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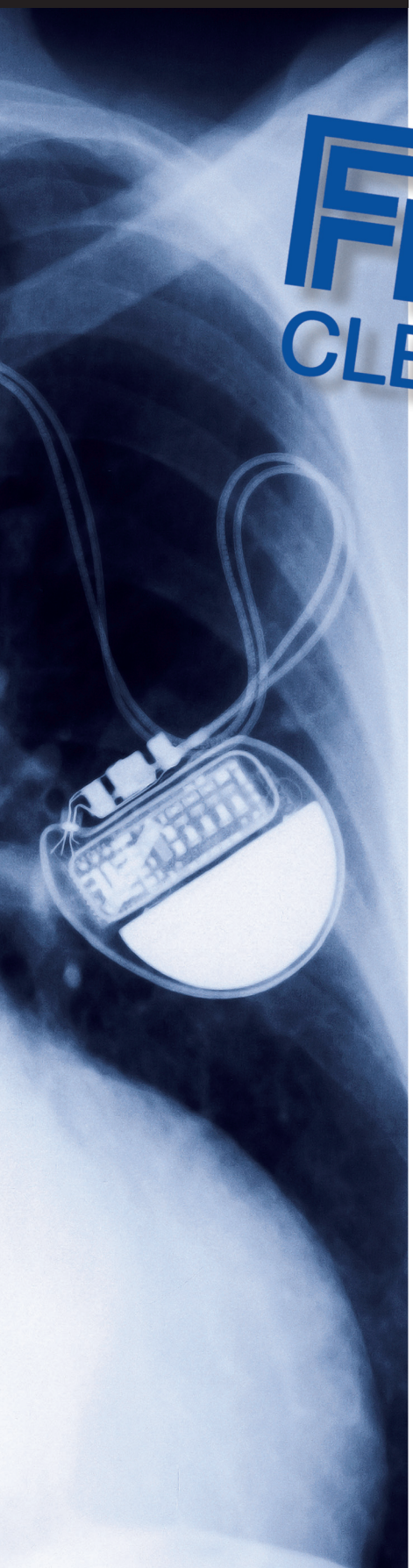
INSIGHTS

FDA's Medical Device Marketing Clearance Process

Impending Changes to the 510(k) Application Process



Medical devices play a critical role in the healthcare of Americans. A medical device can be as simplistic as dental floss and bandages or as complex as pacemakers and magnetic resonance imaging (MRI) machines. The Federal Food, Drug, and Cosmetic Act (FD&C Act) requires a "reasonable assurance of safety and effectiveness" before a device can be marketed, and the U.S. Food and Drug Administration (FDA) is responsible for enforcing this requirement. Devices that pose a moderate risk to patients generally cannot go on the market until they are cleared through the 510(k) process.

Also known as "premarket notification," the 510(k) process has been subject to a considerable amount of criticism over the last several years. Conflicting claims have been made that it is too rigorous, yet not rigorous enough, and legislators are ordering the FDA to scrap recent changes to the 510(k) process in favor of crafting new ones, which have yet to be submitted to Congress. This paper discusses the legislative evolution of the 510(k) process, illustrating how today's process came to be, the perceived need for change, and how these changes can transform the way medical device companies do business today.

Premise of the 510(k) Process

The 510(k) process is built on the premise that if a device has already been cleared under a 510(k), a "substantially equivalent" device should, in theory, be safe for use as well. The legally marketed devices to which equivalence is drawn are known as "predicate" devices.

A device that has been recently cleared under 510(k) is commonly used as a predicate device, though any legally U.S. marketed device may be used. Devices that are cleared through the 510(k) process are still rigorously tested, but generally avoid the costly clinical trials and the substantial premarket application (PMA) fee of $248,000. In comparison, a 510(k) costs less than $5,000 to file. Approximate 90 percent of the devices on the market today were cleared through the 510(k) process.

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Evolution of the 510(k) Process

The 510(k) process has a remarkable 30 year track record of protecting public health, and making safe and effective products available without unnecessary delays. The process originated from the 1976 Amendments to Section 510 of the FD&C Act,[1] which established three regulatory classes for medical devices, Class I, II and III, representing the lowest to highest risk devices, respectively. The classifications are used to determine the device's regulatory controls, which are commensurate with the risk presented by the intended use of the device. In addition, these amendments require that every establishment engaged in the manufacture, propagation, or processing of Class II or Class III devices be inspected at least every two years.

