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What Should the Public Know About Implantable Material and Device Innovation in the US?

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Abstract

Device innovation has potential to improve patient outcomes over time, yet prospective benefits must be considered in light of risks. At the macro level, designers and manufacturers of implantable devices and regulators must balance the need for assurance of devices' safety and effectiveness with industry and clinical investigational enthusiasm about innovation. At the micro level, clinician-investigators need to inform patient-subjects about a particular device's influence, for better or worse, on short- and long-term health goals.

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Risk-Based Regulation

The US Food and Drug Administration (FDA) is the federal agency responsible for providing regulatory oversight of the manufacturing, sales, and distribution of medical devices in the United States. The FDA's mission includes both protecting public health by ensuring the safety and effectiveness of medical devices and "advancing the public health by helping to speed innovations that make medical products more effective, safer, and more affordable."¹ When patients agree to have a device implanted, they expect that it will perform as designed and that it will not expose them to unreasonable risk. The FDA—via authority granted by the US Congress in the Federal Food, Drug, and Cosmetic Act of 1938,² the Medical Device Amendments of 1976,³ and subsequent acts⁴—is **responsible for ensuring** that device manufacturers have taken appropriate actions to meet these expectations.

Because the spectrum of devices ranges from low-risk toothbrushes, band-aids, and reading glasses to high-risk pacemakers, intraocular lenses, and artificial heart valves, the framers of the Medical Device Amendments created 3 classes of devices based on risk.

- Class I devices are the lowest risk and include the aforementioned household items, as well as surgical instruments and gloves; most do not require a premarket submission to the FDA.
- Class II devices are moderate risk and include many devices commonly encountered in health care (eg, electrocardiographs, sphygmomanometers, and other monitoring devices; x-ray and computed tomography imaging devices; syringes; and, as discussed below, some implanted devices). Most require FDA review and clearance of a premarket notification, commonly referred to as a 510(k), before they can be marketed.
- Class III devices are the highest risk or are novel devices that have not previously been classified and, prior to marketing, are subject to FDA review and approval of a premarket approval (PMA) application and inspection of the facility in which a device is manufactured. Most PMA submissions are for implants and novel diagnostic tests.

The concepts of safety and effectiveness as they pertain to medical devices must also be understood within the context of risk and benefit. FDA device regulations state:

There is reasonable assurance that a device is effective when it can be determined, based upon valid scientific evidence, that in a significant portion of the target population, the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warnings against unsafe use, will provide clinically significant results.⁶

There is reasonable assurance that a device is safe when it can be determined, based upon valid scientific evidence, that the probable benefits to health from use of the device for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use, outweigh any probable risks.⁷

What constitutes “clinically significant results” of the effectiveness of a device will vary with the patient population, the disease or condition for which it has been designed as an intervention, and the availability (or lack thereof) of alternative therapies. For example, when a disease or condition is life-threatening and alternatives are few, it may be appropriate to **accept a greater risk** to balance potential benefits. To be clear, safety is not the absence of risk but reflects a balance between prospective risks and benefits. That is, use of a device that results in adverse events in a small portion of a target population does not, in and of itself, mean the device is unsafe.

Moreover, the FDA requires only “reasonable assurance,” not a guarantee, of device safety and effectiveness. The framers of the Medical Device Amendments noted that this standard is “predicated upon the recognition that no regulatory mechanisms can guarantee that a product will never cause injury, or will always produce effective results.”⁸ An FDA decision to allow a device to be marketed reflects a balance between potential benefits that a device might offer a significant portion of a treated population against potential risks that might be experienced by some.

Implantable Device Regulation

Although the subset of implantable devices is generally regarded as high risk, each device presents a distinct **risk profile**. These risk profiles reflect the different conditions the devices are intended to treat (eg, coronary artery disease, diabetes, osteoarthritis), the different procedures required for implantation, and device characteristics (eg, whether the device is electrically powered; whether its function is physiological or

structural; whether it is permanent, removed after some duration, or resorbed over some duration; and whether it delivers a drug).

FDA regulations allow implants to be classified as class II (but not class I) if risks can be identified and appropriately mitigated to offer reasonable assurance of safety and effectiveness.⁹ For example, many orthopedic implants (eg, intramedullary fixation rods that are inserted into the bone canal of long bones for fixation of fractures,¹⁰ polymethylmethacrylate bone cement for fixing prosthetic implants to living bone,¹¹ and many ankle, hip, and knee prostheses¹²) are class II. Since these device types have well-understood risks, performance testing and animal data are generally sufficient to demonstrate performance of class II devices in accordance with established specifications, intended uses, and user needs.

Implantable devices that are high risk or less well understood are class III. These include cardiac pacemakers and heart valves, which are life-sustaining, and breast implants, dermal fillers for wrinkle reduction, and intraocular lenses, which are not life-sustaining. An FDA decision to classify devices as class III reflects the agency's determination that a higher degree of regulatory oversight is necessary to ensure the safety and effectiveness of these devices.

