



**Statement of Diana Zuckerman, Ph.D.
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House Subcommittee on Energy and Commerce
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Thank you for the opportunity to testify about the Subcommittee's discussion draft FDA legislation. I am Dr. Diana Zuckerman, president of the National Research Center for Women & Families, an independent think tank that analyzes and evaluates a wide range of health programs, policies, and agencies, including the FDA.

I am trained as an epidemiologist at Yale Medical School and for more than a dozen years I worked in Congress, the U.S. Department of Health and Human Services, and the White House, determining which health policies were working and which ones were not.

Our center is an active member of the Patient and Consumer Coalition, comprised of nonprofit organizations representing patients, consumers, public health researchers and advocates, and scientists. The Coalition is working to strengthen the FDA and to ensure that FDA approval once again represents the gold standard of safe and effective medical products. Our Center is also an active member of the FDA Alliance, which is a coalition of pharmaceutical companies, medical device companies, former FDA officials, and consumer and patient organizations that work together to support increased resources for the FDA. I am proud to serve on their Board of Directors.

In my testimony, I am speaking on behalf of the National Research Center for Women & Families, not on behalf of other organizations we work with. I will start my testimony by focusing on medical devices and MDUFA, but will also include a brief analysis of PDUFA and other issues that you are considering in your legislation.

Every American relies on medical devices -- whether they use band-aids, contact lenses, or pacemakers. Baby boomers increasingly rely on implanted medical devices, whether hips, heart valves, or wrinkle fillers.

More than 5,000 medical devices were approved 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.

Are medical devices “proven safe and effective”? Not usually.

The American public is very concerned about the FDA drug approval process, wondering how Vioxx, Avandia, and so many other drugs can be prescribed by physicians who are not given accurate information about the risks, and then sold to millions of patients who are unable to make informed decisions about their own medical care. For all its faults, however, the FDA approval process for prescription drugs is much more rigorous than the device approval process.

There are two ways that the Center for Devices and Radiological Health (CDRH) approves medical devices, and neither has the same criteria – to prove that the product is safe and effective – that the drug approval process requires. In a book published this year, FDA officials state, “The FDA is responsible for ensuring that there is reasonable assurance that a medical device will be useful while not posing unacceptable risks to patients.” That standard is certainly more vague and less stringent than the standard for prescription drugs, and yet medical devices are just as important for saving lives and protecting the quality of people’s lives.

The statement is an accurate reflection of the FDA approval process for medical devices. In fact, most medical devices – approximately 98% -- are allowed to be sold after a review that does not usually require any clinical trials. Device companies don’t need to prove that their products are “safe and effective” – they only need to prove that they are “substantially equivalent” to a product that was on the market before 1976. 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 first was given the authority to regulate medical devices in 1976. This authority was the result of thousands of women being harmed by the Dalkon Shield IUD (intra-uterine device), which was found to cause serious infections, permanent infertility, and even death.

When the FDA started regulating medical devices, there were thousands of different devices on the market that had never been proven safe or effective. Most were “grandfathered” -- allowed to stay on the market -- with the FDA requiring some companies to conduct and submit safety studies for the first time. At the same time, to be fair to companies that wanted to sell medical devices that were similar to untested devices that were already on the market, section 510(k) of the Food, Drug, and Cosmetics Act gave the FDA the authority to “clear a product for market” if it was deemed “substantially equivalent” to medical devices already being sold.

We think that decision made sense. If logic had prevailed, however, FDA would have eliminated or at least drastically reduced their use of the 510(k) process in the three decades since 1976. Instead, the process was continued, with the rationale that device manufacturers are 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 assumption has been that a medical device that has been modified very slightly does not need to be tested as carefully as a new product.

Unfortunately, over time the definition of “substantially equivalent” was changed to include almost any product for the same medical condition. The FDA is now using the 510k process for 98% of the medical devices that they review. **As a result, new products, using new materials, or a new mechanism, made by a different manufacturer, are being reviewed as if they were a mere tinkering improvement over previously sold products. In fact, it doesn’t even matter if the previously sold product was subsequently found to be unsafe or ineffective and is no longer for sale.** There are medical devices on the market today that were approved as “substantially equivalent” to products that were subsequently recalled for safety reasons.

Why Clinical Trials are Needed

Even small changes to a medical device can affect safety, 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 a generic drug, 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 and 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. 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.

How does this affect the practice of medicine? According to Dr. Donald Ostergard, past president of the American Urogynecologic Society, many medical devices used to treat incontinence and other urological conditions were not required to conduct clinical trials before being sold. As a result, surgeons considering the use of a new device must rely on colleagues' anecdotal experience or promotional information from the manufacturer. He points out that some have caused serious problems that were not identified until the device had been used on hundreds or even thousands of women. As a result, patients who started out with a minor health problem can end up with many surgeries and with permanent and debilitating health problems.

