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Premarket Notification 510(k)

The most common route to product registration in the USA

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HOW TO CHOOSE THE CORRECT REGISTRATION ROUTE?

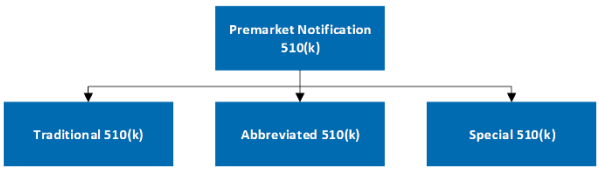
The correct registration route depends on your device and the associated risk. The following risk classes exist in the USA:

- Class I devices are subject to a comprehensive set of regulatory authorities called general controls that are applicable to all classes of devices.
- Class II devices are 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.
- Class III devices are 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 a premarket approval (PMA).

The premarket notification is the process by which a your device is classified into one of these three device classes. Each manufacturer who intends to market a class I, II, or III device for human use, for which a PMA is not required, needs to file a premarket notification. *Note: Some devices are 510(k) exempt.*
In practice, it is often the case that the risk class of the device is already known. Therefore, the theoretical part of the classification of the device within the PMN in class I, II, III is rather secondary.

In case you are unsure about your device class, a Pre-Submission is a useful option to discuss your ideas with the FDA prior submitting a 510(k). The FDA offers this option so that you can clarify your registration strategy or other questions regarding the registration with the FDA in advance. Common aspects of the Pre-Sub are the choice of the predicate device, level of concern for software, and the risk class.

WHICH TYPE OF 510(K) IS THE RIGHT ONE FOR ME?



There are three different types of a 510(k). The most common type is the traditional one. An abbreviated 510(k) can be compiled when special controls or product specific guidelines are available. The special 510(k) is used to modify products that are already registered.

PREPARATION

Before you start to compile one of the three kinds of 510(k) as stated above, we strongly recommend to do some preparations.
The FDA groups products under product codes. Determine the correct product code and find out which regulatory requirements are associated to that code. Also, applicable product specific guidelines and recognized consensus standards may be found using the code.
Another important step is to determine applicable predicate devices. The premarket notification requires that you determine a predicate and that you can proof substantial equivalence to that device. In order to do so, sufficient information about the predicate are required. The predicate might be one of your own devices, then it´s easy to have all information available – But in many cases it´s from another manufacturer and therefore having all required information is much more difficult. It can be necessary to buy a predicate and perform some bench tests to show equivalence. Since the 510(k) is based on the substantial equivalence decision of the FDA, take enough time to choose the predicate and ensure that you can really prove equivalence.

THE PREDICATE DEVICE

A premarket notification is a premarketing submission made to the FDA in order to demonstrate that your device is safe and effective by proving substantial equivalence to a legally marketed device (predicate device) that is not subject to Premarket Approval (PMA).
Within the 510(k), you compare your device to the predicate which is ideally a recently 510(k) cleared device. But in general, you can choose any legally U.S. marketed device as a predicate. A claim of substantial equivalence does not mean your device must be identical to the predicate device. Substantial equivalence is established with respect to the following aspects: intended use, design, energy used or delivered, materials, performance, safety, effectiveness, labeling, biocompatibility, standards, and other applicable characteristics.
A good way to identify predicate devices is using the FDA 510(k) database. For example, you can use that database to search for similar (potentially equivalent) devices on the market, that you already know. Or, if you know the classification of your device, you can search by product code. That database is a good tool in identifying a predicate device.

SUBSTANTIAL EQUIVALENCE

Your whole PMN aims on receiving the SE-statement by the FDA. Thus, being able to prove substantial equivalence is of utmost importance. Luckily, a guidance on evaluating substantial equivalence in premarket notifications is available and provides valuable information that you should use for your 510(k).
As described before, for proving SE, you need to assess the differences between your device and the predicate device with respect to intended use, design, energy used or delivered, materials, performance, safety, effectiveness, labeling, biocompatibility, standards, and other applicable characteristics. We recommend to set up a table containing all these information in sufficient detail.

The following table shows exemplary headings that can be used for a table in the context of the SE discussion. This makes it possible to clearly compare each relevant aspect and assess whether the difference is permissible. It is important to determine whether the your device has the same characteristics as the predicate, and if not, whether the different characteristics raise different questions of safety and effectiveness.

Item of Comparison	Your device	Predicate	Discussion of differences

FORMAT

As with every authority, there are several formal aspects to consider when compiling a 510(k) for the FDA. It is important to stick to these formal requirements in order to prevent unnecessary delays during the submission.
There is a guidance on the format for traditional and abbreviated 510(k)s which clearly describes what chapters you need to include in your submission. This document is the basis for your traditional or abbreviated 510(k) and is a must-read in your project.
In case you are planning to compile a special 510(k), there is another guidance available describing the Special 510(k) Program.
Additionally, the FDA provides the e-Submitter software which is to be used to pack your submission electronically in an FDA-accepted format. Confusingly, the e-Submitter is not used to submit your 510(k). In order to do that, you need a free web-based tool provided by the FDA.

