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# Issue Brief

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## The Medical Device User Fee Act (MDUFA) and Patient Safety

Every American relies on medical devices. Whether they use band-aids, contact lenses, a knee replacement, or a pacemaker, medical devices are part of our daily lives. Baby boomers increasingly rely on implanted medical devices, whether hips, heart valves, or wrinkle fillers.

More than 5,000 medical devices were approved for by the FDA last year. Almost all (98%) were cleared through a “quick and easy” process that usually does not require clinical trials to prove that these medical devices are safe or effective. As a result, some of these devices are neither safe nor effective.

### Is the Approval Process Rigorous Enough?

There are medical devices, such as scalpels, that are exempt from FDA premarket clearance or approval. For the thousands of devices that require more scrutiny every year, the Center for Devices and Radiological Health (CDRH) has two mechanisms for approval. Most devices – approximately 98% --are allowed to be sold after a three-month review that does not usually require any clinical trials. This much less rigorous process is known as the 510(k) process.

The 510(k) process was intended to be a temporary alternative to a full review when the FDA was first given the authority to regulate medical devices in 1976. The authority to regulate medical devices was added after thousands of women were harmed by IUDs (intra-uterine devices) that were designed to temporarily prevent pregnancy, but were found to cause serious infections, permanent infertility, and even death. At the time, there were thousands of different devices on the market that had never been proven safe or effective. Most were allowed to stay on the market, with FDA requiring some companies to submit safety studies for the first time. Meanwhile, to be fair to companies that wanted to sell medical devices that were similar to untested devices already on the market, section 510(k) of the Food, Drug, and Cosmetics Act gave FDA the authority to “clear a product for market” if it was deemed “substantially equivalent” to devices already being sold.

Rather than eliminating the 510(k) process in the decades since 1976, the FDA has used it more often. The process continued in response to device manufacturers’ claims that they were constantly improving their products and that it would stifle innovation to require each small change to be reviewed by the FDA in the more careful premarket approval (PMA) process. The rationale was that a medical device that has been modified very slightly need not be tested as rigorously as a new product.

### Why Clinical Trials are Needed

Even small changes can affect safety, however, and can be very dangerous. For example, when Bausch & Lomb added MoistureLoc to their contact lens solution, the new product was approved through the 510(k) process. No clinical trials were required. The result: severe eye infections causing blindness and the need for corneal transplant surgery.

Although the standard of “substantially equivalent” for devices sounds almost like the standard for generic drugs, the reality is completely different. Many medical devices approved by the FDA through the 510(k) process are not like any medical devices already on the market, and are instead made of different materials, used for different purposes, use a different technology, or are otherwise “new and different” rather than slightly improved.

### A Few Examples of 510(k) Device Disasters

**TMJ Implants:** Vitek jaw implants were cleared as substantially equivalent to silicone sheeting, which was made from a different material that was not developed for use in a joint. The Teflon from the Vitek implants broke off into particles that caused bone degeneration in the jaw joint and skull. Some patients can no longer eat, others have holes in their skulls.

**Bladder Slings:** Boston Scientific won approval for a ProteGen bladder sling to treat stress incontinence. The sling, made of a new synthetic material coated with collagen, caused vaginal erosion.

**Pacemakers and Defibrillators:** Frequently reviewed with the 510(k) process, tens of thousands of pacemakers and defibrillators have been recalled in recent years. When these products are defective, patients can die.

**ReNu with MoistureLoc Contact Lens Solution:** Bausch & Lomb's contact lens solution was found to be an excellent breeding ground for a fungus that caused severe eye infections.<sup>1</sup> One-third of consumers who developed the eye infections needed to have their eyesight restored with corneal transplant surgery. The product was recalled in May 2006.

**Complete MoisturePlus Contact Lens Solution:** Advanced Medical Optics' contact lens cleaning and storing solution was found to not protect against a different bacteria that can cause severe eye infections. It was recalled in May 2007.

