



**Statement of Diana Zuckerman, Ph.D.
President, National Research Center for Women & Families**

**Before the Subcommittee on Health
House Subcommittee on Energy and Commerce
May 16, 2007**

Thank you for the opportunity to testify about the Medical Device User Fee Act. MDUFMA II is one of the most important pieces of legislation to come before Congress this year, and so far it has received very little attention. On behalf of medical researchers, patients, and consumers, I thank you for giving it the attention it desperately needs.

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, and especially the FDA. We are the only think tank that is strongly focused on the safety of medical devices.

I am trained as an epidemiologist at Harvard 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.

While Vioxx and other drug safety issues have attracted most of the attention of Congress as well as patient and consumer groups, medical devices are increasingly important in our lives. All of us use medical devices, and many of us have a loved one with at least one medical device implanted in their bodies. The aging baby boomer population will increase our reliance on medical devices, whether replacement hips or heart valves, and the safety of these devices is therefore becoming even more worrisome.

The vast majority of medical devices that the FDA considers for approval have not been required to prove safety and efficacy through double blind clinical trials. This may seem shocking, since double blind clinical trials are the gold standard

to prove that a medical product is safe and that it actually works. But, at the Center for Devices and Radiological Health (CDRH), most devices are approved under an expedited process, the 510(k) process, rather than the Premarket Approval (PMA) device approval process.

The 510(k) process is intended for products that are “substantially equivalent” to medical devices already on the market. Sometimes that makes sense-- for example, a medical device that has been modified very slightly by the same manufacturer to improve it. But often, the medical devices approved through the 510(k) process are modified in ways that make them potentially very dangerous. For example, when Bausch & Lomb changed their contact lens solution, called ReNu, to ReNu with MoistureLoc, the resulting product caused eye infections and permanent blindness in numerous consumers. ReNu with MoistureLoc was allowed on the market through a 510(k) process, without *any* clinical trials submitted to the FDA.

Changes in heart valves or stents can be deadly, as Congress has learned. Shouldn't FDA always require clinical trials when these implanted devices are modified? Shouldn't MDUFMA II make sure that the approval process protects consumers?

The performance goals of MDUFMA II's goals would drastically speed up the 510(k) process. Instead of 80% of those applications being completed within 90 days, **90%** would be completed in **90 days**. That's just 3 months -- not long enough for anything resembling a careful review. At 80%, the performance goals were already dangerously fast for many products; 90% is worse, not better, for consumers. No wonder ReNu with MoistureLoc, and other devices, are harming consumers. MDUFMA II also requires that **98%** of 510(k)s be completed within **150 days**. So, you see there is truly no wiggle room for any concerns about more than 2% of these devices. This is not safe.

The PMA device approval process, which is more similar to the approval process for prescription drugs, is also faster in MDUFMA II. Instead of **half** the PMA and PMA supplements being completed in **180 days**, that would increase to **60%**. Instead of **90%** of panel track supplements and premarket reports in **320 days**, that would be shortened by almost a month to **295 days**.

At the same time that MDUFMA II would require speedier reviews, **the user fees are being reduced** for each product. For example, the user fee for a 510(k), already a bargain at \$4,158 in 2007, is **reduced 18%** to \$3,404 in 2008, even for multi-billion dollar companies. User fees should be much higher for 510(k) applications, to help ensure that all the safety bases are covered before approval, and to ensure post-market safety standards. Under MDUFMA II, the user fees for a **full PMA review would be reduced more than one-third, from \$281,000 in 2007 to \$185,000 in 2008. The FDA claims that user fees would increase. However, that is only because the workload – the number of products under review – would increase. For each task, the FDA would receive less support from user fees.**

The medical device companies must like MDUFMA II. It reduces their costs and gives them faster reviews.

Let me ask you to consider: What are the benefits to consumers?

We are told that consumers benefit from faster reviews and innovations. But the truth is that contact lens solution has been absolutely fine for millions of consumers for many years. New contact solution with MoistureLoc was not an urgent priority. Innovation is only good if a product is better and safer, not if it is merely new and different.

A quick review with inadequate safeguards harms patients. It also harms companies, pressuring each into developing and marketing their own “new” products so that they can compete – even if their old products work wonderfully and need no improvement.

MDUFMA II has performance goals for speed, but none for public health. Public health performance goals are urgently needed.

In the last year or two, we learned that patients were harmed by FDA-approved stents, heart defibrillators, contact lens solution, and other products. What did the FDA learn from these terrible tragedies? How did it affect their MDUFMA II negotiations? You’d think that the FDA would respond to these and other medical device problems by being more cautious. You’d be wrong. Instead, FDA is making the approval process for devices even easier.

In January, the FDA held a public meeting on a new device called NeuroStar, which is intended to treat depression using magnetic pulses to the brain. For that product, clinical trials were conducted and the results indicated no significant difference whether the product was turned on or turned off.

Depression is a serious and debilitating disease. The use of ineffective treatments can contribute to feelings of hopelessness, which in turn can worsen the symptoms and even result in suicide. It is therefore especially important to make sure that medical products approved for the treatment of depression are proven safe and effective.

The FDA 510(k) process is intended to be for products that are substantially equivalent to other products already on the market. In this case, the company that makes NeuroStar is claiming that it is substantially equivalent to Electroconvulsive Therapy (ECT), even though it is a very different technology.

