

An Engineer Takes on FDA Clearance and Approval Processes

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Developing a medical device that will be subject to scrutiny by FDA often strikes fear in the hearts of design engineers. You might have a great design, but is it enough?

In August, we released the first segment in a series that addresses what engineers need to know about the medical device regulatory process from a design and development standpoint. In Part II of this series, we will look at the regulatory process in the United States.

FDA Clearance and Approval

To obtain FDA approval of a medical device, two main steps must be followed:

- Comply with the applicable FDA regulatory controls required for the regulatory classification of the device.
- Gain product certification (unless the device is Class I, see below) via either a premarket notification 510(k) or premarket approval (PMA)

As in Europe, medical devices in the United States are classified according to the level of risk the device poses to the patient and to the user. FDA classifies devices into three risk categories: Class I, II, and III. Do not confuse the U.S. risk classifications with the EU classifications, even though the nomenclature is similar (e.g. Class I, II, III).

	Risk		Device
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Classification	Level	Description	Examples
I	Low	<ul style="list-style-type: none"> Approximately 50% of all devices. Not life supporting or life sustaining . Many are exempt from 510(k) requirements and do not require a 510(k) submission. 	Tongue depressors, manual stethoscopes, dental floss, elastic bandages, examination gloves, nonprescription sunglasses.
II	Moderate	<ul style="list-style-type: none"> Represent the majority of remaining medical devices not Class I. Non-life supporting or life sustaining. Generally require a 510(k) submission; a very small subset of Class II devices are either exempt from the 510(k) process or require a PMA submission. 	Electrical stethoscopes, electrocardiographs, dental cement, gas analyzers, x-ray systems, powered wheel chairs, fetal cardiac monitors.
III	High	<p>Usually:</p> <ul style="list-style-type: none"> Technologically innovative. Life-supporting or life-sustaining. 	Implantable pacemakers, replacement heart valves, automated external defibrillators, heart

		<ul style="list-style-type: none"> Require a PMA submission. 	pumps.
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FDA determines the classification of medical devices. Appropriate classification of devices can be found by searching the [Product Classification Database](#) ^[4] on the FDA website.

FDA Regulatory Controls

The regulatory requirements applying to the device classes are:

1. Class I: General Controls
2. Class II: General Controls and Special Controls
3. Class III: General Controls and Premarket Approval

General Controls include registration and listing, labeling, and good manufacturing practices. A facility involved in the production and distribution of medical devices must register annually with the FDA for a fee and list the devices that are made at its establishment. A facility must also comply with the device labeling requirements per [21 CFR 801](#) ^[5]. A device manufacturer's quality system must be established in accordance with current good manufacturing practices (CGMPs). For medical devices, the applicable CGMP regulation is [21 CFR 820](#) ^[6].

Special controls that apply to a device depend on the type of the device and its application. Some types of special controls can include special labeling requirements, mandatory performance standards (both international and U.S.), postmarket surveillance, and FDA medical device specific guidance.

Device Exemptions

Certain types of Class I and Class II devices are exempt from some General Controls and Special Controls. Devices that are exempt from the premarket notification process include the following:

- Preamendment devices (devices legally marketed in the US prior to May 28, 1976) that have not been modified in a significant way.
- Class I or Class II devices which are exempted specifically by the regulation.

Approximately 93% of Class I devices and a small number of Class II devices (about 8%) are exempt from the premarket notification process. A small subset of Class I devices are exempt from CGMPs. [An FDA database](#) ^[7] provides a list of Class I and Class II devices that are exempt from premarket notification 510(k), and Class I devices that are exempt from CGMPs (marked with an asterisk(*)).

Browsing this area of the FDA Web site provides a better understanding of the types of devices are exempt. For example, a [manual stethoscope](#) ^[8] (Class I) is exempt from the 510(k) process, while an electronic stethoscope (Class II) is not. Both are subject to CGMP requirements. A [manual toothbrush](#) ^[9] (Class I) is exempt from both the 510(k) process and CGMPs, but a powered toothbrush (Class I) is exempt only from the 510(k) process.

Devices that are exempt from the 510(k) process must still meet general controls for registration, listing, and labeling, and, where applicable, GMPs. These devices must also be suitable for their intended use.