The new subsection 510(k) requires that each person or organization intending to market a device for human use in the United States notify the FDA 90 days prior to marketing the device. More commonly known as "premarket notification," Section 510(k) was designed to ensure that medical device manufacturers do not circumvent the automatic classification of "new" devices into Class III. It was also designed to provide the Center for Devices and Radiological Health (CDRH) the opportunity to challenge a manufacturer's assertion that its device was "substantially equivalent" to a predicate device, and to screen out devices not meeting this requirement. The least risk-laden devices (Class I) would, in theory, be subject to much less regulatory scrutiny and control compared to the devices presenting the highest risk (Class III). Most moderate risk devices (Class II) utilize the 510(k) process as a pathway to obtain market clearance.

Safe Medical Device Act (SMDA)[2]

The 510(k) process has undergone many legislative changes over the years to become the process we know today. The Safe Medical Device Act of 1990 (SMDA) essentially defines "substantial equivalence" by statute, which is an important component of the 510(k) process. Substantial equivalence "means, with respect to a device being compared to a predicate device, that the device has the same intended use as the predicate device and the [CDRH], by order, has found the device has the same technological characteristics as the predicate device; or, has different technological characteristics and the information submitted that the device is substantially equivalent to the predicate device contains information, including clinical data if deemed necessary by [CDRH], to demonstrate that the device is as safe and effective as a legally marketed predicate device, and does not raise different questions of safety and efficacy than the predicate device."

Food & Drug Modernization Act (FDAMA)[3]

With the enactment of the Food & Drug Modernization Act of 1997 (FDAMA), Congress passed the most sweeping legislation on the regulation of devices since the original 1976 amendments to the FD&C Act. Considered the most innovative of all the efforts undertaken by the 510(k) Process Reengineering Team, whose purpose was to examine and reengineer the 510(k) process, was the FDA's document "The New 510(k) Paradigm" which established two alternative approaches that can be used, under appropriate circumstances, to demonstrate substantial equivalence of a new device to a predicate: the "Special 510(k)" and the "Abbreviated 510(k)."

Medical Device User Fee and Modernization Act (MDUFMA)[4]

The Medical Device User Fee and Modernization Act of 2002 (MDUFMA) created a new funding structure for the review of new product applications by introducing a user fee program, for which companies must pay to submit applications to FDA. MDUFMA's goals were twofold: to improve review times and to provide support for the cash- and otherwise resource-strapped FDA. The program was reauthorized in 2007 (MDUFMA II) and in 2012 (MDUFMA III).

Food and Drug Administration Amendments Act (FDAAA)[5]

The Food and Drug Administration Amendments Act of 2007 (FDAAA) incorporated a "least burdensome" principle to the review of device submissions. The least burdensome provision, generally applied to 510(k) submissions, states that when requesting information to demonstrate that devices with different technological characteristics are substantially equivalent, the FDA "shall only request information that is necessary to making substantial equivalent determinations."

1976	1990	1997	2002	2007
Amendments to Section 510 of the FD&C Act – Established three regulatory classes for medical devices, Class I, II and III	**Safe Medical Device Act (SMDA)** – Essentially defined "substantial equivalence" by statute	**Food & Drug Modernization Act (FDAMA)** – Established two alternatives for demonstrating substantial equivalence, "Special 510(k)" and "Abbreviated 510(k)"	**Medical Device User Fee & Modernization Act (MDUFMA)** – Introduced user fee program	**Food & Drug Administration Amendments Act (FDAAA)** Incorporated a "least burdensome" principle to the review of device submissions

Today's 510(k) Process

Industry currently operates under the 1997 FDAMA guidelines, while using the "least burdensome" standard from the FDAAA to bring new products to market. Industry wants this approach to remain static since it provides a range of latitude in deciding how a device makes it to market. Unfortunately, this latitude has been a double-edged sword – it has led to several devices making it through the 510(k) process that have ultimately harmed thousands of Americans. Transvaginal mesh, heart stents and leads, along with metal hip prostheses[6] had all been cleared for market under the current 510(k) process and have since been subject to widespread recalls. As a result of these numerous safety concerns and subsequent recalls, the FDA is faced with the option to impose more rigid oversight of the device to market process.

