U.S. FDA Medical Device Predicate Selection for 510(k) Submissions

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by UL

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What you will learn in this white paper

- **What a primary predicate device is and how to use it in a 510(k)**
- **What a secondary predicate device is and how to use it in a 510(k)**
- **What a reference device is and how to use it in a 510(k)**

In 1976, the Medical Device Amendments were added to the United States (U.S.) Federal Food, Drug and Cosmetic Act (FD&C Act) of 1938, is summarized below.

- Intended to provide reasonable assurance of the safety and effectiveness of medical devices
- Created a three-class, risk-based classification system for all medical devices
- Established the regulatory pathways for new medical devices (devices that were not on the market before May 28, 1976, or had been significantly modified) to get to market: Premarket Approval (PMA) and Premarket Notification (510(k))
- Created the regulatory pathway for new investigational medical devices to be studied in patients (Investigational Device Exemption (IDE))
- Established several key postmarket requirements: registration of establishments and listing of devices with the FDA, Good Manufacturing Practices (GMPs), and reporting of adverse events involving medical devices
- Authorized the FDA to ban devices

Source: **A History of Medical Device Regulation & Oversight in the United States | FDA**

Introduction

This white paper focuses on the selection and use of predicate and reference devices in 510(k) submissions for your 510(k) using various U.S. Food and Drug Administration (FDA) databases.

This white paper assumes a basic understanding of how the FDA's Center for Devices and Radiological Health (CDRH) classifies and regulates medical devices in the United States (U.S.). For those not familiar with this topic, please see the author's accompanying June 2023 white paper, **United States Food and Drug Administration (FDA) Medical Device Classification System**.

We will not discuss how to prepare a 510(k), the differences in a Traditional 510(k), Special 510(k) or an Abbreviated 510(k), or when to submit a new 510(k) for changes made to an existing cleared device. The FDA has guidance documents that address these topics.[1, 2, 3, 4, 5]

A premarket notification, also known as a 510(k), is a premarket submission to the FDA by a device sponsor ("sponsor") to demonstrate that the device they intend to market in the U.S. is as safe and effective as a legally marketed device (aka "predicate device") under the same product code. A 510(k) is relevant for a device that does not require FDA approval under a PMA pathway and is not considered 510(k) exempt.

Most Class I devices are 510(k) exempt and do not require a premarket submission to the FDA before they can be marketed in the U.S. Most Class II devices require 510(k) clearance by the FDA before they can be marketed in the U.S. Most Class III devices require PMA approval by the FDA before they can be marketed in the U.S.

De Novo premarket submissions are for novel, low to moderate-risk devices for which no legally marketed predicate device exists. After the FDA reviews a sponsor's De Novo submission they will either grant or decline the De Novo request for marketing authorization and provide a formal classification (product code and class) for the device.[6]

In a 510(k) premarket submission, the sponsor must compare their device to one or more similar predicate device(s) to make and support their claims of substantial equivalence (SE). Until the sponsor of a 510(k) receives an order from the FDA declaring their device to be substantially equivalent to the predicate device they selected, they cannot market their device in the U.S. A determination of SE is usually made by the FDA within 90 FDA review days and is based on the information submitted by the sponsor. Note the FDA puts a submission on hold from review to ask substantial questions and so the actual time until clearance is generally 4-9 months. The FDA describes substantial equivalence as:[7]

Substantial equivalence means that the new device is as safe and effective as the predicate.

A device is substantially equivalent if, in comparison to a legally marketed predicate it:

- has the same intended use as the predicate and
- has the same technological characteristics as the predicate or
    - has the same intended use as the predicate and
    - the different technological characteristics and does not raise different questions of safety and effectiveness and
- the information submitted to FDA demonstrates that the device is as safe and effective as the legally marketed device.

A claim of substantial equivalence does not mean the new and predicate device needs to be identical. FDA first establishes that the new and predicate devices have the same intended use and any differences in technological characteristics do not raise different questions of safety and effectiveness. FDA then determines whether the device is as safe and effective as the predicate device by reviewing the scientific methods used to evaluate differences in technological characteristics and performance data. This performance data can include clinical data and non-clinical bench performance data, including engineering performance testing, sterility, electromagnetic compatibility, software validation and biocompatibility evaluation, among other data.

