5 Steps to Medical Device Commercialization in the U.S.

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1. Classify Device
2. Choose Premarket Submission
3. Prepare Premarket Submission
4. Premarket Submission to FDA
5. Registration and Device Listing
Step One: Classify Your Device
A medical device is defined by law in the section 201(h) of the FD&C Act

Medical devices are categorized into one of three classes, based on the degree of risk they present. These classes are:

• **Class I – Lowest Risk**
  An example of a Class I device is a manual toothbrush.

• **Class II – Moderate Risk**
  Examples of Class II devices are male condoms and non-invasive blood pressure monitors.

• **Class III – Highest Risk**
  An example of Class III device is a heart valve.
Most medical devices can be classified by finding the matching description of the device in **Title 21 of the Code of Federal Regulations (CFR), Parts 862-892.**

FDA has classified and described over 1,700 distinct types of devices and organized them in the CFR into 16 medical specialty "panels" such as Cardiovascular devices or Ear, Nose, and Throat devices.

http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/ClassifyYourDevice/ucm051530.htm
Class I General Controls
  • With Exemptions
  • Without Exemptions

Class II General Controls and Special Controls
  • With Exemptions
  • Without Exemptions

Class III General Controls and Premarket Approval

Note: Most Class I devices and a few Class II devices are exempt from the premarket notification [510(k)] requirements subject to the limitations on exemptions.
Classification Guidance

• The class to which your device is assigned determines, among other things, the type of premarketing submission/application required for FDA clearance to market.

• If your device is classified as Class I or II, and if it is not exempt, a 510k will be required for marketing.

• All devices classified as exempt are subject to the limitations on exemptions. Limitations of device exemptions are covered under 21 CFR xxx.9, where xxx refers to Parts 862-892.

• For Class III devices, a premarket approval application (PMA) will be required unless your device is a preamendments device (on the market prior to the passage of the medical device amendments in 1976, or substantially equivalent to such a device) and PMA's have not been called for. In that case, a 510k will be the route to market.
More Classification Guidance

- Device classification depends on the *intended use* of the device and also upon *indications for use*. For example, a scalpel's intended use is to cut tissue. A subset of intended use arises when a more specialized indication is added in the device's labeling such as, "for making incisions in the cornea". Indications for use can be found in the device's labeling, but may also be conveyed orally during sale of the product.

- Classification is risk based, that is, the risk the device poses to the patient and/or the user is a major factor in the class it is assigned. Class I includes devices with the lowest risk and Class III includes those with the greatest risk.

- As indicated above all classes of devices as subject to General Controls. General Controls are the baseline requirements of the Food, Drug and Cosmetic (FD&C) Act that apply to all medical devices, Class I, II, and III.
Step Two:
Choose the Correct Premarket Submission
Choose the Correct Premarket Submission

After device classification, you then select the premarket submission required for that regulation. The most common types of premarket submissions include:

- 510(k) (Premarket Notification)
- PMA (Premarket Approval)
- De Novo (Evaluation of Automatic Class III Designation)
- HDE (Humanitarian Device Exemption)
• Some Class I and most Class II devices require a 510(k). In a 510(k), the sponsor must demonstrate that the new device is “substantially equivalent” to a predicate device in terms of intended use, technological characteristics, and performance testing, as needed.

• Some Class I and Class II devices are exempt from 510(k) if they do not exceed the limitations of exemption stated in 21 CFR xxx.9, where xxx refers to 21CFR 862-892.
Most Class III devices require a PMA. A PMA is the most stringent type of premarket submission. Before the FDA approves a PMA, the sponsor must provide valid scientific evidence demonstrating reasonable assurance of safety and effectiveness for the device’s intended use.
De Novo provides a means for a new device, without a valid predicate, to be classified into Class I or II if it meets certain criteria.

For information on how to prepare and submit a De Novo request, please refer to these resources:

- FD&C Act, section 513(f)(2)
- Evaluation of Automatic Class III Designation (De Novo Process)
HDE – Humanitarian Device Exemption

HDE provides a regulatory path for Class III devices that are intended to benefit patients with rare diseases or conditions.

In order for a device to be eligible for an HDE, a sponsor must obtain designation as a Humanitarian Use Device (HUD), which is granted through application to FDA’s Office of Orphan Products Development (OOPD).
Step Three:

Prepare the Appropriate Information for your Premarket Submission to the FDA
Prepare the Appropriate Information for your Premarket Submission to the FDA

Resources

The FDA has developed several types of resources to help you prepare your premarket submission. These include the following:

• Device Advice -- comprehensive Web-based regulatory assistance

• CDRH Learn -- video-based series of teaching modules, seminars, and recorded webinars that cover a variety of policy and guidance efforts

• CDRH Pre-Submission Program -- prospective applicants of future premarket submissions may request feedback from the FDA through this program.
Information to Consider When Preparing your Premarket Submission

• Design Controls

• Nonclinical Testing

• Clinical Evidence

• Labeling
Design Controls

- All Class II and Class III devices must be designed in accordance with Design Controls under the Quality System Regulation (21 CFR 820.30).
- Some Class I devices are exempted from Design Controls.
- For guidance on Design Controls, please see: Design Control Guidance for Medical Device Manufacturers.
Nonclinical Testing

- The types of information and testing required to market your device are determined by the device classification, mechanisms of operation, technological characteristics, and labeling.

