics of the device compare to a legally marketed device identified in paragraph (a)(3) of this section."

- 807.92(b): "510(k) summaries for those premarket submissions in which a determination of substantial equivalence is also based on an assessment of performance data shall contain the following information:"
  "(1) A brief discussion of the nonclinical tests submitted, referenced, or relied on in the premarket notification submission for a determination of substantial equivalence,"
  - A high level summary of the tests that were used to demonstrate substantial equivalence should be included (e.g., fatigue testing, biocompatibility, etc.).
  - If a guidance document was referenced/used for the testing, the guidance document should be referenced in this section.
  - If an FDA recognized consensus standard (e.g., test method or guide) was used/relied upon for testing, please list the standard connotation (e.g., ASTM FXXXX-last 2 numbers of the year).

  "(2) A brief discussion of the clinical tests submitted, referenced, or relied on in the premarket notification submission for a determination of substantial equivalence. This discussion shall include, where applicable, a description of the subjects upon whom the device was tested, a discussion of the safety or effectiveness data obtained from the testing, with specific reference to adverse effects and complications, and any other information from the clinical testing relevant to a determination of substantial equivalence,"
  - FDA is interested in collecting an appropriate degree of detail within this section to be informative regarding the level of evidence that was necessary to support an SE determination.
  - As applicable, FDA recommends the following details be included regarding the clinical evidence provided to support an SE determination:

    - Level of Evidence (identify one)
      - Randomized, multi-arm, "blinded" study with concurrent sham (placebo) control
      - Randomized, multi-arm, "blinded" study with concurrent ("active") control

- Randomized, multi-arm, un"blinded" study with a control (control that is either active or consists of no treatment)
- Non-randomized study with concurrent ("active") control
- Single-arm study with patient serving as own control (include designed single-arm crossover)
- Single-arm study with Historical Control (using patient-level data)
- Single-arm study with Literature Control (historical control)
- Single-arm study with Objective Performance Criteria
- Single-arm study with Performance Goals
- Registry
- Observational study
- Systematic review (meta-analysis with patient-level data)
- Meta-analysis based on summary information only
- Literature Summary
- Uncertain

- Location of Study (specify one of the following)
  - United States only
  - outside of United States only
  - both in United States and outside of United States

  - Identify applicable IDE number [Gxxxxxx]

- Primary Safety Endpoint Identified?
  - If Yes, describe

- Primary Effectiveness Endpoint Identified?
  - If Yes, describe

- Primary Composite Safety/Effectiveness Endpoint Identified, if applicable?
  - If Yes, describe

- Patient Accountability (Enter number of patients reported at each stage):

Stage	Investigational Device Arm Total	Control Arm Total	Total
Enrollment			
Treatment			
Primary Safety Endpoint Analysis			
Primary Effectiveness Endpoint Analysis			
Primary Composite Safety/Effectiveness (if app)			

The content of the table may need to be modified depending upon the specifics of the clinical data provided and the endpoints studied.

- Identify whether the study met the primary endpoint
  - Whether Yes or No, describe