It is important to note that demonstrating SE requires the new device to have the same intended use and the same or similar technological characteristics as the predicate device. However, the FDA clears devices under a 510(k) based on the device's stated indications for use that is included in the 510(k) submission. For the FDA to find the new device SE to the predicate device, the indications for the use of the new device must fall within the intended use of the predicate device. Also, while the intended use and indications for the use of a device can be the same, often they are not. This makes selection of the predicate device particularly important as the new device should have the same indications for use, or be a subset of, the predicate device's indications for use.[8, 9, 10] However, it is also important to note that when selecting a predicate device, one should check to see that the predicate device has a history of safe use and that there are no known unmitigated use-related or design-related safety issues or associated design-related recalls for the predicate device being proposed, as discussed in the referenced guidance document *Best Practices for Selecting a Predicate Device to Support a Premarket Notification [510(k)] Submission*.

Therefore, if the indications for use of the new device are different from the predicate device and you cannot locate a better predicate device, you may need to introduce an additional predicate device(s) to your 510(k) to cover the rest of the indications for use and/or technological characteristics. The additional predicate device(s) must also have the same intended use as the new device. If an additional predicate device(s) is added to your 510(k), you should designate the predicate device that is most like the new device in terms of indications for use and technological features as the primary predicate device and any other device(s) as a secondary predicate device(s) to cover those parts of the indications for use and/or technological characteristics features in the new device that are not found in the primary predicate device. If it is not clear which should be the primary predicate device, then, in general, the one that has a higher apparent risk should be chosen.

Additionally, there are instances when the sponsor of a new 510(k) may only find one or two devices under the same product code as their new device. Further complicating matters could include that the identified predicate device was cleared fifteen or more years ago where there is often little, if any, substantive information on the device in the FDA database. Therefore, while older devices can be used as a predicate in a new 510(k) submission, using predicate devices that are older than fifteen years often makes demonstrating SE difficult given the lack of publicly available information.

Since clearance of the first 510(k) under K760001 in 1976, thousands of 510(k)s have been cleared by the FDA using this regulatory pathway. Of the three main premarket regulatory pathways for devices at the FDA (510(k), De Novo and PMA), more devices are processed through the 510(k) pathway every calendar year. In 2022, 3,194 510(k)s were cleared by the FDA, vs. 22 original PMA approvals and 23 De Novos that were granted marketing authorization.

What is a predicate device?

A predicate device is a legally marketed device (in the U.S.) that has already been cleared by the FDA through the 510(k) or granted under a De Novo or was in commercial distribution on or before May 28, 1976. The sponsor of a new 510(k) must demonstrate that their device is SE to the predicate they select in terms of its intended use and technological characteristics. Demonstrating SE to a predicate device is only relevant to 510(k) submissions.

Once a sponsor has determined the product code of the new device, they are ready to begin looking for suitable predicate devices in the FDA's 510(k) database seen in **Figure 1** or the similar De Novo database.[11]