The FDA admits that NeuroStar is not really substantially equivalent to ECT because it 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. But the FDA decided to change the definition of “substantially equivalent.” They publicly stated that the product can be considered substantially equivalent as long as the **benefit to risk ratio is similar**. 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 it does not cause memory loss.

If the FDA broadens the definition of the 510(k) criteria in this way, based on the benefit to risk ratio rather than similarities to other products on the market, any medical device can be eligible for the speedy 510(k) process. This could certainly help speed up the approval process, but at the risk of flooding the market with medical devices that either don't work or work but are not safe.

That kind of change will make MDUFMA II performance goals possible, but opens a Pandora's box that is very dangerous for everyone in this room.

Who is minding the store at the FDA to make sure that medical devices are safe and effective before they can be sold in the United States?

The FDA claims that any medical product will have risks, and that they will do a better job to figure out those risks **after** a product is approved by the FDA. My final concern is that MDUFMA II does not provide adequate user fees for the review of direct-to-consumer (DTC) advertising or other post-market safety measures. The recently passed Senate drug safety bill does a better job, although not enough, on PDUFA user fees and enforcement of post-market drug safety issues, and those provisions should be expanded and improved upon as you consider much-needed post-market improvements to MDUFMA II.

Please ask the FDA how many employees review medical device DTC ads to make sure they are accurate. I have been told that it is only one person. However many reviewers there are, the result is not reassuring. The number of DTC ads for implanted medical devices, such as gastric lap bands and injections to the face to reduce wrinkles, is on the rise. DTC ads for breast implants are currently under review. Based on the DTC ads that I have personally seen for implanted medical devices on TV and on company Web sites, these ads often feature personal testimonials that present a rosy view of the product with no meaningful risk information. The patients giving the testimonial are paid by the company, which often provides the treatment for free – a huge gift for just a few minutes of their time.

I have expressed my views on these ads and the lack of post-market surveillance to Dr. von Eschenbach when meeting with him face-to-face. He assures me that the FDA will enforce post-market study requirements. However, MDUFMA II clearly does not provide the funding needed to make that possible. It would be an unfunded mandate, requiring FDA to do more with fewer resources to follow through on those promises.

With Congressional leadership and appropriate revisions to MDUFMA II, you can make sure that CDRH has the resources, the enforcement powers, and the performance goals needed to protect your families, your constituents, and the American public.

14

A consumer advocate's perspective on medical device epidemiology and surveillance

Diana M. Zuckerman, PhD

National Research Center for Women & Families, Washington, DC, USA

Consumers show their confidence in the safety of medical devices when they spend the equivalent of more than \$200 billion worldwide annually [1]. Nevertheless, consumers are not necessarily familiar with the term 'medical device' and might not be able to name any if asked. Virtually every consumer uses medical devices, and many have friends and family members with implanted medical devices. In recent years, the number of men, women, and even children with implanted medical devices has increased dramatically, as artificial knees, hips, heart valves, and shunts have become increasingly common [2,3]. Medical implants come in a very wide range of shapes, sizes, and substances, including the increasingly popular oils and gels that are injected into millions of faces every year to fill wrinkles and scars [4]. The use of implanted devices, either to replace aging body parts or to help people look younger, will certainly continue to increase as the baby boomers age. Lasers are also widely used medical devices, with more than 2 million eye laser surgeries performed in the USA in 2004, more than 1 million laser hair removal procedures, and numerous other laser procedures [5].

Medical devices received relatively little public attention throughout most of the twentieth century, with a few exceptions, such as: the excitement followed by disappointment about lives prolonged with an artificial heart; widespread media attention about infertility and deaths caused the Dalkon Shield in the mid-1970s; serious illness and death from toxic shock syndrome caused by tampons in 1980; and the growing popularity of replacement knees and hips in the last two decades. It was especially difficult to obtain

useful safety data about devices prior to 1976, when the Food, Drug and Cosmetic Act was amended to give the US Food and Drug Administration (FDA) substantial authority to regulate medical devices. At that point, there were thousands of medical devices already on the market, most of which were 'grandfathered' so that they could continue to be sold until the FDA determined whether studies of safety and effectiveness would be required.

In the 1990s, very few consumer advocates or nonprofit organizations focused any attention on medical devices. Even so, the few groups that were concerned about medical devices generated considerable public attention regarding the questionable safety of specific devices, such as breast implants, jaw implants, and fetal monitors, especially in the USA, Canada, and the UK. Organizations such as the National Women's Health Network, Canadian Women's Health Network, Public Citizen Health Research Group, and the TMJ (temporomandibular joint) Association were vocal critics of specific implants, and they were joined by the National Research Center (NRC) for Women & Families when that research and advocacy organization was founded in 1999. In the last few years, increased attention has been given to the benefits of medical devices for life-saving procedures as well as common age-defying cosmetic solutions, and the risks have also come under greater scrutiny. In 2001, while working with an informal coalition of approximately a dozen organizations called the Patient & Consumer Coalition, NRC for Women and Families and the National Women's Health Network brought the issue of improving legislation regarding medical devices to the Coalition for the first time. As a result, broad-based consumer organizations in the USA, such as National Consumers League, Consumer Federation of America, Center for Medical Consumers, Gray Panthers, International Union of UAW, and The Title II Community AIDS National Network, have become knowledgeable about medical devices and started to raise questions about safety data and surveillance. Although consumer groups in or outside the government have been less vocal in other countries, medical devices have attracted the attention and concerns of organizations such as the Canadian Women's Health Network, Health Canada's Women and Health Protection, Women's Implant Information Network New Zealand, and Silicone Support UK.