- Nonclinical testing performed in support of a premarket submission for a medical device must comply with the Good Laboratory Practices (GLPs) of 21 CFR 58.
Clinical Evidence

• PMAs, HDEs, some 510(k)s, and many De Novo submissions will require objective clinical evidence.

• Prior to initiating a clinical study, the study sponsor may need to obtain approval of an Investigational Device Exemption (IDE) by the FDA. This will depend on the risk of the device.

• The study will also need to be approved by the appropriate Institutional Review Board (IRB).

• Clinical studies must comply with all applicable IDE regulations and Good Clinical Practices (GCPs).

• For additional information on the IDE and GCP regulations, see Device Advice Investigational Device Exemption (IDE).
The labeling for a device must be written according to labeling regulations and included in your premarket submission.

For additional information, see [Device Labeling](#).
Step Four:

Send your Premarket Submission to the FDA
Once you have assembled the appropriate information necessary for your Premarket Submission, you send your submission to the FDA and interact with FDA staff during review.

- **User Fees:** There is a user fee associated with the submission of a 510(k) or a PMA.

- **eCopy:** Premarket submissions must include an electronic copy (eCopy) on a CD, DVD, or a flash drive.

- **Administrative Filing Review:** After a premarket submission is received, the FDA conducts an administrative review to assess whether the submission is sufficiently complete.

- **Interactive Review:** While a submission is under review, FDA staff communicates with applicants to increase the efficiency of the review process.
Table 1 – Medical Device User Fees for FY 2016

<table>
<thead>
<tr>
<th>Application Type</th>
<th>Standard</th>
<th>Small Business</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premarket Application (PMA, BLA, PDP)</td>
<td>261,388</td>
<td>65,347</td>
</tr>
<tr>
<td>Premarket Report (for a reprocessed single-use device)</td>
<td>261,388</td>
<td>65,347</td>
</tr>
<tr>
<td>Panel-Track PMA supplement</td>
<td>196,041</td>
<td>49,010</td>
</tr>
<tr>
<td>BLA Efficacy Supplement</td>
<td>261,388</td>
<td>65,347</td>
</tr>
<tr>
<td>180-Day PMA Supplement</td>
<td>39,208</td>
<td>9,802</td>
</tr>
<tr>
<td>Real-Time PMA Supplement</td>
<td>18,297</td>
<td>4,574</td>
</tr>
<tr>
<td>Premarket Notification (510(k))</td>
<td>5,228</td>
<td>2,614</td>
</tr>
<tr>
<td>30-day notice</td>
<td>4,182</td>
<td>2,091</td>
</tr>
<tr>
<td>513(g) request for classification information</td>
<td>3,529</td>
<td>1,765</td>
</tr>
<tr>
<td>Annual fee for periodic reporting on a class III device</td>
<td>9,149</td>
<td>2,287</td>
</tr>
</tbody>
</table>

**Establishment Registration Fee** - There is no reduced fee for a small business. If this is the only fee you expect to pay during FY 2016, do not submit an FY 2016 Small Business Qualification and Certification request.

<table>
<thead>
<tr>
<th>Type of Fee</th>
<th>Annual Fee</th>
</tr>
</thead>
<tbody>
<tr>
<td>Establishment registration fee</td>
<td>3,845</td>
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</tbody>
</table>
Typical Review Times

Initial Traditional or Modular PMA

• 140 days for manufacturing section review and site inspection
• Assumes one 30 day cycle to address deficiencies
• Greater delay if deficiencies are not addressed satisfactorily or on time

PMA Supplements (Changes)

• Small changes can be handled in 30 or 135 days
• Major changes take 180 day review and may require an additional site inspection
510(k) Review Times

- Traditional 510(k) requires 90 days
- Feedback at 60 days
- Request for Additional Information allows 30 days for response, may allow up to 180 days.
- Failure to respond within 180 days and must start over.
Changes to Approved 510(k) Devices

Minor Design Changes

• Use Special 510(k)
• 30 day review

Changes in Intended Use or Technology

• Use Abbreviated 510(k) if Guidance Documents or Consensus Standard are applicable
• Traditional 510(k) for all other cases
• Same 90 day review for both

New Draft Guidance Issued

Step Five:
Complete the Establishment Registration and Device Listing
• A device facility must register its establishment and list its devices with the FDA.

• If a device requires premarket clearance or premarket approval prior to marketing (i.e., the medical device is not exempt), the device firm must wait until it receives FDA clearance or approval before registering and listing.

• Registration of a device establishment, assignment of a registration number, or listing of a medical device does not in any way denote clearance or approval of the establishment or its products by the FDA.
FDA Inspections

FDA inspections are based on priority

- Manufacturer with pending PMA approval
- Class III manufacturer never inspected
- Compliance Follow Up/For Cause Inspections
- Manufacturer of High Risk Devices

Class III device manufacturer should expect FDA to visit every 2 years

Programs to reduce FDA inspection work load include

- ISO 13485:2003 Voluntary Audit Report Submission Pilot Program
- Single Audit Program (MDSAP)

No additional fees for FDA inspections
Additional Market Entry Requirements

- OSHA and local regulations govern safety in the workplace – hospital or medical office.

- FCC regulates interstate and international communications by radio, television, wire, satellite and cable in U.S.

- NFPA and NEC provide consensus standards addressing fire and electrical safety.