**Shelhigh heart valves and other implants:** In April 2007, the FDA seized all implantable medical devices from Shelhigh, Inc., after finding deficiencies in manufacturing. The devices are used in open heart surgery in adults, children and infants, and to repair soft tissue during neurosurgery and abdominal, pelvic and thoracic surgery. "Critically ill patients and pediatric patients may be at greatest risk," according to the FDA.

For example, stress incontinence is a condition that affects 15 million American women, especially athletes, women who have had children, and women over the age of 50. Medical implants, often called "bladder slings," have been used to surgically correct this problem, but many of the slings are not very effective over the long-term and can cause serious complications. Manufacturers are regularly developing new slings that they hope will work better, virtually all of which have been cleared through the 510(k) process. One of these slings, ProteGen, made by Boston Scientific, was made of a new material, a synthetic mesh coated with bovine collagen, which was implanted in many women before it was recalled because it was determined that the sling caused vaginal erosion.

According to Dr. Donald Ostergard, past president of the American Urogynecologic Society, the manufacturers of such devices should be required to present substantial safety and efficacy data before approval. Those data could be used by surgeons and consumers to make educated decisions about treatment options. "In the current climate, there is no incentive for manufacturers of new devices to provide such data to the public" and surgeons considering the use of a new device must therefore rely on "expert opinion, anecdotal experience of colleagues, or marketing information from the manufacturer. Without adequate information, the possibility that associated problems will not be identified until a new device has been used on hundreds or possibly thousands of women is significantly increased."<sup>2</sup>

A device for the treatment of depression is another example of the 510(k) approval process and the implications for patients. In January 2007, the FDA held a public meeting on a new device called NeuroStar, which is designed to treat depression using magnetic pulses to the brain.

The FDA reviewed an application by the company that makes NeuroStar, claiming that it is substantially equivalent to Electroconvulsive Therapy (ECT). The FDA has stated publicly that NeuroStar is a different kind of product using a different kind of mechanism – magnetic pulses rather than electric shocks. It is also used on an outpatient basis, rather than inpatient.

However, the FDA stated that the product can be considered substantially equivalent if it treats the same illness (in this case, depression) and the risk to benefit ratio is similar to ECT. In this case, the product is not more effective than placebo, and is less effective than ECT, but it is also less risky than ECT. It can cause pain, muscle twitching, and several other serious adverse reactions, but unlike ECT it does not cause permanent memory loss.

The FDA is now regularly using this loose definition of "substantial equivalence" as part of the FDA's 510(k) process. For NeuroStar, the FDA required clinical trials, which indicated no significant difference whether the product was turned on or turned off; in other words, the product is no more effective than a placebo treatment. However, for most 510(k) reviews, clinical trials are not required. When no clinical trials are required, however, it is not possible for the FDA to accurately determine if the risks and benefits are similar for a new device.

In addition to other safety concerns about the 510(k) process, current law permits manufacturers to hire a third party to review their devices, instead of the FDA. The goal is to speed up the review process and reduce the FDA workload. However, according to the FDA, the program has not measurably reduced the FDA workload because of the use of FDA staff to administer the program. The benefit to device manufacturers is modest since the companies must pay the third parties and the review time is reduced by an average of less than two weeks.<sup>3</sup>

### **Why are 98% of Medical Devices Reviewed Through the Expedited Process?**

Since CDRH has a modest budget and fewer resources than the Center for Drug Evaluation and Research (CDER), it is not surprising that the FDA has increasingly relied on the less labor intensive 510(k) process to review the thousands of products submitted for review every year.

Under the current law, 80% of 510(k) reviews are completed within 90 days. This is a very short turnaround time, making it difficult for the more complicated applications to receive careful evaluations.

Physicians and consumer advocates have suggested changes in the 510(k) review, designed to increase information for physicians and improve safeguards for patients. These changes include:

- ▶ Excluding implanted medical devices from the 510(k) process;
- ▶ Requiring clinical trials for all medical devices that could harm patients and consumers; and

► Reverting to the original intent of the 510(k) process: the review of products that are substantially equivalent in terms of intended treatment, form, substance, mechanism, and function.