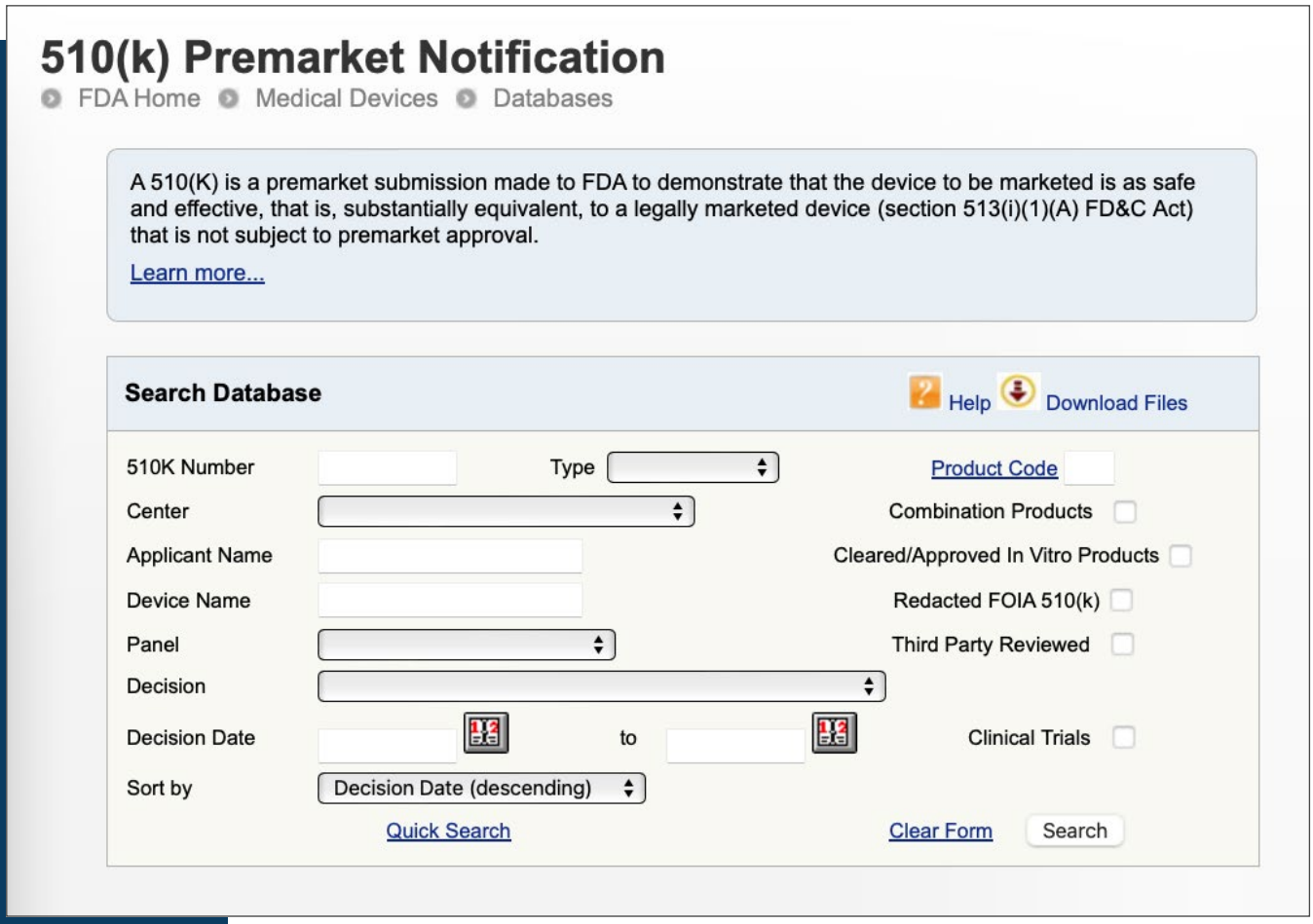

Figure 1 – 510(k) Premarket notification page to database

It is important to note that when searching in the databases for a predicate device, there are multiple fields that can be used to narrow your search, with some of those fields having drop-down menus for additional search features. There are also additional boxes that can be checked to further refine your search. From a practical standpoint for companies making a 510(k) submission for the first time, we recommend starting your initial predicate device search by entering the product code of your device into the "Product Code" field and clicking on the "Search" button.

This will list all devices that have been authorized under the relevant submission type under a product code in chronological order with the most recent authorizations shown first. The more 510(k)s that have been issued for a particular product code, the better the chance of finding a suitable predicate device.

It is also important to remember that there can be more than one product code assigned to the same regulation number.

Some predicate device examples

Demonstrating SE of a new device to a legally marketed predicate is based on the new device having the same intended use and the same or similar technological characteristics as the predicate device. The intended use of a device is generally described in part (a) Identification of its regulation number or can also be shown on the product classification landing page under Definition for a specific product code. This usually happens when there are several product codes in the same regulation number and part (a) Identification of the regulation number does not accurately describe the product code in that regulation or when a new product code is granted under a De Novo pathway and no regulation has been published yet by the FDA. Examples of these include product codes **NUC** (Lubricant, Personal) under regulation number **884.5300 (Condom)** and **QMJ** (Powered Radiofrequency Toothbrush) under regulation number **872.6866 (not currently published)**, respectively.

Therefore, when looking for a predicate device, it is preferable to locate one with the same indications for use as your device, or be a subset of the predicate device's indications for use. Additionally, the technological features should be the same or similar where any differences in the new device does not raise new questions of the safety and effectiveness when compared to the predicate device. Having these two things clearly described in your 510(k) helps minimize any questions from the FDA concerning SE, and may result in a faster clearance time for your device.