Until 1993, medical device regulation within Europe was the responsibility of the health ministries of each country. Although few countries required clinical trials to determine safety, the regulatory process was nevertheless considered burdensome because different countries posed different requirements for inspecting and authorizing the sale of medical devices [6,7]. These variations made it difficult for European manufacturers to obtain approval to market their products in other countries. When the European Union (EU) established a harmonization program in 1993, however, the program mandated only general requirements for medical devices, and although the criteria include product safety and protection of health, clinical trials are not required to establish either [6]. Manufacturers need only demonstrate compliance in one EU country in order to sell a medical device throughout Europe. Conformity assessment bodies (CABs) are hired by the companies to determine and certify whether a company's product meets the minimum technical requirements. Few consumers are knowledgeable about the specific safety requirements or approval process for medical devices in their

¹at which time it was called the National Center for Policy Research (CPR) for Women and Families; the name was changed in 2004.

country. From the consumer perspective, the main concern is one's health: do the benefits of a medical device outweigh the risks? Consumers want medical devices that can save their lives or improve their quality of life, and that means that the device should work, last as long as possible, and not have dangerous side effects. However, for many medical devices sold around the world, there is often limited clinical and epidemiological research to determine the risks and benefits. A brief history of the medical devices receiving the greatest public attention in recent years is instructive in illustrating the concerns expressed by consumers and the organizations that advocate on their behalf.

Examples of widely publicized problems with selected medical devices

Dalkon Shield

Medical devices were not systematically regulated in the USA and most other countries when the Dalkon Shield intrauterine contraceptive device (IUD) was studied in 1970 (see Figure 14.1). The inventor, Dr Hugh Davis, published a study claiming exceptional effectiveness with no serious risks [8]. The study's shortcomings were overlooked: only 700 women participated in the study, they were followed for less than 6 months, the researchers did not report that the women used additional contraceptive foam for the first several months, and efficacy statistics were compiled within a week after the study was completed, so that later pregnancies were not reported.

After the study was completed and publicized, Davis revised the IUD, adding copper and using a smaller size; the revised product was not tested for safety or efficacy. Approximately 2 million Dalkon Shields were inserted in women in the USA and Puerto Rico [8].

By 1974, pelvic inflammatory disease, ectopic pregnancies, septic abortions, sterility, and 12 deaths had been reported among women who used the Dalkon Shield, and the FDA requested that the manufacturer of the Dalkon Shield, A. H. Robins, remove the IUD from the US market. The company complied, but continued selling it in other countries. It was not until 1980 that the company advised doctors to remove the Dalkon Shield from women who still had them in their bodies, and the IUD was not recalled until 1985. By then, about 9500 cases had been litigated or settled, 6000 more cases were pending, and 16 new cases were being filed each day. Robins filed for Chapter 11 (bankruptcy) protection in 1985, and the settlement included a \$2.5 billion trust fund for compensation of more than 100 000 women who sought damages [8].

In response to the Dalkon Shield disaster, and the increased recognition of the risks of medical products, Congress passed the 1976 Medical Device Amendments, which gave the FDA authority to systematically regulate all medical devices [9].

Tampons

A few years later, in May 1980, investigators reported to the US Centers for Disease Control and Prevention (CDC; at that time the agency was called the Center for Disease



Figure 14.1 Dalkon Shield poster from the 1970s. Courtesy of the FDA History Office

Control) 55 cases of toxic shock syndrome (TSS), a newly recognized illness characterized by high fever, sunburn-like rash, desquamation, hypotension, and abnormalities in multiple organ systems [10]. Fifty-two (95%) of the reported cases occurred in women, and the onset of illness occurred during menstruation in 38 (95%) of the 40 women from whom menstrual history was obtained. In June 1980, a follow-up report described three studies that found that women with toxic shock syndrome were more likely to have used tampons: case-control studies in Wisconsin and Utah and a national study by CDC.

Subsequent studies established that toxic shock syndrome was more likely among women who used a new, highly absorbent tampon called Rely™. By September, Rely tampons were voluntarily withdrawn from the market by the manufacturer. During 1980, 890 cases of toxic shock syndrome were reported, 91% of which were associated with menstruation; there were 28 deaths. In response, tampon makers reduced the absorbency of tampons and the FDA began to require that all tampon packages include package inserts explaining the risks of toxic shock syndrome.

Silicone gel breast implants

In the late 1970s and early 1980s, following the addition of medical device regulation to the FDA's responsibilities, the agency was overwhelmed with an enormous number of devices that had previously been on the market and now needed to be classified and possibly evaluated. Breast implants were among the many devices that were allowed to stay on the market until those reviews were completed. Silicone breast implants had been sold since the 1960s and remained on the market while decisions were made about what kind of safety and efficacy studies might be required. Meanwhile, numerous other silicone implants were considered under the law to be 'substantially equivalent' to breast implants, and therefore allowed to be sold without any clinical trials to prove safety. Scientists and physicians started expressing strong concerns about the safety of silicone breast implants, and by the early 1980s, the suspected risks were officially described in the US government Federal Register [11]. However, it was not until 1988 that the FDA held a public meeting that focused on these risks, and an advisory committee recommended that the FDA establish a national registry of women who have breast implants. The US registry was never established. By 1990, approximately one million women in the USA and Canada, and unknown numbers in other countries, had breast implants, and a scientist at Health Canada had lost his job after publicly urging the agency to remove them from the market. Meanwhile, no government regulatory agencies had yet required the manufacturers to evaluate their safety and no empirical studies had been published regarding their effects on human health.