- Describe the study results in appropriate parameters

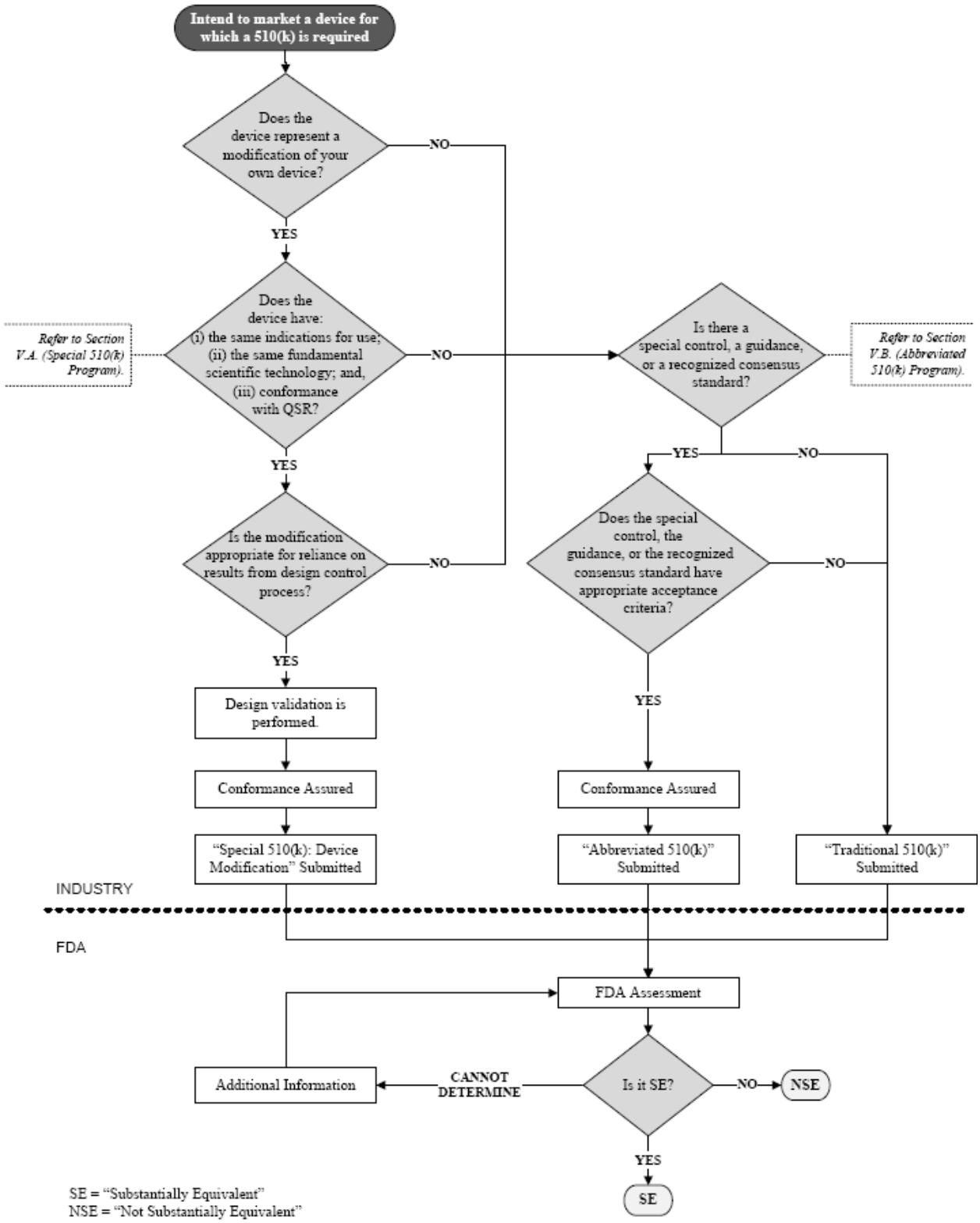
- Identify the adverse events and complications observed in the study, including those associated with the device.

"(3) The conclusions drawn from the nonclinical and clinical tests that demonstrate that the device is as safe, as effective, and performs as well as or better than the legally marketed device identified in paragraph (a)(3) of this section."
  - A brief summary of why the device is substantially equivalent to the predicate.

- 807.92(c): "The summary should be in a separate section of the submission, beginning on a new page and ending on a page not shared with any other section of the premarket notification submission, and should be clearly identified as a '510(k) summary'."

- 807.92(d): "Any other information reasonably deemed necessary by the agency."
  - If the FDA determines that other information needs to be included within the 510(k) Summary, such information must be included within this document.

Appendix C. 510(k) Process



This Flowchart is not intended to be used as a 'stand-alone' document and should only be considered in conjunction with the accompanying text in this guidance.

Appendix D. Content of a Special 510(k) Submission

A Special 510(k) for a device modification should include:

- A coversheet clearly identifying the submission as a "Special 510(k): Device Modification;"
- The name of the manufacturer's legally marketed (unmodified) device and the 510(k) number under which it was cleared;
- Information required under § 807.87, including a description of the modified device, a comparison to the cleared device, the indications for use of the device, and the proposed labeling for the device;
- If the Special 510(k) includes reference to a standard, then we recommend that you include Form FDA 3654, **Standards Data Report for 510(k)s**.
- A concise summary of the design control activities. (See the example provided in **Appendix F**). A tabular presentation of this information should be provided. FDA may consider the information generated from the design control activities to be "appropriate supporting data" within the meaning of 21 CFR 807.87(g). The summary should include the following:
  - An identification of the Risk Analysis method(s) used to assess the impact of the modification on the device and its components as well as the results of the analysis;
  - Based on the Risk Analysis, an identification of the verification and/or validation activities required by 21 CFR 820.30, including methods or tests used and the acceptance criteria applied.
- Indications for Use enclosure; and
- A declaration of conformity with design controls. The declaration of conformity should include:
  - A statement** that, as required by the risk analysis, all verification and validation activities were performed by the designated individual(s) and the results demonstrated that the predetermined acceptance criteria were met; and
  - A statement** that the manufacturing facility is in conformance with the design control procedure requirements as specified in 21 CFR 820.30 and the records are available for review.