There are several ways to begin your search for a predicate device which depends on what information you have available. In this section we will look at some specific examples of predicate device selection using different product codes to highlight some of the challenges of trying to locate an ideal predicate device, as well as reference device (if needed), for your submission.

Example 1 – Challenges of using older predicate devices vs. newer predicate devices

Selecting older predicate devices for use in your 510(k) submission is acceptable by the FDA, and sometimes you may have no other choice as the last clearance may have been many years ago. Devices cleared fifteen or more years ago typically do not have a lot of useful information about them in their 510(k) Summary related to the technological characteristics of the device or what type of testing it underwent.

As examples, **K973926** in product code **DZE** (Implant, Endosseous, Root-Form) **K973133** in product code **FRN** (Pump, Infusion) both were cleared in 1997 and there is very little in the way of detailed information in the 510(k) Summaries. This is fairly typical for older 510(k)s.

This exercise is repeated with two more devices cleared under the same product codes DZE and FRN with **K222778** and **K223607**, but these devices were cleared in 2023. This example contrasts the significant differences in the amount of information that is made available in the 510(k) Summary of recent submissions vs. older submissions and what the FDA expects to see in 510(k)s for these types of devices currently.

We suggest that you always review recent 510(k) summaries to get a better perspective on current FDA expectations for clearing a particular product code, even if you have elected to use an older predicate device in your 510(k) submission.

Example 2 – Differences in indications for use

In this example, we highlight how some devices under the same product code can be cleared with different indications for use while the intended use of the device remains the same. For this example, we use product code DZE (Implant, Endosseous, Root-Form) again, which falls under regulation number **872.3640**. Many of the devices cleared under this product code have significantly different indications for use depending on the design of implants, how they are to be used, and what sort of abutments are supplied with them as part of the overall dental implant system. Abutments are classified under product code NHA (Abutment, Implant, Dental, Endosseous) and regulation number **872.3630** and may be submitted in the same 510(k) with the implants.

The intended use of all endosseous dental implants is the same irrespective of their indications for use as described in part (a) Identification of its regulation. These devices are surgically placed in the bone of the upper or lower jaw arches to provide support for prosthetic devices, such as artificial teeth, in order to restore a patient's chewing function. The intended use of all endosseous dental abutments is the same irrespective of their indications for use as described in part (a) Identification of its regulation, as these devices are connected to the endosseous dental implant and intended for use as an aid in prosthetic rehabilitation.

Table 1 shows the indications for use statements for three different endosseous dental implant systems (implants + abutments) cleared by the FDA, and the difference in their indications for use, while the intended use of these devices remains the same as described in part (a) Identification of 872.3640 and 872.3630 for the implants and abutments, respectively.

Table 1 – Cleared indications for use for dental implant systems (product codes DZE + NHA)

510(k) number	Indications for use
K231426	8plant Implant System is indicated for use in partially or fully edentulous mandibles and maxillae, in support of single or multiple unit restorations, including cemented retained, screw-retained, or overdenture restorations and final or temporary abutment support for fixed bridgework. It is intended for delayed loading. Implant bodies with a diameter of 5mm or more are intended to be used in the molar region.
K233137	Ticare Dental Implant Systems are endosseous dental implants intended to be implanted in the maxilla or mandible jaw bone to serve as a union between the jaw bone and a dental prosthesis for partial or total replacement of teeth in edentulous patients. They are indicated for single-stage or two-stage procedures to support screw-retained restorations and can be used for immediate loading when good primary stability is achieved and with appropriate occlusal loading. Small diameter (3.3mm) implants are indicated to replace a lateral incisor in the maxilla and/or a central or lateral incisor in the mandible and should not be used in the molar region. Ticare Osseous Quattro and InHex Quattro implants are indicated to support permanently fixed restorations. Ticare Inhex and Osseous implants of 6 mm length are intended for use in a two-stage surgical procedure and are indicated for delayed loading to support permanently fixed restorations. These implants are indicated only for straight abutments.
K223714	UniFit Dental Implant System is intended for surgical placement in the maxillary and/or mandibular arch to support crowns, bridges or overdentures in partially or completely edentulous patients to restore masticatory function. UniFit Dental Implants may be immediately loaded when good primary stability is achieved and with appropriate occlusal loading. UniFit short implants (6 mm L) are intended to be used only with straight abutments. All digitally designed custom abutments for use with Ti Base abutments or Pre-milled Blank abutments are to be sent to an Adin Dental validated milling center for manufacture.