In 1991, pressured by Congressional hearings and enormous news media attention in Canada and the USA regarding non-medical grade polyurethane coverings and reports of implant patients' illnesses and complications, the FDA finally required the manufacturers to submit safety studies on silicone gel breast implants [11]. The company that made polyurethane-covered breast implants removed their product from the market amid studies indicating that the foam broke down to a known carcinogen, 2,4-toluene diamine (TDA), which was found in the breast milk of women with breast implants. Other implant companies, including Dow Corning, submitted safety data, which FDA scientists reviewed and found to be inadequate [11].

Despite being on the market for almost 30 years, the studies submitted by the breast implant makers were deficient in many respects: they included small sample size and all the women were studied for less than 1 year. However, silicone gel breast implants had been widely available for more than two decades and had become increasingly popular,

providing considerable income for implant manufacturers and plastic surgeons; both groups lobbied heavily to keep them on the market. That pressure, however, was counterbalanced by implant company documents, made public in the course of several lawsuits, indicating that company scientists had expressed concern about the lack of safety data, and the leaking of silicone from intact silicone implants [11,12].

In 1992, as a compromise, silicone gel breast implants were allowed to remain available as a 'public health need', with the FDA limiting their availability to clinical trials, primarily for women who have mastectomies, breast deformities, or to replace a broken gel implant. A similar compromise was instituted in Canada. At the same time, other countries considered similar restrictions. In most countries, these restrictions were lifted several years ago and silicone gel breast implants are available to virtually any patients who want them, but the restrictions were not lifted in the USA and Canada until Fall 2006, and even then extensive long-term post-market safety studies were required. In 2001, after years of consumer advocacy pressure by Silicone Support UK, using information published in medical journals and compiled by consumer organizations, the European Commission adopted plans to improve informed consent for women considering breast implants, and urged member countries to establish minimum age limits and to establish registries in all 15 EU Member States [13]. The UK had previously established the first registry of breast implant patients in 1993. Several countries, including Australia and Denmark, have followed suit. All registries are voluntary, which limits the number of patients.

Meanwhile, patients won multimillion dollar law suits against implant companies in the early 1990s, so the manufacturers entered into an international legal settlement with patients totaling more than \$3 billion dollars, all the while claiming that their implants were safe and not responsible for the health problems that the settlement compensated.

TMJ Implants

In 1992, Congressional hearings brought attention to even more obvious health problems caused by jaw implants used to treat temporomandibular joint (TMJ) disorder. Several companies sold TMJ implants made of silicone or other materials, and Dow Corning sold silicone sheeting that could be used for custom-made TMJ implants. Another company, Vitek, made TMJ implants with Teflon and proplast. Most adverse reactions that were reported to the FDA were for implants made from silicone or Teflon; the friction of the joint caused the jaw implant to flake or break, and the body reacted to the particles with an immune reaction that could cause debilitating pain, bone loss, and in some cases with the Vitek implants, bone degeneration in the joint and skull [14,15]. Like breast implant patients, TMJ implant patients reported systemic autoimmune symptoms and reported that their physicians often assumed that the symptoms were unrelated to their implants. However, patients with TMJ implants reported many symptoms in the jaw joint area, so that at least some of the risks of the implants were identified relatively quickly.

In response to law suits from patients with permanent jaw damage, Vitek declared bankruptcy, but their implants continued to be sold under the names Novamed, Inc., and Oral Surgery Marketing, Inc. When the FDA required them to stop selling their implants, the head of the companies, Dr Charles Homsey, left the USA and sold the TMJ implants in other countries [14]. In 1993, the FDA notified the World Health Organization of its concerns about the proplast implants, and in 1994 the FDA wrote to regulatory agencies in Japan, Italy, Switzerland, Canada, Mexico, Australia, and New Zealand, and the Director General of the European Union, to describe the serious and debilitating complications of proplast implants among TMJ patients in the USA [14].

The examples of the Dalkon Shield, tampons, silicone gel breast implants, and TMJ implants all indicate that there can be substantial risks for medical devices used within the body. The latter three examples also indicate how, even in a country that regulates medical devices, pre-1976 'grandfathered' devices have been allowed to be sold that can have devastating effects on human health. Also, when regulators in one country demand that a product be removed from the market, companies can continue to sell their products in other countries with less stringent regulations for medical devices. Particularly in small countries, where the number of patients using the products is modest, or in products that work well at first but fail over time, the risks of a defective or poorly designed device may not be noticed for many years.