Part of the problem is the very loose definition of "substantial equivalence." As long as a product is used for the same general purpose – such as the treatment of depression or cancer – and if its risk to benefit ratio seems to be similar, a product can be approved as "substantially equivalent." Not to be glib, but this would be like saying that cheese is substantially equivalent to peanuts or bread because all three are food that provide nutrition, and each has risks and benefits for the general population. But, if you are allergic to peanuts, or sensitive to milk products, you know that there is a world of difference regarding how those foods will affect you, and the percentage of people who can be harmed by them. They are not interchangeable.

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 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.

Why are 98% of Medical Devices Reviewed Through the 510(k) Process?

CDRH has a modest budget and fewer resources than the Center for Drug Evaluation and Research (CDER). And yet, they have a greater workload in terms of number of devices submitted to them for review every year. 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.

In speaking with physicians, scientists, and consumer advocates, we have developed several suggested changes in the 510(k) review. The goal is to increase useful information for physicians and improve safeguards for patients. These changes, supported by most members of the Patient and Consumer Coalition, include:

- Excluding implanted medical devices from the 510(k) process;
- Requiring clinical trials for all medical devices that could harm patients and consumers; and
- The FDA needs to establish an appropriate definition of “substantial equivalence.” They should revert to the original intent of the 510(k) process: the review of products that are substantially equivalent in terms of intended treatment, form, what they are made of, mechanism, and function.

We know that device manufacturers believe that the 510(k) process is safe enough and necessary to get products to patients more quickly. From a policy point of view, however, 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. For many important products, the patient will not benefit at all until those studies are done.

If medical devices are not reimbursable until peer reviewed studies are published, then the 510(k) process is NOT getting many new, innovative products out to patients more quickly. Research will still need to be conducted. Wouldn't it be better to make sure that the studies are evaluated by the FDA through the PMA process, to make sure that the analyses are not manipulated to minimize the risks?

We strongly support the Committee's plan to require a study of the 510(k) process. Either the IOM or GAO could do a credible study and report, and we urge you to determine which can do the best job in the next 12-18 months.

The “Full Review” Premarket Approval Process

The more rigorous approval process, which is similar to the process for prescription drugs, is called the premarket approval (PMA) process. 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 merely a “reasonable assurance of safety and effectiveness.”

That rather vague definition is not an appropriate standard. In our Center's review of thousands of pages of FDA advisory committee transcripts, we found how dangerous this vague definition can be. For example, at an FDA advisory panel meeting on the Kremer LASIK device, a physician explained that she recommended approval “because I did not see from the data that this was totally unsafe or totally ineffective.” At a different FDA advisory panel meeting for a device to treat Alzheimer's Disease, a neurosurgeon recommended approval after saying, “Only time will tell whether or not this will pan out to be helpful.” The FDA went along with advisory panel recommendations for approval almost every time. With standards like these, patients and their families will waste billions of dollars on

products that are not proven safe and effective, do not benefit them, and that replace products that might have helped save their lives or improve the quality of their lives.

There is no logical reason why the standard for the PMA should be any different than the standard for prescription drugs. All medical products should be required to be proven safe and effective. That does not mean that the product has no risks, but it should mean that the benefits outweigh the risks for the people who will be using the product.

Post-market Studies, Surveillance, and Advertising

Since so many medical devices are approved through the 510(k) process, and the rest are approved on the basis of the vague criteria of “reasonably safety and effectiveness” it would make sense for CDRH to devote a great deal of resources to post-market surveillance. In fact, the CDRH often requires post-market studies be conducted, but they do not monitor those studies to make sure that they are done appropriately.

For example, in 2000 CDRH approved saline breast implants on the condition that 10-year post-market studies be conducted. Because of the enormous media attention and controversy, the CDRH required the implant makers to present their 5-year data at a public meeting in 2003. At the meeting, it was shown that one of the companies, Mentor Corporation, had lost track of 95% of their augmentation patients after 5 years.

Any epidemiologist will tell you that when you lose track of 95% of your patients, your study does not provide useful safety information. The FDA criticized the company, and encouraged them to re-contact more of the patients in their study. However, even with more extensive follow-up, more than two-thirds of the patients were missing from the post-market study at the six-year follow-up. And yet, the company continued to sell their product with no penalties. They even came back for approval of their more controversial silicone gel breast implants two years later, and those implants were approved on the basis of the company’s promise to study those women for 10 years. In other words, they made the same promise that they had previously broken, and the FDA approved their product anyway.

In a recent book, the director of CDRH wrote that “the premarket evaluation program alone cannot assure continued safety and effectiveness of marketed devices” and explained the need for post-market surveillance to determine the risks after a product is approved and widely used. Thus far, those efforts have been under-funded and ineffective. 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.