Example 3 – Multiple predicate devices and product codes

Some 510(k)s need to be submitted with multiple product codes to cover the different features of the device and in situations like this more than one product code will be listed on the 510(k) landing page for that device, with two categories of product codes identified. The classification product code (aka the primary product code) for the primary predicate device and any subsequent product code(s) (aka the secondary product code(s)) for any secondary predicate device(s) used in the submission. As there can only be one primary predicate device and product code in a 510(k) submission, you want to locate a predicate device that has indications for use and technological characteristics that are the same (or most similar) to the new device, but any changes in the technological characteristics do not raise new questions of safety and effectiveness.

For this example, we use a device that was cleared under **K231086** that used primary product code **MWI** (Monitor, Physiological, Patient (Without Arrhythmia Detection Or Alarms) that is regulated in **870.2300** cardiac monitor (including cardio tachometer and rate alarm). This type of device can measure one or more patient physiological parameters in a healthcare or home setting. The device selected for this example can measure six different physiological parameters under six different secondary product codes as seen in **Figure 2**, which are further described in **Table 2**. Therefore, six other secondary product codes are included in this 510(k).

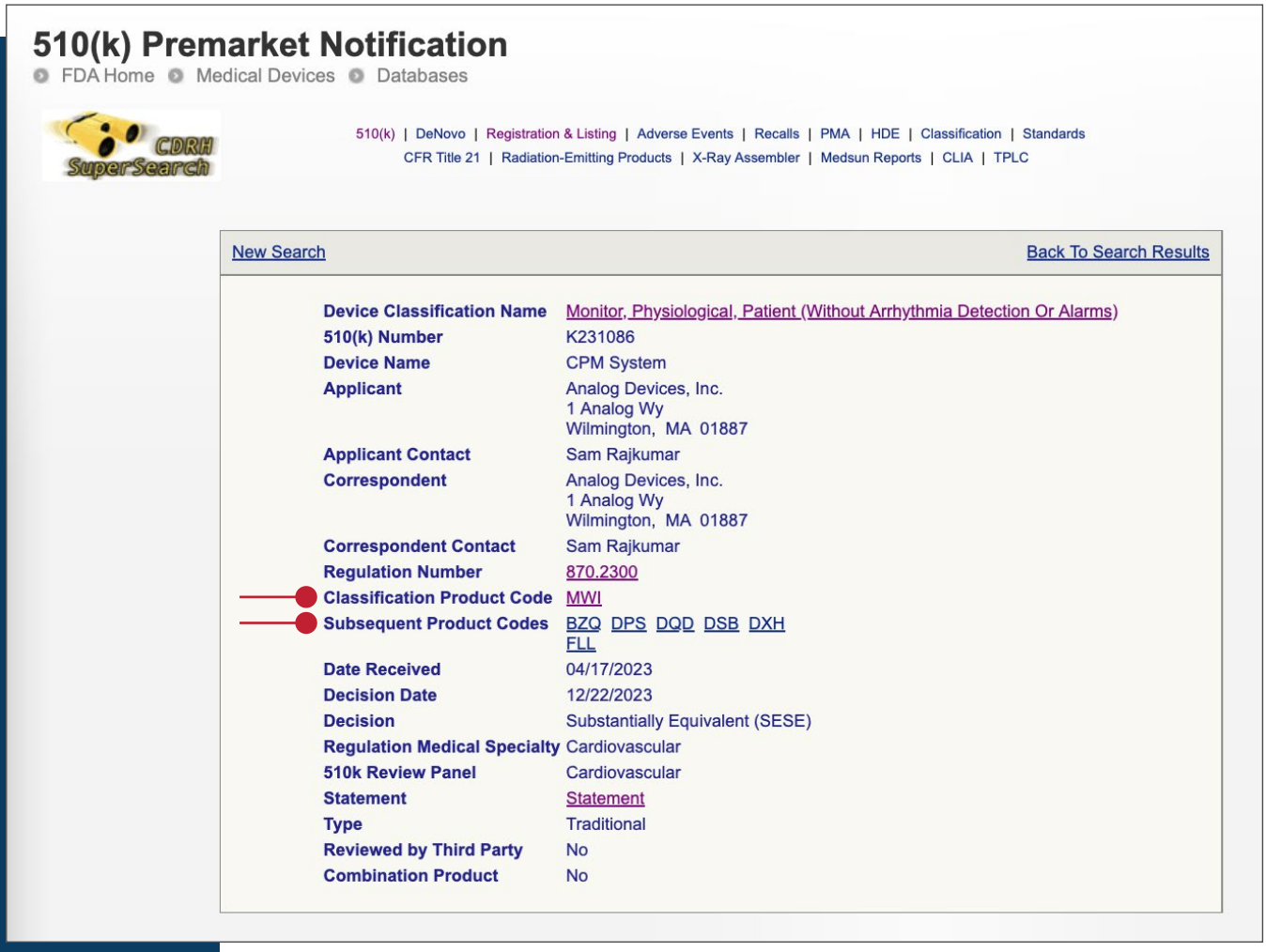

Figure 2 – Product Codes for Patient Physiological Monitor (K231086)

Table 2 – Product code descriptions used in K193391 (BeneVision Central Monitoring System)

Product codes	Regulations	Intended use	Indication for use
Primary product code			
MWI Monitor, Physiological, Patient (Without Arrhythmia Detection Or Alarms	870.2300	Used to measure the heart rate from an analog signal produced by an electrocardiograph, vectorcardiograph or blood pressure monitor.	See K193391
Secondary product codes			
BZQ Monitor, Breathing Frequency	868.2375	Used to measure or monitor a patient's respiratory rate.	
DPS Electrocardiograph	870.2340	Used to process the electrical signal transmitted through two or more electrocardiograph electrodes and to produce a visual display of the electrical signal produced by the heart.	
DQD Stethoscope, Electronic	870.1875	Used to project the sounds associated with the heart, arteries, and veins and other internal organs.	
DSB Plethysmograph, Impedance	870.2770	Used to estimate peripheral blood flow by measuring electrical impedance changes in a region of the body.	
DXH Transmitters And Receivers, Electrocardiograph, Telephone	870.2920	Used to condition an electrocardiograph signal so that it can be transmitted via a telephone line to another location.	
FLL (Thermometer, Electronic, Clinical)	880.2910	Used to measure the body temperature of a patient by means of a transducer coupled with an electronic signal amplification, conditioning, and display unit.	

Summary of examples 1-3