SUBMISSION

For submitting documents to the FDA, you need to create a WebTrader account with the FDA electronic submission gateway (ESG). WebTrader / ESG is the free online tool mentioned before and it is the same tool you need to use when reporting an incident to the FDA.

A checklist on what steps to perform is available online and needs to be followed stepwise. Special attention needs to be payed to the user name and the personal digital certificate.
The user name cannot be changed, but the assigned person to your account can. So, in case your user name is the name of a certain employee and that employee leaves your organization, you can assign another employee to the account. But the user name will always be as before.
The personal digital certificate is used for a secure transmission of your submission via the ESG. It´s a certificate with a private and a public key that in most cases needs to be payed on annual basis. There are different providers for theses certificates and we recommend to compare these before choosing one.
After setting up the WebTrader account, you need to setup your PC for the electronic submission gateway by installing the client you can download after logging in into your WebTrader account.

After compiling the content of the 510(k), the eSubmitter packs it into an accepted format. That package is then submitted to the FDA using the WebTrader account via electronic submission gateway.

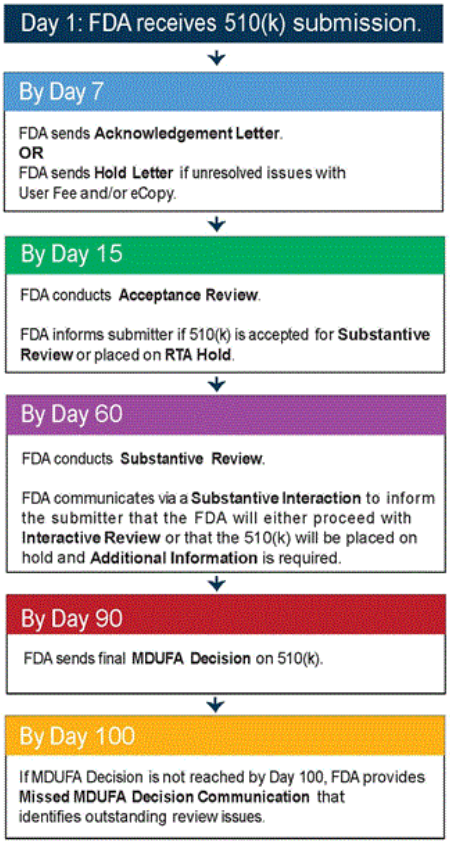
SEQUENCE OF A PREMARKET NOTIFICATION

There are different steps on the way to product registration by means of a PMN. The following points provide an overview of the typical process.

1) Pre-Submission (optional)
2) Compile and submit the PMN
3) Refuse to accept policy (within 15 days)
4) 510(k) review by the FDA
5) Letter of substantial equivalence (SE) or non-substantial equivalence (NSE)

TIMELINE

The FDA provides information on the timeline of communication during a traditional and abbreviated 510(k) review summarized in the following figure:



Note: Days are calendar days.

The review durations for different submission types are as follows:

Pre-Sub	75 – 90 d.
Traditional & Abbreviated 510(k)	90 days
Special 510(k)	30 days

These timelines represent the timelines for the FDA. In some cases, the 'clock' may be stopped. For example, this is the case when during substantive review, an additional information request is sent by the FDA allowing the manufacturer to respond within 180 days. In that case, of course, the clock for the FDA timelines is on hold.

ACCEPTANCE REVIEW

The FDA conducts an acceptance review within 15 calendar days after your submission. During that time, the FDA verifies formal aspects of your submission. In case the 510(k) does not meet these formal requirements, the FDA sends a so-called RTA Hold Letter. Then you have 180 calendar days left to respond. Otherwise, the 510(k) will be withdrawn and the submission is closed by the FDA.
In order to avoid a RTA Hold Letter, the FDA provides specific RTA checklists for a traditional, for an abbreviated, and for a special 510(k).

SUBSTANTIVE REVIEW

By day 60, the FDA conducts a substantive review of your submission. There are two ways how the FDA may proceed.

1) The 510(k) will not be placed on hold and deficiencies will be resolved during an interactive review. This is an information interaction between the FDA and the manufacturer during the submission.
   During an interactive review, it is very important to respond in a timely manner.

2) The 510(k) will be placed on hold and the FDA sends an AIR (additional information request). The AIR outlines the outstanding deficiencies that need to be addressed, such as missing test data required to demonstrate substantial equivalence. The timeframe to respond is 180 calendar days.

510(K) CLEARANCE

After successfully passing the substantive review, the product is 510(k) cleared. The FDA publishes the substantial equivalence letter together with an indications for use form and the 510(k) summary or 510(k) statement on their website. These are the information you might already know from the predicate device after using the 510(k) database.

ABOUT THE AUTHOR

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Please do not hesitate to contact us for further information. We look forward to facilitating your access to the US market!

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