Under current law, if an implanted device is recalled, it is unlikely that the men, women, or children who have that device in their bodies will be notified. Doctors and medical centers will be notified, but they may not be able to notify all – or even most – of their patients. Registries for implanted devices, using unique identifying numbers, are needed to help

ensure that patients will be notified as quickly as possible if there is a defective implant inside their body.

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 inserted 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

The MDUFA Discussion Draft would not speed up the 510(k) process, which is already very fast, reviewing 80% of the products within 90 days. That is a wise decision. It is important that the legislation focuses on decreasing the cost of user fees for the smaller companies, but does not reduce the already very inexpensive user fees for 510(k) reviews.

The decrease in funding for the PMA process seems reasonable, as long as the process is not required to speed up. The total funding, and the increase in appropriations authorized, would help ease the stress on CDRH staffing levels and improve their ability to conduct careful reviews.

Third Party Inspections

Rather than FDA conducting inspections of manufacturing facilities, device companies can directly pay a 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 MDUFA discussion draft wisely does not expand this program. Critics have compared third party inspections to allowing parents to select and pay a third party to determine school grades for students, 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 this program, but it has very rarely been used. We urge the Committee to ask the GAO or IOM to evaluate whether this program is workable and cost-effective, or whether the funds should instead be used to hire more FDA inspectors.

Progress on PDUFA and Safety Issues for Drugs, Devices, and Biologics

The FDA discussion draft legislation includes many important provisions that will greatly improve the safety of drugs and potentially the safety of all medical products.

We strongly support the proposed addition of **\$225 million** over five years in new safety money, and urge Congress to make sure that funding is used to improve resources to conduct post-market surveillance and modernize the FDA's computer systems, including **software for reporting and analyzing adverse reactions for drugs and devices**. We also strongly support the provision that **would include patient and consumer organization representatives in the negotiations for any PDUFA renewal and MDUFA renewal**. The patient and consumer organizations represented should be full partners at the negotiations, and should not have financial ties to pharmaceutical or medical device companies.

The proposed legislation builds on the best **REMS provisions** in the Waxman-Markey bill (HR 1561), giving the FDA the authority it needs.

For drugs and medical devices, it is important that there be required registration of all Phase II thru IV trials. We agree with the discussion draft provision that the results of all these studies should be made publicly available, and that should apply to studies on medical devices as well as drugs.

In **Section 5**, the discussion draft includes the Senate bill's section 201, which is based on a suggestion by former FDA Commissioner Dr. Mark McClellan and introduced in a bill by Senators Gregg, Burr, and Coburn (S. 1024). In combination with REMS, these **databases** from Medicare and elsewhere are very important because they can be used to detect short- and long-term safety problems in **drugs and devices**.

We support the discussion bill's recognition that **nothing in these FDA bills pre-empts state tort laws**.

Additional Suggestions for Devices and Drugs

As a member of the Patient and Consumer Coalition, our Center strongly supports several recommendations to strengthen provisions in your discussion draft of PDUFA and other FDA legislation.

Although the conflicts of interest" provision is a clear improvement over the Senate bill, we believe that **conflicts of interest should be eliminated in FDA advisory committees for drugs and devices**, by excluding any members with stock, stock options, or other financial ties to companies that have stakes in the topic under discussion. The discussion draft includes a good provision on conflicts of interest, but it is essential that "conflicts of interest" be defined in the law as a financial relationship within the last 36 months. Otherwise, FDA advisory committees could include members who received million dollar honoraria from the company whose product is under review just 13 months prior to the committee meeting. And, since stock and stock options are so strongly affected by FDA decisions, either should always be unacceptable for advisory committee members.

Better consumer protections regarding DTC advertising is needed. The discussion draft section on DTC advertising is a good start, but needs to be strengthened by making pre-clearance of all DTC advertising for drugs and devices mandatory rather than

voluntary. An effective system of civil monetary penalties is also needed, and those must be substantial to be an effective deterrent.

Strong whistle-blower protection provisions are needed, as well as a provision clarifying the **right of FDA officers and employees to publish scientific articles**, with proper disclaimers. The right to publish could have meant earlier warnings about the risks of Vioxx, Avandia, Actos, and other blockbuster drugs and devices, saving the lives and improving the quality of life of many Americans.

In addition to the provisions in the discussion drafts on making data available, we strongly urge that you consider the Senate provisions making **FDA reviews, evaluations, and approval documents promptly available to the public**, including dissents and disagreements. In addition, the FDA should be required to **publish observational study results**, in addition to clinical trial results.

We support legislation by Representatives Tierney, Emerson, and Stupak that would create a separate **Center for Post-market Evaluation and Research** with real clout within the agency, but strongly urge that the Center include devices as well as drugs and biologics.

In conclusion, thank you for the opportunity to testify and share our views about the discussion drafts. You have made important progress, and we appreciate your consideration of provisions that would strengthen this legislation to help ensure that safe and effective medical products are available to all Americans.