Regulatory Requirements

An FDA decision to classify a device as class III reflects its greater perceived risk or greater uncertainty about the information needed to determine reasonable assurance of safety and effectiveness. Devices in this class require a PMA submission¹³ that provides the clinical evidence necessary not only to demonstrate that the device will provide reasonable assurance of safety and effectiveness but also for users to understand its prospective risks and benefits. Furthermore, a PMA submission must describe how a device's manufacture will accord established quality practices, and a PMA submitter's manufacturing facilities must also pass FDA inspection.¹³

As mentioned, most class II devices require FDA review and clearance of a premarket notification, or 510(k). The **510(k) pathway** is sometimes incorrectly described as being a loophole or fast track. A device submitted through the 510(k) pathway must be found to be "substantially equivalent" to a legally marketed predicate device, but safety and effectiveness still underlie each 510(k) review and substantial equivalence determination.¹⁴ For implantable devices, a 510(k) submission includes the same bench and animal testing demonstrating that the materials are biocompatible and appropriate for the intended use as would be provided in a PMA submission, as well as the same electrical safety and software testing when needed. Most 510(k) submissions, however, do not require clinical testing (only 10% to 15% of 510(k) submissions include clinical data¹⁵), as many devices' performance can be fully evaluated using bench and animal studies and many class II devices already have a long history of safe use. For example, polypropylene sutures have been used since 1969,¹⁶ and their risks and benefits are well understood. Nevertheless, the FDA generally requires clinical studies for implantable devices with new designs or materials or for devices in which bench testing is insufficient to demonstrate performance.

In addition to following premarket submission requirements, all manufacturers of implantable devices must follow good manufacturing practices specified in the Quality System Regulation.¹⁷ The Quality System Regulation requires that specifications and controls be established for devices and that devices be designed to meet these

specifications (design controls); that devices be manufactured under a quality system; that finished devices meet these specifications; that devices be correctly installed, checked, and serviced; that quality data be analyzed to identify and correct quality problems; and that complaints be processed. The Quality System Regulation helps ensure that implantable devices are appropriately designed to meet user needs and intended uses and are consistently manufactured in accordance with established specifications.

Labeling

The Code of Federal Regulations requires device labels to include instructions, risk and benefit information, and other essential information for safe and effective use.¹⁸ Labeling is also important for risk mitigation and key to FDA review of PMA and 510(k) submissions. The FDA generally requires manufacturers of implantable devices, which are only for prescription use, to develop both physician- and patient-appropriate labeling. Physician labels are not supposed to substitute for professional judgment and should facilitate physicians' explanations to patients of why they recommend a particular device and its potential risks and benefits. Importantly, implantable devices' labels are not expected to include all possible adverse situations that could occur. Patient labels should educate patients about what to expect from the device, including potential risks and benefits. FDA guidance about patient labeling is intended to assist device manufacturers' preparation of labels that are readable at an eighth-grade level, define terms, summarize points, and promote understanding.¹⁹

Implantable devices available in the United States can save lives, restore lost function, and provide benefits to many patients. No implantable devices are risk free, and FDA device regulation helps ensure their safety and effectiveness.

References

1. What we do. US Food and Drug Administration. March 28, 2018. Accessed December 29, 2020. <https://www.fda.gov/about-fda/what-we-do>
2. Federal Food, Drug, and Cosmetic Act, Pub L No. 75-717, 52 Stat 1040 (1938) (codified as amended at 21 USC §§301-399 (2000)).
3. Medical Device Amendments, Pub L No. 94-295, 90 Stat 539 (1976).
4. A history of medical device regulation and oversight in the United States. US Food and Drug Administration. June 24, 2019. Accessed June 7, 2021. <https://www.fda.gov/medical-devices/overview-device-regulation/history-medical-device-regulation-oversight-united-states>
5. Classification of Devices Intended for Human Use, 21 USC §360(c) (2021).
6. Determination of Safety and Effectiveness. 21 CFR §860.7(e)(1) (2021).
7. Determination of Safety and Effectiveness. 21 CFR §860.7(d)(1) (2021).
8. HR Rept 94-853 (February 29, 1976). Accessed July 12, 2021. <https://www.congress.gov/bill/94th-congress/house-bill/11124>
9. Implants and Life-Supporting or Life-Sustaining Devices. 21 CFR §860.10 (2021).
10. Intramedullary Fixation Rod. 21 CFR §888.3020 (2021).
11. Polymethylmethacrylate (PMMA) Bone Cement. 21 CFR §888.3027 (2021).
12. Prosthetic Devices. 21 CFR §888 pt D (2021).
13. Application. 21 CFR §814.20 (2021).
14. US Food and Drug Administration. The 510(k) program: evaluating substantial equivalence in premarket notifications [510(k)]. Guidance for industry and Food

and Drug Administration staff. July 28, 2014. Accessed July 12, 2021.
<https://www.fda.gov/media/82395/download>

15. Faris O; Center for Devices and Radiological Health. Clinical trials for medical devices: FDA and the IDE process. US Food and Drug Administration. Accessed April 26, 2021. <https://www.fda.gov/media/87603/download>
16. Levine H. Stitch in time: 18 fascinating facts about the history of sutures. Johnson & Johnson. October 5, 2016. Accessed April 26, 2021.
<https://www.jnj.com/our-heritage/history-of-sutures-ethicon>
17. Quality System Regulation. 21 CFR §820 (2021).
18. Labeling. 21 CFR §801 (2021).
19. Center for Devices and Radiological Health. Guidance on medical device patient labeling; final guidance for industry and FDA reviewers. US Food and Drug Administration. April 19, 2001. Accessed July 12, 2021.
<https://www.fda.gov/media/71030/download>

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