    ** The above two statements should be signed by the 510(k) holder's designated individual(s) responsible for those particular activities.

Appendix E. Sample Risk Analysis Summary - Definitions

This section provides information with respect to the risk analysis summary to be provided with a Special 510(k). In particular, the summary consists of 9 elements for which each device modification and corresponding risk analysis are identified.

The elements, and the corresponding description/definition, are provided here:

Device Modification: Identify each change made from the manufacturer's previously cleared device (predicate).

Cause of Risk: For each risk associated with the modification, identify the normal condition, fault condition, or failure mode that causes it.

Hazardous Situation(s): For each cause, identify the hazardous situation that may occur. If the normal condition, fault condition, or failure mode can be the cause of more than one hazardous situation, identify each one.

Consequences: For each hazardous situation, describe the worst-case consequence and the consequence most likely to occur.

Risk Control Measure(s): For each cause, describe the control measure used to mitigate the risk. If the control measure is used in combination with other control measures, list the measures and describe the function of the combination.

Risk Acceptability Criteria: For each cause not originating in software, provide the verifiable acceptability criteria and the basis (rationale) for the criteria. (If software, see Verification Method(s) below). If the basis is a standard, identify the standard, the applicable provision, and the performance requirement(s). If the basis is a direct comparison to properties of the predicate device or other marketed devices, identify the device and the properties. If the basis is a safety principle such as no single-fault, state the principle and provide reference(s). For each cause of a use-related risk or control measure requiring operator-intervention to prevent harm, provide the user needs criteria and the basis (or rationale) for that criteria.

Verification Method(s): For each control measure or combination of control measures, describe the verification method. If testing was conducted, state whether the same test protocol submitted in the predicate submission was used (reference the section of prior submission, including page number, where this information is available); or, provide the new test protocol. If the new test protocol conforms to that of a standard, provide a statement indicating whether the test method was in full accordance with a particular standard, a description of all deviations to the protocol made during testing, if any, and a complete description of parameters not defined in the cited standard. If the protocol does not conform to that of a standard, describe the protocol and provide a summary of test conditions. For all tests, identify the specific device components tested, the number of components tested, and provide a rationale for why the test conditions and components tested were considered

"worst-case." For each cause originating in software, provide the pass/fail criteria for verification and pass/fail criteria for validation.

Validation Method(s): Note that the specific change being proposed may necessitate the performance of verification activities only, or both verification and validation activities. For each control measure or combination of control measures for each cause of a risk originating in software, each use-related risk or each control measure requiring operator intervention to prevent harm, describe the validation method. Provide a summary of the relationship of the method to (1) actual conditions of use and (2) the extent to which test participants represent actual users.

Summary Conclusion: A summary conclusion confirming (1) verification of the specified acceptability criteria for each control measure or combination of control measures and (2) validation of the specified criteria for each control measure or combination of measures for each cause of a risk originating in software, each use-related risk, or each risk control measure requiring operator-intervention to prevent harm.

It is recommended that the information described above be presented in a very clear manner such that the nine elements for each modification are clearly identified, such as in a table:

Device Modification	**Cause of Risk**	**Hazardous Situation(s)**	**Consequences**	**Risk Control Measure(s)**	**Risk Acceptability Criteria**	**Verification / Validation Method(s)**	**Summary Conclusion**
mod #1							
mod #2							

Appendix F. Sample Risk Analysis Summary

In this section, we present sample risk analysis summaries for changes involving mechanical engineering (and bench testing), materials (biocompatibility), and software. As discussed in Appendix E, this information should be presented in a very clear manner, such as in a table format.