Consumer concerns

Consumer concerns about device manufacturers and their research

As these examples illustrate, consumers or their physicians were the first to complain about the adverse reactions to these medical devices, and in most cases the manufacturers defended their products and challenged consumers in court. In some examples, such as tampons, healthcare professionals were instrumental in bringing attention to the problem; in others, physicians tended to assume that the medical devices were safe and unrelated to the problems being reported. In the case of breast implants, it was only when it became clear that there were no safety data to back up company claims, and internal corporate documents indicated the possibility of a cover-up, that the products were withdrawn from the market or restricted, usually with belated pressure from the regulatory agencies of countries such as the USA and Canada. In recent years, the European Commission has applied pressure on EU countries to institute safeguards that implant manufacturers and plastic surgeons were not providing, such as informed consent that provides information about specific risks.

All these examples have a fundamental scientific problem in common: the lack of meaningful short-term or long-term safety research. It was only when unexpected adverse reactions were reported – by the CDC, as part of law suits, or by physicians – that there was pressure on government regulatory agencies to require that research be conducted. In the case of breast implants, this was initiated by a Health Canada engineer who served as a whistleblower, generating media attention in Canada that spread to the USA [11].

Manufacturers defend the lack of research for medical devices, stating that, unlike pharmaceutical companies, devices tend to be modified frequently in response to the requests and recommendations of physicians. For example, AdvaMed, the largest medical technology trade association in the world, claims that:

‘Medical device innovation development differs significantly from pharmaceutical innovation in that most devices on the market today result from a series of incremental improvements to preexisting devices. These improvements result from continued vigilance by the manufacturer and substantial input from the provider community. Although well-designed research plays a significant role, formal research projects cannot substitute for the one-to-one interaction between the researchers tasked with developing and improving a technology and the clinical personnel who use it in their therapeutic and diagnostic interactions with patients’ [16].

AdvaMed represents 800 companies selling more than half of the healthcare technology products purchased worldwide [16]. Based on their view, a study of an implant made 10 years ago or even 2 years ago might be irrelevant to the product being sold today. However, in some cases described in this chapter, there was evidence that research indicating risks was not published or made public.

Consumer concerns about regulatory safeguards for medical devices

Concerns about insufficient regulatory safeguards for medical devices reflect the differences between these devices and prescription drugs. Historically, most devices were used outside the body (such as scalpels and band-aids), and there was a perception that ‘what you see is what you get’, making research seem less important. As implanted medical devices have become more common, long-term research has become more important, but the safeguards and resources for regulatory agencies, in the USA and other countries, has not kept up with the increased importance of those devices.

In most countries, medical devices are routinely approved for marketing on the basis of short-term studies. This is also true in the USA, although manufacturers of high-risk devices are often required to do longer-term postmarket studies as a condition of device approval. Postmarket studies that are required because of concerns that arise after product approval, rather than as a condition of approval, are limited by FDA regulations. For example, 3 years is the maximum time that the FDA can impose for postmarket research requirements on medical devices ordered after approval without the agreement of the manufacturer; that is not sufficient to examine long-term safety [17]. Moreover, recent reports by the Institute of Medicine and the FDA indicate that postmarket studies, imposed as a condition of approval, have been inadequately monitored, and that the studies were often not performed or finished [18,19]. Add to that the corporate rationale that devices are constantly being improved and therefore regulatory flexibility is necessary, and there is a clear conflict between consumer demand that products be proven safe and corporate demands that products be approved quickly and be allowed to change without the need for new approval applications. These issues are raised in countries all over the world, and there is not one country that has insisted on or

consistently enforced long-term postmarket surveillance of medical devices, not even of those implanted for very long-term use.

FDA regulations differ in the safety criteria for medical devices compared to new drug approvals, and these differences are similar in other countries as well. Drugs must be safe for the uses recommended in labeling, which is interpreted as meaning that the benefits outweigh the risks. In contrast, a medical device must have a 'reasonable assurance of safety', which is more ambiguous; the law requires that the 'probable benefits to health' should outweigh 'any probable risks' (21CFR860.7). This has been interpreted as a less stringent criterion for safety and effectiveness, where scientific proof that the benefits outweigh the risks is not necessarily required.

In racially and ethnically diverse countries such as the USA, the potential for racial and ethnic differences in responses to implanted medical devices has become an issue of concern among consumer groups. The NRC for Women & Families, the National Medical Association, and the Congressional Black Caucus of the US Congress have all expressed their concern that implant makers rarely include racial and ethnic minorities in their studies. Since individuals of African or Asian ancestry are more likely to have keloid scarring, and since individuals of African ancestry are more susceptible to autoimmune diseases, medical implants may be more risky for those groups. However, it is impossible to know whether this is the case if no studies have been done.

Consumer groups have the opportunity to influence regulatory decisions in countries using independent advisory panels, such as is the case in the USA and Canada. Consumers are represented on the advisory panels and also have the opportunity to speak during the open public comment periods. However, whatever the roles consumers play, there is reason to be concerned that advisory panels tend to be a rubber stamp for approval. In a study released in 2006, NRC for Women & Families compared recommendations from FDA advisory panels for medical devices with advisory panels for prescription drugs. Votes between 1998 and 2005 were compared for five randomly selected device advisory panels and six randomly selected drug advisory panels. During those 8 years, the advisory panels recommended approval for 82% of medical devices that they reviewed, compared to 76% of prescription drugs under review. Some panel members always voted for approval for any product during their entire tenure on the advisory panel. NRC for Women & Families concluded that the less stringent criteria for approval for medical devices created an expectation that most medical devices were 'reasonably safe' and therefore suitable for FDA approval. Although panel members often expressed concern about the lack of safety information, they apparently assuaged those concerns by recommending postmarket studies and other conditions of approval. Unfortunately, as discussed later in this chapter, postmarket studies and surveillance are often not enforced [18].

