US FDA Regulation of Medical Devices: The Basics

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What is a medical device?

The US Food, Drug and Cosmetic Act (Act) defines a device as:

"…an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is—

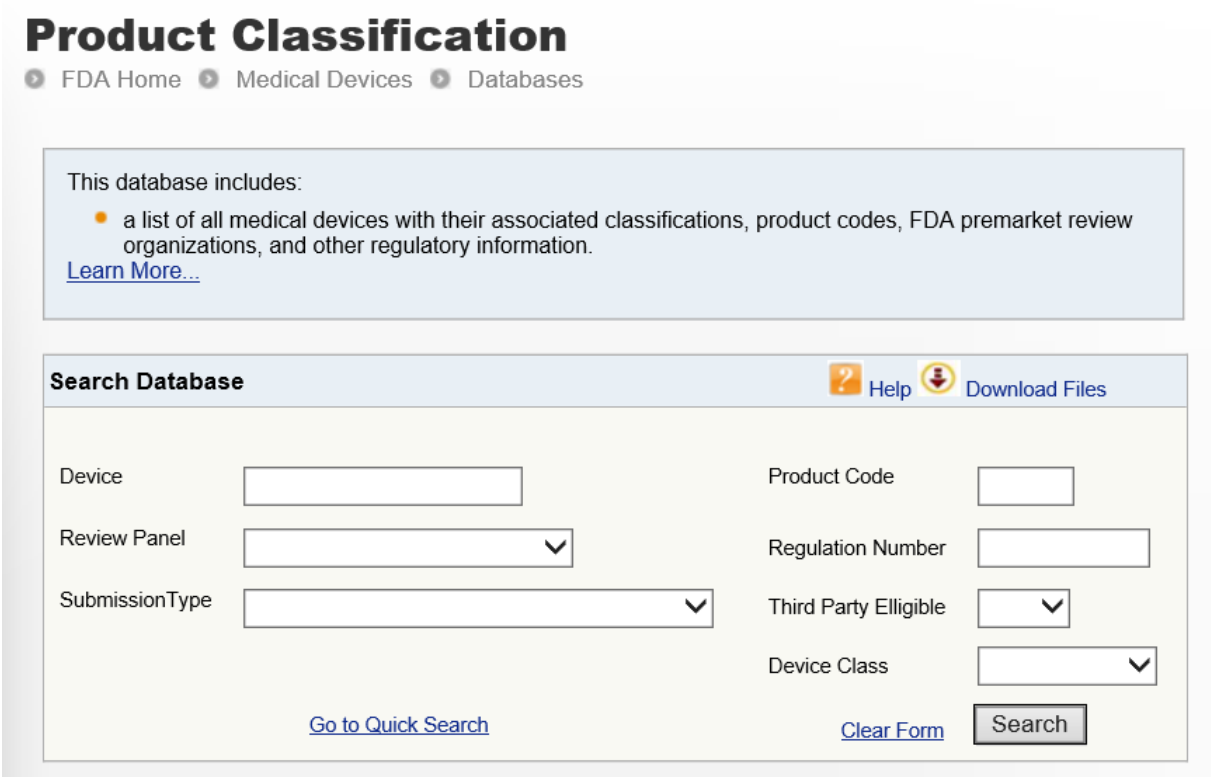
1. *recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,*
2. *intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or*
3. *intended to affect the structure or any function of the body of man or other animals, and*

which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes".

FDA regulates medical devices based on risk

- Section 513(a)(2) of the Act requires FDA to determine safety and effectiveness of a device by weighing any probable benefit to health from the use of the device against any probable risk of injury or illness from the use
- FDA has established classifications for approximately 1,700 different generic types of devices and grouped them into 16 medical specialties referred to as panels.
- Each of these generic types of devices is assigned to one of three regulatory classes based on the level of control necessary to assure the safety and effectiveness of the device.

FDA's Classification Database



http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPCD/classification.cfm

Classification

- If you are not sure how to classify your device, you can submit a 513(g) request to FDA, and within 60 days FDA will provide you with information about how they believe the device is classified.

  http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM209851.pdf

- If you are not sure if your product is a drug, biologic, or device, you can submit a "Request for Designation" to the FDA Office of Combination Products.
  - In the RFD you should define the "primary mode of action (PMOA)" of your product
  - FDA will use the PMOA to determine which FDA center has the lead and which regulatory authorities (drug, device, biologic, or a combination) will apply.

    http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM251544.pdf

Determining submission type

Class	Premarket requirement
I	Exempt from premarket review, unless 510(k) is specifically required by regulation
II	Requires a 510(k), unless specifically exempted by regulation
III	Requires a PMA or an HDE

510(k)

