Medical Devices: Roadmap to Market
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The last installment of Regulatory 360 discussed the FDA organization in general — where it came from and a broad overview of how it operates, as well as how it affects product development and marketing. This installment of the series looks further into medical device regulation, beginning with classification, premarket notice, and premarket approvals — the first steps in bringing your product to the marketplace.

The medical device landscape is extremely broad and, as discussed last month, the FDA attempts to tailor the approval process to the particular risks of the device. It is not a perfect system, but given the vastness of the device field, it makes some inroads into the effective application of effort and resources according to the degree of risk presented by a given category of device.

Medical devices are classified into different categories: Class I, General Controls (with and without exemptions); Class II, General Controls and Special Controls (with and without exemptions); and Class III, General Controls and Premarket Approval. But what does this mean for a manufacturer? In short, your device's classification is its roadmap to the market, informing you whether the submission of an application for approval will be required and the pre-market steps your company will need to complete.

This article examines how the regulatory process changes with the particular device at issue by examining a few different sample products.

What is a medical device?

How can you be sure your product is actually a medical device? Sometimes it is obvious, for example, if you are manufacturing a pacemaker. What about less complex and less inherently “medical” products? The FDA defines a medical device as “an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is (1) recognized in the official National Formulary, or the United States Pharmacopoeia, 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 any of its primary intended purposes.” 21 USC § 321(h).

By definition, the intended use of the product often determines whether the product is regulated as a device. If you are making a product that is intended to affect a disease of
the body or mitigate disease symptoms, or to affect a normal structure or function of the body in a physical manner – meaning that the product is not ingested or absorbed into the body and metabolized to produce its effects, which would be a chemical mode of action – then your product is likely a medical device.

What does it mean to affect disease or to affect a structure or function of the body? How can you be sure your product has a physical mode of action? Think about products you use every day, such as a toothbrush, for example. A toothbrush is intended to clean the teeth, removing bacteria and debris that can lead to cavities or gum disease. The teeth are a structure of the body, and by brushing your teeth, you are physically removing materials that might otherwise cause this structure to become diseased. As such, a toothbrush is a medical device.

Once you realize you have a medical device on your hands, you must determine how the FDA classifies your device – you need to set your roadmap to market. This can be difficult to get a handle on in the abstract, so the following examples illustrate device classification in action.

**Device Classification**

**Example 1: Teething Ring (Non-fluid filled)**

Medical devices cover nearly every corner of the consumer product market. Teething rings are just one example. The hypothetical product is a simple food grade, nubby, solid plastic ring – something that most people might never think would be governed by FDA regulations. However, think back to the toothbrush analysis above. Teeth are a structure of the body, and development of teeth is a normal function; further, pain is a normal side effect of teething. Non-fluid filled teething rings work in two ways. First, the baby’s repetitive biting on the textured ring can help to soften the gum tissue, making it easier for the teeth to break through. Second, the nubby textures and the pressure of biting on the ring can help to soothe teething pain. Given these intended functions, teething rings are medical devices subject to FDA regulation.

In order to confirm the analysis, the next step is to consult the FDA [Medical Device Classification Database](#) to see whether and how the product is classified. Within the
search box, as shown below, you can enter a general term in the “Device” field, and any classifications containing that term will be returned. For this product, enter “teething” and discover two regulated categories of products—fluid filled and non-fluid filled teething rings.

From the results screen, one can see the device class, and clicking on the appropriate product link provides the remainder of the information needed to complete the product’s roadmap.
What does this screen reveal?

- The device is a Class I device and regulated per 21 CFR § 872.5550.
- It is exempt from the 510(k) premarket notification process; therefore it is not necessary to notify the FDA that the product is intended to be marketed.
- The device is subject to Good Manufacturing Practices, so the manufacturer will need to develop and implement an appropriate quality system.
- The manufacturer is required to register its establishment with the FDA and provide a list of all regulated products manufactured in its establishment.
- As a medical device, the product must be appropriately labeled as required per 21 CFR § 801 et seq., which applies to all regulated devices.

When marketing a Class I, exempt device, the roadmap is quite simple. But what if the device is just slightly different—for example, a fluid filled teething ring?

**Example 2: Teething Ring, Fluid Filled**

Photo courtesy of diapers.com
The analysis remains the same—the product is a medical device, but how does the roadmap change with the addition of freezable fluid to the mix?