Sample 1 - Bench Testing for a Mechanical Engineering Change

- **Device Modification**: Decreased diameter by 2mm for component "A" in valve assembly (to improve operational clearance).

- **Cause of Risk:** Fatigue fracture of component "A."

- **Hazardous Situation(s):** Loss of primary device function (requiring replacement of the valve assembly); broken pieces from component "A" introduced into patient airway.

- **Consequences:** Worst-case: Surgical intervention to remove broken pieces from airway.

  Most likely: Loss of primary device function resulting in delayed therapy.

- **Risk Control Measure(s):** A combination of measures is used to control risk: Use of the existing particulate filter to prevent broken pieces from entering airway, as described in the predicate device cleared in Kxxxxxx; fatigue testing of modified component "A" to ensure reliability of the life of the assembly.

- **Risk Acceptability Criteria:** Acceptability criteria for the particulate filter described in our predicate device cleared in Kxxxxxx. Fatigue fracture acceptability criteria: When tested in accordance with ASTM F000, the component tested will maintain a fatigue load of 1000N, R=0.1, frequency of 1 Hz, for 2 million cycles without failure. All components will be tested to 3 million cycles or failure. Any failure mode shall be consistent with those reported for predicate device (i.e., fatigue fracture at the critical dimension). These criteria are equivalent to those previously reported for the predicate device cleared in Kxxxxxx.

- **Verification Method(s):** Verification of the effectiveness of the particulate filter described in our predicate device cleared in Kxxxxxx. Verification of the reliability of component "A": Testing conducted in full accordance with ASTM F000, as in our predicate submission. The following parameters, not defined by ASTM F000, were used: testing was performed on 5 samples at a fatigue load of 1000N, R=0.1, frequency of 1 Hz, for 3 million cycles. Component "A.0001" was tested. Each component tested had the smallest critical dimension possible for Component "A", and therefore, were considered "worst-case." These testing parameters are the same as those used in the clearance of Kxxxxxx.

- **Validation Method(s):** not applicable in this case.

- **Summary Conclusion:** The summary conclusion confirming verification for the filter for the specified criteria are described in our predicate device cleared in Kxxxxxx. Summary conclusions for verification of fatigue fracture criteria: All samples tested (n=5) met the acceptability criteria. One device that was tested beyond 2 million cycles failed due to fatigue fracture at the critical dimension (cycle = 2,500,306). The other four devices performed for 3 million cycles without failure. Thus, verification of the criteria is confirmed.

Sample 2 - Biocompatibility Testing for a Materials Change

- **Device Modification**: Change in the material contacting the patient from polyurethane to polyethylene.

- **Cause of Risk:** Patient contact with the material may elicit a biological response.

- **Hazardous Situation(s):** Patient skin in prolonged direct contact with the material.

- **Consequences:** Worst-case: Foreign material/body induces an immunological reaction to the patient or produces a toxic effect on the patient. Most-likely: Irritation of the skin-contacting region.

- **Risk Control Measure(s):** (Note: Risk is controlled by the selection of the appropriate biological evaluation test(s) and use of the test(s) to verify that acceptability criteria are met. The rationale for selection should be provided and take into account all relevant factors for the new material including the causes of risk, the hazardous situations, the consequences, as well as the nature, degree, frequency, and duration of exposure of the body to the material.)

  The biocompatibility test serves as the risk control measure. The specific cytotoxicity test is for a surface device with prolonged contact of the skin. It was selected using Required Biocompatibility Training and Toxicology Profiles for Evaluation of Medical Devices, May 1, 1995 (G95-1) and ISO 10993.

- **Risk Acceptability Criteria:** (Note: The basis for the criteria should be provided, such as published findings associated with a history of safe use. The specific acceptability criteria for each test/assay should be stated.)

  The cytotoxicity test acceptability criterion is < X% lysis.

- **Verification Method(s):** (Note: Specific tests/assays should be listed, e.g., cytotoxicity, intracutaneous toxicity, sensitization, etc., with either a copy of, or reference to, the test protocols.)

  Cytotoxicity testing was conducted in accordance with ISO 10993 and FDA Bluebook Memorandum G95-1. A description of specific test used, the applicable requirements in the standard, and anomalies from the requirements are attached.

- **Validation Method(s):** not applicable in this case.

- **Summary Conclusion:** (Note: Any observed deviations or anomalies and the rationale for accepting them should be fully described.)