Time for Change

In August 2010, the FDA released for public comment the preliminary reports on the "Utilization of Science in Regulator Decision Making from the 510(k) Working Group and Task Force." The Task Force was charged with making recommendations on how the FDA can quickly incorporate new science into its decision-making process regarding 510(k) clearance determinations. The FDA published "A Plan of Action for Implementation of 510(k) and Science Recommendations" with a timeline on its website.[7]

In addition to the plan, FDA officials requested the Institute of Medicine (IOM), an independent organization that provides information and advice concerning health and science policy, to review the 510(k) process in response to widespread recalls of medical devices. The results of the review were published on July 29, 2011, stating that "the current 510(k) process is flawed," and that "the FDA's finite resources would be better invested in developing an integrated premarket and postmarket regulatory framework that provides a reasonable assurance of safety and effectiveness throughout the device life cycle."[8]

The FDA released a new guidance document, "510(k) Device Modifications: Deciding When to Submit a 510(k) for a Change to an Existing Device," in July of 2011. Issuance of this guidance document was in the first task in the FDA's plan toward a new framework. Subsequently, numerous medical device industry analysts noted that this guidance would significantly increase the number of required 510(k) applications, potentially creating a backlog and further slowing the device regulatory process.

Looking Ahead

Due to unrelenting criticism from the medical device industry, the 2011 guidance went before Congress, which at the time was considering reforms to the 510(k) process under the FDA Safety and Innovation Act (FDASIA).[9] Legislators, already focused on other alleged problems in the medical device clearance process, were receptive to the criticism, and in July 2012 ordered the FDA to withdraw the guidance. The agency was further ordered not to issue any other 510(k) guidance until it has briefed Congress on the proposed content; the 1997 guidance remains in effect until that time.

FDASIA, passed in July 2012, requires the FDA to submit a report to Congress within 18 months outlining possible processes to determine whether a new 510(k) is required for modifications to an existing device. The report must include an interpretation of the key phrases "safe and effective" and "significant change." Additionally, it must explain how to leverage existing quality systems requirements to reduce premarket burden, facilitate continual device improvement, and provide reasonable assurance of the safety and effectiveness of modified devices.

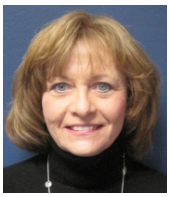
The FDA stated that any policy put forth must ensure accurate, consistent decision-making, and effective oversight of modifications made to devices, especially those that could significantly affect safety or effectiveness. The policy options the FDA is considering are:

1. ***Risk Management** – This concept would involve a risk management process for device modifications to help manufacturers and the FDA determine when a 510(k) is appropriate.*
2. ***Design Controls** – The concept of using design control activities, such as design verification and validation, intends to ensure that device modifications are appropriately evaluated prior to marketing.*
3. ***Critical Specifications** – This concept involves defining a range of specifications prior to marketing that would be acceptable to ensure safe and effective devices.*
4. ***Risk-Based Stratification** – This option would stratify medical devices requiring 510(k)s by risk, where lower risk devices would not require 510(k)s for most modifications. This option would likely be combined with another, such as periodic reporting, listed below.*
5. ***Periodic Reporting** – This would require companies to submit periodic reports of any updates to their medical devices, and would help the FDA stay informed of all device changes, including minor modifications.[10]*

Industry Involvement to Improve 510(k)

In the meantime, the FDA is advertising its intent to involve industry stakeholders in the 510(k) reform process. On June 13, 2013, in a meeting entitled "510(k) Device Modifications: Deciding When to Submit a 510(k) for a Change to an Existing Device," the FDA met with industry representatives, public agencies, and consumer advocacy groups to discuss policy proposals for modifying the 510(k) approval process. The meeting was held in preparation for the FDA's scheduled January 2014 briefing of Congress to discuss whether industry can continue to take the fast track to medical device approval via 510(k) or when more oversight should be applied.

In general, both industry representatives and consumer groups expressed support for risk management and design control processes to be incorporated into the premarket process. Regardless, companies should stay informed of potential 510(k) changes, considering how increased scrutiny and regulations could impact time to market, industry competition, and their bottom line. In the medical device sector, being first to market with a quality product is imperative. After all, lost market share is difficult and expensive to regain.



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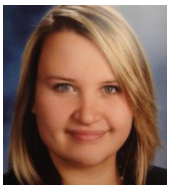

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