The addition of fluid to the teething ring has:

- Modified the classification of the device from Class I to Class II;
- Removed the 510(k) exemption, so that now a premarket notification submission and finding of substantial equivalence by the FDA is required; and

**The 510(k) Premarket Notification**

The 510(k) as a regulatory mechanism applies to an extraordinary breadth of the device market, covering some devices in all three classes. For example, a Class III automated external defibrillator, the intended use of which is to restore a normal cardiac rhythm following an incidence of cardiac arrest, also enters the market by way of the 510(k), just as the fluid-filled teething ring does. For this reason, the Center for Devices and
Radiological Health (CDRH) within the FDA has a number of different evaluative review panels so that experts in each branch of medicine are reviewing technology in which they have developed expertise. While the teething ring would be reviewed by the dental review panel, the defibrillator would be reviewed by the cardiovascular review panel.

The 510(k) is the document through which a company notifies the FDA of its intent to market a medical device and provides the FDA with sufficient evidence to demonstrate that the new product is “substantially equivalent” to a product already on the market by means other than approval of a full premarket application. This predecessor device is referred to as a “predicate.”

A finding of “substantial equivalence” indicates that the new product is at least as safe and effective for its intended use as the predicate device. A device will be considered “substantially equivalent” if 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
- Has different technological characteristics, BUT
  - Does not raise new questions of safety and effectiveness AND
  - Demonstrates that the device is at least as safe and effective as the predicate.

As seen here, the second option offers great flexibility to manufacturers in terms of what can be used as a predicate device. The new device can be quite different from the predicate as long as the intended use and safety and effectiveness profile are consistent. A 510(k) filing is required not just when a product enters the market, but also when the product is changed or modified in a way that significantly affects its intended use and/or safety and efficacy.

There are three types of 510(k)s: traditional, special, and abbreviated. The special and abbreviated 510(k)s were created with the intent of streamlining the process, and are available in limited circumstances. The traditional 510(k) is governed by 21 CFR § 807.87. There is no form to complete; rather, the regulations spell out the elements of the document that must be submitted for review. The FDA has also prepared a Guidance Document to assist industry participants in drafting appropriate 510(k) submissions. See “Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s,” available here. More than 95% of 510(k) submissions that are cleared will be cleared within a year; the review process timeline varies, but is averaging around 140 days. A product subject to the 510(k) requirement may not be marketed until the submitter receives notice of substantial equivalence from the FDA.

**Premarket Approval**
The highest FDA scrutiny is reserved for devices presenting the greatest risk. The earlier example of the toothbrush illustrates circumstances when a device has a preventive purpose. However, in the event a tooth becomes diseased despite preventive measures, greater intervention is required, perhaps through a root canal.

**Example 3: Root Canal Filling Resin (with Chloroform)**

As seen above, root canal filling resin, when it contains chloroform as an ingredient, is a Class III medical device. Note in the “Submission” field, a Premarket Application (PMA) is required.

PMAs are reserved for devices that support or sustain life, or that present a significant risk of illness or injury with appropriate use. A PMA requires significant scientific evidence of the device’s safety and effectiveness for its intended use. It more closely resembles a New Drug Application than a 510(k) in its preparation, requiring substantial technical and clinical data in support of its approval. As with the 510(k), the FDA has published numerous Guidance Documents intended to assist industry in PMA preparation, which are available on the FDA’s website. By regulation, the FDA allocates 180 days for reviews of PMAs, but in practice, that timeframe is generally longer; the average review time is more than one year.
Asking for FDA Assistance

The FDA recognizes the challenges inherent in this process and has developed procedures through which industry participants can seek CDRH counsel regarding the FDA’s opinion on the appropriate classification and premarketing steps required for their devices. This process is referred to as the “513(g),” as it is codified in Section 513(g) of the FDA Act (21 USC § 360c(g)). Under a 513(g), the FDA will respond to requests for information within 60 days, although the response will be limited to questions asked and only as they relate to device classification and the premarket requirements. The FDA will not address matters of safety, efficacy, substantial equivalence, or clinical data requirements, nor will any such material be reviewed pursuant to a 513(g) request for information. The 513(g), like 510(k)s and PMAs, is subject to a user fee.

Conclusion

Although the medical device market is extremely broad and diverse, entrance to the market is not always a simple and straightforward process. The key is establishing a proper identity and classification for a device in order to set a clear path forward, allowing the device-maker to gather the most appropriate data and prepare the best possible submission to the FDA, if one is required. In the event the path remains unclear, the FDA has endeavored to assist industry both through numerous guidance documents and through direct contact per the 513(g) process. Also consider taking advantage of the resources available through Medmarc’s Loss Control Department, whether in our publications, listening to archived webinars, or through our staff.

Next month’s series installment will further discuss bringing a product to the market and will provide an overview of clinical trials.

http://www.emergogroup.com/research/fda-510k-review-times-research

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