Consumer concerns about long-term safety of implants

Of all the concerns that consumers have about medical devices, the long-term safety of implanted devices has attracted the most attention. There is widespread agreement

among consumer advocates that in most countries the current statutes regulating medical devices are inadequate for ensuring adequate safety studies, especially for life-saving and implanted devices. In the USA, the Patient and Consumer Coalition has participated in meetings with individual FDA officials, FDA forums, meetings with Members of Congress and their staff, and Congressional briefings to urge policy makers to require better research, including long-term safety studies, and better postmarket surveillance to improve the safeguards for implanted medical devices. These concerns are similar to those expressed by consumer advocates in Canada, the UK, and other countries.

The lack of long-term safety studies is a particular problem for implanted devices. Medical devices are allowed to be sold without proof of long-term safety. Solutions that have been suggested by consumer groups include the following:

- Government regulatory agencies must devote more resources to postmarket surveillance that focuses on long-term efficacy, reliability, and safety.
- Government regulatory agencies should be required to closely monitor, document, and audit all medical device Phase IV trials. The studies should be monitored for the adequacy of informed consent and human subject protection, the quality of study design, and the accuracy of results. Registries should be used more often to keep track of adverse reactions to devices and as a mechanism to inform patients of recalls or other problems.
- Adverse event reporting must be improved for medical devices, especially implanted devices. All hospitals, Health Maintenance Organizations (HMOs), nursing homes, and other healthcare providers should be required to immediately submit all adverse event reports to government regulatory agencies, and this should be stringently enforced. Information technology must be employed to facilitate the submission of adverse event reports.
- Government regulatory agencies or health agencies should be required to write and distribute consumer guides that provide unbiased, clearly-worded research-based information about the risks and benefits of medical devices used by consumers, such as implanted medical devices. This need is exemplified by the fact that, although US health experts have focused increasing efforts to provide understandable materials for consumers, there is little effort to develop consumer-oriented written materials for medical devices, since devices are often 'used' by medical professionals (sometimes by surgically implanting them in patients) rather than by patients.

In the rare instances when postmarket studies or surveillance are required (which is more likely in the USA than in other countries) consumer advocates are concerned that such studies and surveillance are not monitored adequately to ensure that they are conducted appropriately, or to ensure that companies or physicians provide information relevant to adverse reaction reports. Whether this is due to inadequate resources or inadequate

regulatory authority, it has become increasingly obvious in recent years that patients can not be assured they have the information they need to avoid medical disasters resulting from insufficiently safe medical devices, particularly those implanted in their bodies.

For example, a study by the FDA of all 127 premarket agreements (PMAs) approved during 1998–2000 found that 45 required postapproval studies. Although the law requires manufacturers to include information about these studies in their annual reports, only 19 of the 45 legally required studies (42%) were mentioned in annual reports. For the 11 PMAs where the results were due, final results had not been submitted in six (54%) cases [19]. This would make it impossible for consumers to obtain the information they need about the long-term safety of these devices. In 2006, the FDA announced initiatives to improve the enforcement of postmarket requirements; future reports will evaluate the results of those FDA initiatives [20].

Given the failure of device companies to submit required data, government regulatory agencies would benefit from subpoena power to compel manufacturers and healthcare providers to deliver documents relevant to all mandated regulatory functions regarding medical devices. Since premarket studies for medical devices are often small and of short duration, these postmarket studies take on even greater significance. That manufacturers agree to these studies as a condition of approval for their medical device and then do not finish them should be adequate reason for withdrawal of the product from the market, until such a time as adequate studies are completed.

Regulatory mechanism recommendations

Recalls

Several well-publicized recalls have brought attention to shortcomings in removing defective products from the market. For example, in 2002, a defect in a bronchoscope manufactured by Olympus led to persistent bacterial contamination of the instruments (see Chapter 17, ‘Medical device-related outbreaks’). A recall was delayed for two months, and problems continued even after the recall. As reported in newspapers across the country, the recall notice to Johns Hopkins Hospital was sent by Olympus to a loading dock instead of the department using the bronchoscope. As a result, Johns Hopkins continued using the defective instruments for several months after the recall was initiated [21]. Apparently, other medical centers also were unaware of the recall, which was not widely publicized and which we found was posted on neither the company’s nor the FDA’s websites.

As a result of this and other examples, consumers and their advocates have become increasingly concerned about medical device recalls. In the USA, an article in a mainstream women’s magazine, *Good Housekeeping*, in March 2004, explained that neither device companies nor physicians are required to send patients a notification that a medical device implanted in their body has been recalled. The magazine encouraged readers to respond, resulting in more than 10 000 consumers joining a campaign to

change these policies – the largest response the magazine has ever received [22]. Similarly, consumer organizations agree that government regulatory agencies need to have a more active role in the oversight of medical device recalls, for example:

- Government regulatory agencies need a clear and explicit legal mandate to assume primary responsibility for the supervision, monitoring, and enforcement of all medical device recalls, rather than requesting that the companies provide recall information to the public. The agencies should be required to quickly and efficiently disseminate accurate and pertinent information regarding the recall of medical devices to patients and healthcare providers.
- An office or agency independent of the health regulatory agency is needed to investigate the circumstances surrounding the withdrawal of any approved medical device from the market.