In Example 1 we saw how an older predicate device may not have much, if any, relevant information on the technical characteristics of that device in the FDA database. Technical characteristics are key requirements for demonstrating substantial equivalence in a 510(k). The lack of significant information is also true for the type of performance testing the predicate device went through.[12] Therefore, whether selecting a relatively new predicate device or an older one for use in a 510(k) submission, it is always best to look at the most recent 510(k) clearances for a particular product code to get a better understanding of the type of information the FDA will expect to see for that product code.

In Example 2 we saw how differences in indications between devices cleared under the same product code cannot change the intended use of the new device when compared to the predicate in order to be considered a potential predicate device.

In Example 3 we saw how some 510(k) submissions need more than one product code, but only one of the product codes can be designated as the classification or primary product code from which a primary predicate device must be selected. Other product codes are designated as the subsequent or secondary product codes to cover the other technological features of the device.

It should be noted that if the new device being submitted under a 510(k) based on its classification product code also has a new intended use and/or new technological characteristics that are different than other devices cleared under the same classification product code, and the level of risk this device would pose to the patient/user is considered low to moderate, the device may be a candidate for a De Novo Classification Request and should initially be discussed with the FDA under their Q-Submission Program.

Using reference devices in 510(k) submissions

Some device sponsors submitting a 510(k) to the FDA may need to use a reference device in their submission to clear their device. In this section we discuss what a reference device is and what it is not, and when it can be used in a 510(k).

As described in the FDA's guidance document, **The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]**, a reference device is not considered to be a predicate device and cannot be used to address decision points 1-4 on the 510(k) Decision-Making Flowchart found in Appendix A (page 27) of the guidance (legally marketed, same intended use, and no different questions related to safety or effectiveness based on technological characteristics). A reference device can only be used in a 510(k) after decision point 4 of the SE flowchart (that is to consider whether methods are acceptable and data demonstrates substantial equivalence) to support scientific methodology or standard reference values.

The FDA's guidance defines a reference device as:

A legally marketed device that is intended to provide scientific and/or technical information (e.g., test methodology) to help address the safety and effectiveness of a new technological characteristic. Reference devices are not predicate devices and may only be used after Decision Point 4 on the 510(k) Decision-Making Flowchart.