There has been no objective evaluation by the Government Accountability Office (GAO), the Institute of Medicine, or Inspector General to determine if the extensive use of the 510(k) process is putting patients at risk. It is important to note that many medical devices cleared for sale by the FDA under the 510(k) process are not reimbursable under Medicare or Medicaid, or by private insurance companies. The Center for Medicare and Medicaid Services (CMS) and insurance companies have higher standards for reimbursement than the FDA has for device approval. Although thousands of medical devices are cleared for market by the FDA through the 510(k) process every year, many Americans will not have access to all those products because insurance companies require published research to prove that the products are safe and effective.

### **The “Full Review” Premarket Approval Process**

The more rigorous device approval process, which is similar to the process for prescription drugs, is called the premarket approval (PMA) process. In these reviews, drug companies and device companies must conduct clinical trials and other tests to determine that their products work well and are safe. However, the drug approval process requires that the products be “proven safe and effective.” The approval process for medical devices has a lower standard: the products must provide a “reasonable assurance of safety and effectiveness.” For medical devices, that might mean that many patients do not benefit and a substantial number may be harmed.

### **Post-market Studies, Surveillance, and Advertising**

The criteria for device approval indicate that medical products will have risks, and the FDA has repeatedly testified that it will improve post-market surveillance to determine the risks after a product is approved and widely used. Registries for implanted medical devices and improvements to the adverse reporting systems would provide important information to doctors and patients about devices already on the market. The Energy & Commerce Discussion Draft of MDUFA authorizes additional funding that would make post-market surveillance possible, but does not require specific post-market surveillance activities.

MDUFA does not include any user fees for the review of direct-to-consumer (DTC) advertising, which has been increasing greatly for medical devices. For example, in the spring of 2007, Allergan Corporation has extensive DTC ad campaigns for three medical devices: gastric lap bands (which are surgically implanted for weight loss), Botox, and Juvederm; the latter two devices reduce wrinkles, and are injected by a physician. Allergan is currently preparing an ad campaign for silicone gel breast implants. The ads on their Web site and on TV feature enthusiastic patient testimonials with no meaningful risk information. According to the Allergan Web site, the patients receive free treatment, worth thousands of dollars, as compensation for their testimonials.

### **Speed and Safety**

As negotiated by the FDA and the device companies, the medical device user fee agreement of 2007 would speed up the 510(k) process so that 90% (instead of 80%) of the products would be reviewed within 90 days. This would mean that even the most complicated applications would need to be decided very quickly. In addition, the negotiated agreement would have required that 60% of PMAs and PMA supplements would be completed within just six months. The application process for devices is already remarkably fast compared to drugs, and shortening it would mean more stress on an understaffed CDRH, and even less time to examine safety concerns. In addition to requiring a speedier review, the user fee agreement negotiated by the FDA and device companies would decrease the cost of each user fee, 18% for the 510(k) fees and by more than one-third for the PMA. This decrease in funding could further jeopardize safety if there are insufficient staff and resources to conduct careful reviews. The Energy & Commerce MDUFA Discussion Draft decreases the PMA user fees, but would not speed up the approval process. This would create less stress on CDRH staffing levels and ability to conduct careful reviews.

### **Third Party Inspections**

Rather than FDA conducting inspections of manufacturing facilities, device companies can directly pay an FDA-approved third party to do the inspection, and can negotiate the price of the inspection. The current law includes very modest restrictions on third party inspections of Class II and Class III medical devices, which are the most stringently regulated devices. The current law allows two consecutive third-party inspections, after which the FDA must conduct the next inspection (unless the FDA issues a waiver).

The current third party inspection process creates an incentive for third party inspection companies to please their customers if they want to stay in business, and an incentive for third parties to be more positive about their findings when companies pay more generously. Critics of the program have compared third party inspections to allowing parents to select and pay a third party to determine students' school grades, or allowing employees to hire a third party to make salary and promotion decisions.

According to 2007 FDA testimony, the agency has spent millions of dollars on the third party inspection program, but it has very rarely been used. Neither the GAO nor the Inspector General has evaluated the program to determine whether it is workable and cost-effective, or whether the funds should instead be used to hire more FDA inspectors.

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