Background: 510k

- A 510(k) must demonstrate that a new device is “substantially equivalent” to a “predicate device”

- A predicate device is a legally marketed device that does not require a PMA, including:
  - A device that has been cleared by FDA (most common approach)
  - A device that was legally marketed prior to the 1976 medical device amendments (you must provide evidence)
  - A device that has been classified by a de novo petition
  - A device that has been reclassified by FDA from Class III to Class II

Background: 510k

- A device is substantially equivalent to a predicate device if:
  - It has the same intended use, AND either
    - Has the same technological characteristics as the predicate, OR
    - Has different technological characteristics and the information submitted to FDA:
      - does not raise new questions of safety and effectiveness; and
      - demonstrates that the device is at least as safe and effective as the legally marketed device.

Prepare the 510(k) submission

- FDA has strict requirements about what must be included in a 510(k) submission. If your submission is not administratively complete, FDA will refuse to accept (RTA) it.
- You must pay the required User Fee before making a 510(k) submission
- FDA generally requires both a paper copy and an electronic eCopy
- If this is your first 510(k) for a device, or you are making significant modifications or changing the indications for use for a previously cleared device, then you must submit a Traditional 510(k).
- If you are making modifications to a device that has been previously cleared, then you may be eligible to submit a Special 510(k).

The 510(k) review process

- FDA will determine if your 510(k) is administratively complete within 15 days and will notify you by email when the 510(k) is accepted
- FDA will generally complete its initial review of a traditional 510(k) submission within 60 days. You will be notified of any deficiencies that FDA identifies. FDA's review clock pauses at this point.
- You have 180 days to prepare your response. FDA does not grant any extensions. Once FDA receives your response, the review clock will start up again.
- FDA will then attempt to work with you interactively to address any remaining issues. FDA's performance goal is to review the majority of submissions in 90 total FDA days.
- If all issues can be resolved, FDA will issue a letter stating that your device has been found substantially equivalent (SE). If FDA is unable to determine that your device is substantially equivalent, FDA will issue a letter stating that your device has been found Not Substantially Equivalent (NSE).

De novo

- Devices that are low to moderate risk for which there is no predicate may be candidates for the “de novo” program
- This program allows FDA to classify new types of devices into Class I or Class II, if FDA determines that it can identify the appropriate special controls to ensure a reasonable assurance of safety and effectiveness
- From the perspective of a submitter, this generally involves more work than a 510(k), but much less than a PMA
- Some recent examples are: colon capsule imaging system, a foot wrap for restless leg syndrome, TENS for migraine, and a cooling device for lipolysis.

PMA

Background: PMA

- The regulatory standard that a PMA must meet is a "reasonable assurance of safety and effectiveness"
- PMAs almost always include clinical studies, and these studies must constitute "valid scientific evidence"
- Valid scientific evidence includes:
  - Well-Controlled Studies
  - Partially Controlled Studies
  - Objective Trials Without Matched Controls
  - Case Histories (rare)
  - Robust Human Experience (rare)

Typical pathway for PMA device

1. Conduct preliminary bench and proof of concept testing
2. Develop a clinical study plan
3. If the clinical study is to be conducted entirely within the US, submit an IDE for a feasibility study.
4. When the feasibility study is complete (either in US or OUS), develop an outline for the pivotal study and submit to FDA as a preSub.
5. When you are ready to begin the pivotal study, submit an IDE (if the study is to be done in the US).
6. You may chose to submit parts of the PMA as modules while you conduct your pivotal study. You should make every effort to minimize device changes during the pivotal study
7. After the pivotal study is complete, submit a prePMA to obtain FDA's comments on the layout of the PMA submission

“Typical” PMA review process

- Unless you meet the definition of a small business, there is a PMA User Fee that must be paid when the first module is submitted.
- FDA will conduct a “Filing” review to determine if the PMA is administratively complete, and then complete a full initial review within 90 days.
- If the PMA is complex or novel, FDA may take the PMA to apublic Advisory Committee meeting for review and recommendation.
- FDA’s review of a PMA also includes a review and inspection of your Quality System/Manufacturing procedures and facilities.
- FDA’s performance goals for PMA’s are to complete those that do not need an Advisory Committee meeting in 180 days, and those that do need such a meeting in 320 FDA days.

Useful websites

- CDRH Learn
  http://www.fda.gov/training/cdrhlearn/default.htm
- Device Advice
  http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/default.htm
- Registration and Listing
  http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/RegistrationandListing/default.htm
- User (MDUFA III) Fees
  http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MDUFAIII/ucm313673.htm
- Searchable 510(k) database
  http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm

Thank you!

In the beginner's mind there are many possibilities, but in the expert's mind there are few.
Shunryu Suzuki

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