If a reference device is used in a 510(k) submission, it should be identified in the appropriate sections of the submission including the 510(k) Summary.

Below are some examples of the use of reference devices in 510(k) submissions.

Example 4 – Dental implant coating

Company XYZ wants to submit a 510(k) for their dental implant system under product code DZE (+ NHA for their abutments) and has three different product families of titanium implants in different sizes (diameters and lengths) and shapes as each product family is for specific indications for use. One of the three product families of dental implants has a hydroxyapatite (HA) coating that is applied to the titanium threads of the implants to enhance osteointegration of the patient's bone to the implant surface. Company XYZ has identified a predicate device with all of the same sizes of implants with similar shapes as their proposed implants that were also cleared for the same indications for use, except none of the predicate implants are coated with HA to enhance osteointegration. Instead of trying to find another predicate device with the same indications for use in all of the same sizes and shapes, including some with HA coating, company XYZ was able to locate another titanium dental implant system cleared under product code DZE that uses HA to coat the threads of their dental implants to enhance the osteointegration process. Company XYZ selects this cleared device as a reference device to support the scientific methodology of coating titanium dental implants with HA.

Example 5 – Surgical gown durability testing

Company XYZ manufactures reusable surgical gowns made of polyester that are classified under product code FYA and wants to submit a 510(k) for them. As these devices can be used up to 50 times, they are provided nonsterile to the end user and are required to be reprocessed and sterilized after each use. The durability testing requirements for these surgical gowns are described in the FDA-recognized standard, ANSI AAMI PB70:2012 Liquid barrier performance and classification of protective apparel and drapes intended for use in healthcare facilities, and the new surgical gowns must demonstrate a barrier level of protection with a rating of the appropriate barrier level when tested. Company XYZ selected a predicate that is a single-use disposable gown that is made from polyester. However, since the predicate device is a single-use device that is supplied sterile to the end user, durability testing for that device is not required. Therefore, a reusable reference device that also underwent durability testing would be needed for this 510(k).

Summary of examples 4-5

In Example 4, we saw how a technological feature such as HA coating, has a long history of being applied to the surface area of the threads of titanium implants to enhance the process of osteointegration of the patient's bone to the implant surface. In the case of Example 4, because the primary predicate device did not use any HA coating a reference device was introduced to the 510(k) to cover this technological feature.

In Example 5, we saw how a manufacturer of non-sterile, reusable surgical gowns that can be reprocessed by the end user up to 50 times selected a sterile, single-use primary predicate device for their 510(k) submission. Because the new device can be reprocessed up to 50 times, it needed to undergo durability testing by an FDA-recognized consensus standard, which the primary predicate device did not need to undergo. Therefore, a reusable surgical gown that underwent the same durability testing as the new device was selected as a reference device for inclusion in the 510(k) to demonstrate the durability of the new device.

Summary

We have discussed some of the challenges regarding predicate device selection under the FDA's 510(k) premarket notification pathway. While selecting an appropriate predicate device for a 510(k) submission can often be a fairly easy exercise, there are also times when identifying an appropriate predicate device for a 510(k) submission may prove challenging and require additional time and research. In cases like this, more than one predicate device and/or a reference device may be needed in the 510(k) submission.

End Notes

1. Electronic Submission Template for Medical Device 510(k) Submissions
2. How to Prepare a Traditional 510(k)
3. The Special 510(k) Program
4. The Abbreviated 510(k) Program
5. Is a new 510(k) required for a modification to the device?
6. Premarket Submissions: Selecting and Preparing the Correct Submission
7. Premarket Notification 510(k)
8. The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]
9. Best Practices for Selecting a Predicate Device to Support a Premarket Notification [510(k)] Submission
10. How to Find and Effectively Use Predicate Devices
11. 510(k) Premarket Notification (fda.gov)
12. Recognized Consensus Standards: Medical Devices

About the author

Stuart R. Goldman has over thirty years of combined RA/QA experience in medical devices, including fifteen years in industry working on high-risk Class III/II implantable devices. At Emergo by UL, Stuart focuses on the United States market and has extensive expertise in device classification and testing requirements; regulatory pathway strategies; Q-Submissions and clearance of over forty 510(k)s and submission of over twenty 513(g)s.

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