Pre-market Approval—510(k)s and PMAs

A 510(k) submission is required for most Class II devices and for a small number of Class I devices. Submission requires demonstration that a medical device is substantially equivalent to another device (or devices) already cleared by the FDA. A legally marketed device used for such a comparison is called a predicate device. A small percentage of 510(k)'s (approximately 10%) also require the submission of clinical data for acceptance. In general, the number of 510(k)s that require clinical data has been increasing. FDA is authorized to charge a fee for 510(k) reviews; small businesses are eligible for a reduced fee. FDA reviews approximately 4,000 510(k) applications each year.

A 510(k) application commonly includes some of the following elements:

- Device indications for use.
- Predicate device comparison.
- Summary of safety and effectiveness.
- Product risk analysis.
- Biocompatibility results.
- Software design documents.
- Sterilization information, if applicable.
- Labeling, including instructions for use.

A premarket approval (PMA) is required for Class III devices that pose a significant risk of illness or injury, or for devices that are found to not be substantially equivalent to a Class I or Class II predicate device via the 510(k) process. A PMA requires a significant amount of information to support the claims made for the device, including the submission of clinical data. Manufacturers must also undergo a facility inspection by FDA prior to a product's approval and release onto the market. FDA charges a fee for a PMA review; as with a 510(k) review, the fee may be reduced or even waived for small businesses. FDA reviews between 30 and 50 PMA applications each year.

A PMA application must include "valid clinical information and scientific analysis on sound scientific reasoning ^[10]" to demonstrate the safety and effectiveness of the device, and in order to be reviewed and approved by the FDA in a timely manner.

A PMA application commonly includes many of the same elements as a 510(k) application, along with the following:

- Summary of results of technical data (nonclinical and clinical studies)
- Conclusions drawn from studies
- Results of clinical investigations involving human subjects

FDA Regulatory Process

Once a device has been classified in accordance with the FDA regulation, the regulatory strategy can be implemented. As with the European process, a higher-risk device requires a more thorough and demanding regulatory process than a low-risk device.

Classification	General Regulatory Process
I	<ul style="list-style-type: none"> • Quality System per FDA Regulation 21 CFR 820 (QSR) (a few devices are exempt). • Facility must meet FDA labeling, registration, and listing requirements. <p><u>Most Class I devices</u> ^[11] are exempt from 510(k) requirements</p>
II	<ul style="list-style-type: none"> • Quality System per FDA Regulation 21 CFR 820. • Facility must meet FDA labeling, registration, and listing requirements. • Prepare and submit 510(k) application. • Less than 10% of 510(k)s require clinical data for acceptance. • FDA reviews application within 90 days. • FDA issues 510(k) clearance letter. • Manufacturer is subject to random FDA inspection per 21 CFR 820.
III	<ul style="list-style-type: none"> • Quality System per FDA Regulation 21 CFR 820. • Facility must meet FDA labeling, registration, and listing requirements. • Develop clinical trial protocol, obtain FDA approval, conduct clinical trial. • Prepare and submit PMA application. • If FDA accepts application, review within 180 days. • FDA conducts facility inspection. • FDA issues PMA acceptance letter. • Manufacturer is subject to random FDA inspection per 21 CFR 820.

Conclusion

When designing a product requiring FDA approval, fear not. This quick-reference can help you to better understand how your designs and resulting documentation are being reviewed during each step of the process for a device that will be commercialized in the United States.

More in this series:

[An Engineer Takes on CE Marks and European Commercialization](#) ^[12]

[An Engineer Takes on Global Regulator Processes: Asia, Latin America, and More](#) ^[13]

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Karen Brentnall is senior quality engineer at [Stratos Product Development](#) ^[14]. She has 16 years in product development and quality engineering, during which she developed expertise in class II and III medical device product development. Prior to joining the quality and regulatory world, she worked for eight years as a mechanical design engineer. She has played an active role in the design, development and manufacture of numerous medical devices including the SuperSonic Imagine Aixplorer diagnostic ultrasound system, the Boston Scientific Rotablator rotational artherectomy system, several therapeutic catheter devices and LVADs, and a hemodialysis machine. Her expertise includes development and maintenance of documentation to support medical device regulatory submissions, including risk management, quality planning and verification. Her capabilities also include implementation and maintenance of quality management systems per the FDA medical QSRs and ISO 13485.

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