Legislative and regulatory changes requested

As a result of the EU's streamlined process, which rarely requires clinical trials to examine the safety of medical devices, the USA came under pressure to ease their approval process for medical devices. In 2002, the US Congress passed the Medical Device User Fee and Modernization Act (MDUFMA), and this law was amended in 2004 [23]. Consumer groups opposed many aspects of these bills, which weakened rather than strengthened FDA's regulatory muscle. In their opposition, consumer groups pointed out three general concerns:

- The law favors rapid medical device approval over medical device safety.
- The law ignores the need for improved postmarket surveillance.
- The law sets time limits on reviews of medical device safety, which could divert resources from other important FDA functions.

Consumer groups were especially concerned that the bill supports privatization of several essential regulatory functions of the FDA, by allowing for third-party reviews and inspections. The bill extended a previous law implementing 510(k) review by third parties of most Class II devices. In addition, the law initiated/expanded the use of non-FDA 'accredited persons' to conduct inspections of medical device facilities, including Class II and Class III devices that are permanently implantable, life-sustaining, or life-supporting. The third parties must be selected from a list of accredited persons compiled by the FDA; however, the specific accredited third party can be chosen by medical device manufacturers. Compensation for accredited persons is determined by medical device manufacturers in agreement with the third parties, and is paid by the manufacturer. Consumer groups point out that this arrangement creates a clear financial conflict of

interest; if a company wants to be hired for these tasks, it is in their financial interest to please their customers.

Consumer concerns about the need for legislative and regulatory changes have increased during the early years of the twenty-first century, in response to several well-publicized failures of medical devices. Although consumer groups have been concerned about how recalls are handled, recalls also bring attention to issues with the approval process, not just the recall process. For example, recent recalls of heart valves and defibrillators have brought public attention to life-threatening problems that can result from defective medical devices [24–28]. Thus far, however, consumer groups have been unsuccessful in their efforts to strengthen the regulation of medical devices. On the contrary, medical device companies can get new products approved in an expedited process that does not necessarily require clinical trials if the new product is considered ‘substantially equivalent’ to another product on the market. The definition of ‘substantial equivalence’ is very vague, and has included products made of different materials and/or for very different intended uses – differences that could substantially affect safety and effectiveness.

Consumer group accomplishments: mixed results

As a reflection of the growing clout of consumer organizations, in September 2005, Health Canada held its first-ever public meeting of an advisory panel, for the review of a controversial medical device: silicone gel breast implants. The public meeting was in response to consumer complaints about a secret meeting that took place in March 2005, with an ‘independent’ advisory panel. The controversy arose when it became known that the ‘expert advisors’ who participated in the panel meeting included two men who were paid consultants to one of the breast implant manufacturers, Inamed, whose products were being reviewed by Health Canada. In fact, both ‘expert advisors’ had testified on behalf of the safety of Inamed silicone gel breast implants at an FDA advisory panel in April of the same year. When consumer groups pointed out that paid consultants were unlikely to make unbiased judgments about the product, Members of Parliament joined them in demanding a more open, balanced process. As a result, Health Canada officials held a public advisory panel meeting, modeled after the FDA public meetings. However, consumer groups were shocked to learn that the same industry-paid consultants who were on the panel for the secret meeting would remain on the panel for the public meeting, as well as other consultants to one or both implant manufacturers. Only one consumer advocate was on the panel, and patients and advocates were given only 3 minutes each to testify during the public comment period. The expense and inconvenience of traveling to Ottawa, and concerns that the panel vote for approval was preordained, apparently outweighed patients’ desire to publicly testify for 3 minutes, and few consumer representatives or patients testified.

Recent consumer efforts in the USA indicate similarly mixed results. In response to consumer and Congressional pressure about inadequate postmarket surveillance of medical devices, the FDA announced its intention to address shortcomings in 2006,

and held the first in a series of 'workshops' on this topic in early February 2006. The first workshop was described afterwards in the FDA's press release as a meeting 'between the FDA and AdvaMed', the organization that represents device manufacturers. Consumer groups were not included in the planning or agenda of the workshop, and were not notified that it was held until after the meeting was over. Moreover, the meeting was organized by AdvaMed rather than the FDA, and participants were charged several hundred dollars each to attend, which likely reduced the participation of government employees and representatives of nonprofit organizations. Presumably consumer groups will be invited to a later workshop organized by the FDA, but the question arises as to why they were not included as an integral part of all FDA meetings on the topic.

These examples indicate that consumer organizations are actively pushing for better regulatory processes and safeguards for medical devices, but are meeting with limited success to even 'be at the table' and have their voices heard. As device manufacturers savor their victories in streamlining the approval process, consumer advocates complain that they are tilting at windmills in the face of regulatory agencies that seem oblivious to conflicts of interest, unconcerned about long-term safety data, and indifferent to the shortcomings of postmarket surveillance. Nevertheless, consumer advocates continue to make their voices heard, and partly as a result of those efforts the news media are focusing more attention on dangerous defects and numerous recalls of specific medical devices. In the USA, Canada, and the UK, legislators have joined consumer advocates in their demands for greater safeguards, and the combined forces of consumer groups, Members of Congress, Members of Parliament, and the attention of the news media may eventually influence government regulatory agencies and device manufacturers, resulting in improved safety studies and postmarket surveillance.