  The cytotoxicity test was performed in accordance with ISO 10993 with no deviations or anomalies in the test methodology. The results met the specified criteria.

Sample 3 - Software Verification and Validation for a Software Change

- **Device Modification**: (Note: The software change and the version to which it applies should be described. The level of concern for the predicate device software should be identified. Explain if and how the software modification affects the level of concern.)

  For the predicate device, the patient-activated EMERGENCY STOP automatically changed therapy settings to default safe-state conditions. When EMERGENCY STOP is activated, the modification stops therapy but causes those therapy settings to be retained until the operator manually resets the device.

  The software version is xx-xxxx-xx and level of concern remains moderate.

- **Cause of Risk:** (Note: All direct and indirect cause(s) of each risk associated with the change should be provided. A revised Device Hazard Analysis identifying any changes to the Device Hazard Analysis for the predicate device should be provided.)

  When EMERGENCY STOP is activated, the therapy settings (system-state) are not retained. Thus, the therapy settings causing harm are unknown to the operator.

  The revised Device Hazard Analysis xx-xxxx-xx highlighting changes associated with the modification is attached.

- **Hazardous Situation(s):** Restarting the device at therapy settings that will cause pain and could cause tissue damage for the patient.

- **Consequences**: Worst-case: Tissue damage requiring surgery.

  Most likely: Temporary pain and discomfort.

- **Risk Control Measure(s):** EMERGENCY STOP places device in a safe state, disables the START control, and retains and displays therapy settings for the operator.

  Manual RESET by the operator is then required before therapy can be restarted. Manual RESET (1) automatically changes settings to default conditions, (2) allows new therapy settings to be selected by the operator, and (3) enables the START therapy control.

  New user manual EMERGENCY STOP/RESTART instructions are attached.

- **Risk Acceptability Criteria:** (Note: New functional and operational requirements should be provided in the revised Software Requirements Specifications, and Software Design Specification for moderate and major level of concern software.)

  The new functional and operational requirements are described in the following revised documents, which are attached:

  Software Requirements Specification xxxx-xx-xx.

  Software Design Specification xxxx-xx-xx.

  The risk control measure specifications and verification pass/fail criteria are described in EMERGENCY STOP/RESTART Test Plan xx-xxxx-xx.

  New user requirements and validation pass/fail criteria are described in EMERGENCY STOP/RESTART Human Factors Analysis and Use Study xx-xxxx-xx.

- **Verification/Validation Method(s):** (Note: For minor level of concern, a summary of software functional and operational test plans should be provided. For moderate and major levels of concern, a summary of verification and validation activities at unit, integration, and system levels should be provided.)

  (Note: A traceability analysis demonstrating traceability among prior and new requirements, specifications, identified hazards and control measures, verification and validation tests, and regression tests should be provided.)

  The verification methods including hazard analysis and regression testing verifying that the modification met applicable specifications and did not adversely affect the safety designed into the system are described in the attached test plan.

- **Validation Method(s):** The validation method included is described in the attached human factors analysis and use study.

  The revised Traceability Analysis xx-xxxx-xx highlights changes associated with the modification and is attached.

- **Summary Conclusion:** (Note: The conclusions should take into account revisions to existing documentation as well as the results of testing, including failed tests.)

  The Summary Conclusion xx-xxxx-xx confirming verification of the specified pass/fail criteria and validation of the pass/fail criteria is attached.

Appendix G. Abbreviated 510(k) Content

FDA's recommendations for the content of an Abbreviated 510(k) submission may be found in the guidance document entitled **Format for Traditional and Abbreviated 510(k)s**.[57]

In addition to the information specified in the guidance document, we recommend that you include Form FDA 3654, **Standards Data Report for 510(k)s**, if the 510(k) references a national or international standard.[58]

When applicable, Abbreviated 510(k)s should also include a "Declaration of Conformity" to recognized consensus standards. In preparing a declaration of conformity, please refer to the guidance document entitled, **Recognition and Use of Consensus Standards**.[59]

[57] http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm084365.htm

[58] http://www.fda.gov/AboutFDA/ReportsManualsForms/Forms/default.htm. The Standards Data Report for 510(k)s should be completed by the manufacturer submitting the 510(k). A separate form for each standard referenced in the 510(k) should be submitted.

[59] http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm077274.htm