

Medical Device Regulation: A Review

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It is sometimes taken for granted that the devices used in practice are safe and effective. It was not all that long ago, however, that medical devices were not subjected to the regulatory scrutiny that is required today. Medical devices first came under the US Food and Drug Administration's (FDA) authority with the passage of the Food, Drug, and Cosmetic Act in 1938; however, the FDA was given the right only to remove adulterated or misbranded products and could not prevent medical devices from being commercialized.

Although many of the devices available in 1938 when the act was passed were simplistic, making any defects easily noticeable, the technology boom following World War II prompted an increase in medical devices and their complexities. At this time, it became clear that more regulation on the safety and effectiveness of devices would be necessary. A government report documenting more than 10 000 injuries resulting from medical devices in the early 1970s,^{1,2} the thousands of women injured by the Dalkon Shield intrauterine device, and other therapeutic disasters prompted the Medical Device Amendments Act of 1976, giving the FDA the authority to approve medical devices. Consequently, the approval and regulation procedures for drugs and devices are separate and regulated by the Center for Drug Evaluation and Research and the Center for Devices and Radiological Health, respectively.

CLASSIFYING A MEDICAL DEVICE

The 1976 amendments defined 3 regulatory classes: Class I, class II, and class III devices (Table 1). These classes place devices according to their degree of risk—the higher the class, the greater the degree of regulation.² Device classification is also based on the intended use and indications for use of the device and will determine the type of premarketing strategy required for FDA clearance or approval.³ All 3 classes are subject to general controls, conditions of the 1976 amendments to the Food, Drug and Cosmetic Act of 1938 that require devices to be properly packaged and labeled, be suitable for the proposed use, be manufactured under a quality system, and be listed with the FDA.⁴ These

controls also state that in order to market a class I, II, or III device that does not require premarket approval (PMA) and is not exempt, a premarket notification must be submitted. The notification is commonly called a 510(k) after the section of the Food, Drug and Cosmetic Act that outlines its use.

Class I devices require the least regulatory control, as they are low risk and are subject to general controls only.⁴ Class II devices are moderate-risk devices and comply with special controls in addition to general controls, including special labeling requirements and mandatory performance standards.⁴ Class III is the most rigorous regulatory category, as devices in this category are considered high risk. Devices in Class III include many implantable devices, products that are life-supporting, and other diagnostic devices that pose considerable risk of illness or injury.^{4,5} In general, Class III devices require PMA, including extensive safety and effectiveness data in humans.

THE 510(K), DE NOVO, AND PMA PROCESSES

Most class II and class III devices enter the market through 1 of 2 pathways: through a 510(k) notification by demonstrating substantial equivalence to a previously cleared or legally marketed "predicate" device, or through a PMA by demonstrating safety and effectiveness. Some devices, however, are exempt from these procedures, and others may achieve marketing authorization through the de novo process, described below.

Class I and class II devices are cleared through the 510(k) process, which demonstrates that the device is as safe and effective (ie, substantially equivalent) as a predicate device.⁶ Devices are considered substantially equivalent if they have either the same intended use and materials as a predicate device or have the same intended use with different materials but a similar safety and efficacy profile.⁶ Companies submitting 510(k) applications should compare and contrast the new device with predicate devices in order to establish substantial equivalence. Generally, most of the devices in class I and some class II devices are exempt from the premarket notification requirements;⁷ that is, they are

TABLE 1. RETINAL DEVICES AND THEIR CLASSIFICATIONS¹¹

Product Code	Device Name	Device Class
LPO	Gases Used Within Eye To Place Pressure on Detached Retina	Class III
HJO	Biomicroscope, Slit-lamp, Ac-powered	Class II
HKL	Retinoscope, Ac-powered	Class II
OBO	Tomography, Optical Coherence	Class II
HQB	Photocoagulator and Accessories	Class II
MLZ	Vitrectomy, Instrument Cutter	Class II
MYC	Ophthalmoscope, laser, scanning	Class II
HNQ	Hook, Ophthalmic	Class I

either nonaltered preamendment devices (considered to be “grandfathered” as they were marketed prior to 1976) or specifically exempted by regulation. Although considered exempt from the premarket notification process, such devices must still adhere to other general controls. A small number of class I devices are exempt from manufacturing in accordance with good manufacturing practices (GMP) but are still required to maintain complaint files and general record keeping obligations.⁷ Class III postamendment devices that are substantially equivalent to preamendment devices and do not yet require PMA data by the agency may also be marketed with a 510(k).

As part of the FDA Modernization Act of 1997, the de novo classification was added to provide an alternative pathway for novel devices. This classification process is for medical devices that are low to moderate risk but that have been placed in class III because no predicate exists,⁸ making them not substantially equivalent by default. If a novel device has received notification that it is not substantially equivalent as a result of a 510(k) submission, the submitter may put forward a de novo petition within 30 days requesting that the FDA make a risk-based assessment of the device.⁸ Should the de novo petition be granted, the device can be reclassified from class III into class I or II. Moving forward, devices that have been classified through this process can be used as a predicate for future 510(k) submissions.

A PMA is the second main route to market for medical devices and is reserved for class III devices to ensure their safety and effectiveness. One exception, as previously mentioned, is a postamendment class III device substantially equivalent to preamendment class III device for which the FDA has not published a regulation requiring a PMA, which can utilize a 510(k).

Because class III devices are high-risk, the path to market is much more stringent and typically requires that a device be approved rather than cleared, as is the case with a 510(k) application. Although the specific data required depend on the device under review, these applications almost always involve clinical data to support claims made for the device. Clinical studies utilizing investigational devices to collect safety and effectiveness data will require an investigational device exemption (IDE). IDEs are generally used to support a PMA, as few 510(k)s require clinical data, and they must be in place before a study is initiated. An IDE must be approved by the appropriate institutional review board, and if the study involves a significant risk device the FDA must approve the IDE as well.

PRESUBMISSION PROCESS

In July 2012, the FDA issued a draft guidance outlining the presubmission (presub) process, an extension of the agency's existing pre-IDE program. Instead of being limited to providing feedback prior to the intended submission of an IDE, the program now extends to additional medical device premarket regulatory pathways, including PMA, 510(k), and de novo submissions. The goal is for companies to obtain agency feedback to questions related to product development prior to the formal application process.⁹ The presub process is entirely voluntary and involves generating a formal written request for feedback from the FDA on a particular question or topic. Subsequent feedback from the FDA may come in the form of a written response, or should the applicant request, through a face-to-face meeting or teleconference.¹⁰ It is also important to remember that just because the agency has reviewed particular study designs and protocols does not guarantee the approval or clearance of

submissions in the future. Again, although presubs are not required, they are strongly encouraged by the FDA to streamline the development process and to help avoid regulatory hurdles along the way.¹⁰

CONCLUSION

The device development path can be rigorous and demanding, and for good reason. After establishing that your product is a device and identifying which class it falls into, moving forward appropriately with the necessary data or information in a prompt but thorough manner will help your device obtain FDA clearance or approval to market. Utilizing the presub process is a valuable asset that will help facilitate this process and future submissions. ■

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