References

1. Medical device regulations: global overview and guiding principles. World Health Organization, 2003: http://www.who.int/medical_devices/publications/en/MD_Regulations.pdf
2. Kojic EM, Darouiche RO. *Candida* infections of medical devices. *Clin Microbiol Rev* 2004; **17**: 255–267.
3. Garver D, Kaczmarek RG, Silverman BG, Gross TP, Hamilton PM. The epidemiology of prosthetic heart valves in the United States. *Texas Heart Inst J* 1995; **22**: 86–91.
4. American Society of Plastic Surgeons. Procedural statistics: http://www.plasticsurgery.org/public_education/2004Statistics.cfm [accessed October 10 2005].
5. American Society for Aesthetic Plastic Surgery. Beam me up Scotty: plastic surgeons find better results and fewer complications with new laser treatments. October 6 2005 press release: <http://surgery.org/public/news-release.php?iid=414andsection=>
6. The US–EU Recognition Agreement: its implications for the US medical device industry: <http://www.devicelink.com/mddi/archive/01/05/003.html>
7. Medical device reporting. Improvements needed for FDA's system for monitoring problems with approved devices. GAO/HEHS-96-65, 1997: <http://www.gao.gov/archive/1997/he97021.pdf> [accessed October 13 2005].
8. Sobol RB. *Bending the Law: The Story of the Dalkon Shield Bankruptcy*. Chicago, IL: University of Chicago Press, 1991; 1–6.

9. FDA milestones in women's health: <http://www.fda.gov/womens/milesbro.html> [accessed February 15 2006].
10. Historical perspectives reduced incidence of menstrual toxic-shock syndrome – United States, 1980–1990: <http://www.cdc.gov/mmwr/preview/mmwrhtml/00001651.htm> [accessed October 10 2005].
11. The FDA's Regulation of Silicone Breast Implants. Staff report prepared by the Human Resources and Intergovernmental Relations Subcommittee of the House Government Operations Committee, December 1992.
12. Gladwell M. Documents tell risks of implants. *Washington Post* February 11 1992; 1.
13. BBC News. Victory for breast implant victims, November 15 2001: <http://news.bbc.co.uk/1/hi/health/1657856.stm>
14. TMJ implants. A consumer information update, April 2001: <http://www.fda.gov/cdrh/consumer/tmjupdate.pdf>
15. Congressional Hearing. Are FDA and NIH ignoring the dangers of TMJ (jaw) implants? Hearing before the Human Resources and Intergovernmental Relations Subcommittee of the Committee on Government Operations, House of Representatives, June 4 1992.
16. AdvaMed: testimony to the House Energy and Commerce Health Subcommittee on 'Assessing HIPAA: how federal medical record privacy regulations can be improved', March 22 2001, available at: <http://www.advaMed.org/publicdocs/hipaatestimony3-22-01.html>
17. Postmarket Surveillance Studies: www.fda.gov/cdrh/devadvice/352.html [accessed October 14 2005].
18. Zuckerman, DM. *FDA Advisory Committees: Does Approval Mean Safety?* National Research Center for Women & Families, 2006, available at http://www.center4research.org/pdf/FDA_Report_9-2006.pdf.
19. Brown S, Bezabeh S, Duggirala H. Center for Devices and Radiological Health condition of approval studies as a postmarket tool for PMA approved cohort 1998-2000. Rockville, MD: Food and Drug Administration: http://www.fda.gov/oc/whitepapers/epi_rep.pdf [accessed October 10 2005].
20. Field MJ, Tilson H (eds). Committee on Postmarket Surveillance of Pediatric Medical Devices, Institute of Medicine. *Safe Medical Devices for Children*, 2005: <http://www.iom.edu/report.asp?id=28277> [accessed October 14 2005].
21. Medical Device Postmarket Transformation Initiative: <http://www.fda.gov/cdrh/postmarket/mdpi.html> [accessed February 15 2006].
22. Patterson P. Bronchoscope recall falls through cracks. *OR Manager* 2002; **18**: 20.
23. *Good Housekeeping*. Dangerous devices. Article and campaign described on: http://magazines.iviillage.com/goodhousekeeping/hb/health/articles/0,,284594_651884-14,00.html [the characterization as the magazine's largest response was made by editor Toni Hope in a personal communication].
24. Medical Device User Fee and Modernization Act (MDUFMA) of 2002: <http://www.fda.gov/cdrh/mdufma/> [accessed October 10 2005].
25. Medtronic announces a nationwide, voluntarily recall of small subset of two implantable cardioverter-defibrillator models: http://www.fda.gov/oc/po/firmrecalls/medtronic04_04.html
26. Medtronic announces additional devices affected in voluntary recall of certain monophasic LifePak[®] 500 automated external defibrillators: http://www.fda.gov/oc/po/firmrecalls/lifepak04_25.html
27. FDA updates consumers on Guidant Corporation's implantable defibrillators: <http://www.fda.gov/bbs/topics/NEWS/2005/NEW01198.html>
28. FDA issues nationwide notification of recall of certain Guidant implantable defibrillators and cardiac resynchronization therapy defibrillators: <http://www.fda.gov/bbs/topics/NEWS/2005/NEW01185.html>