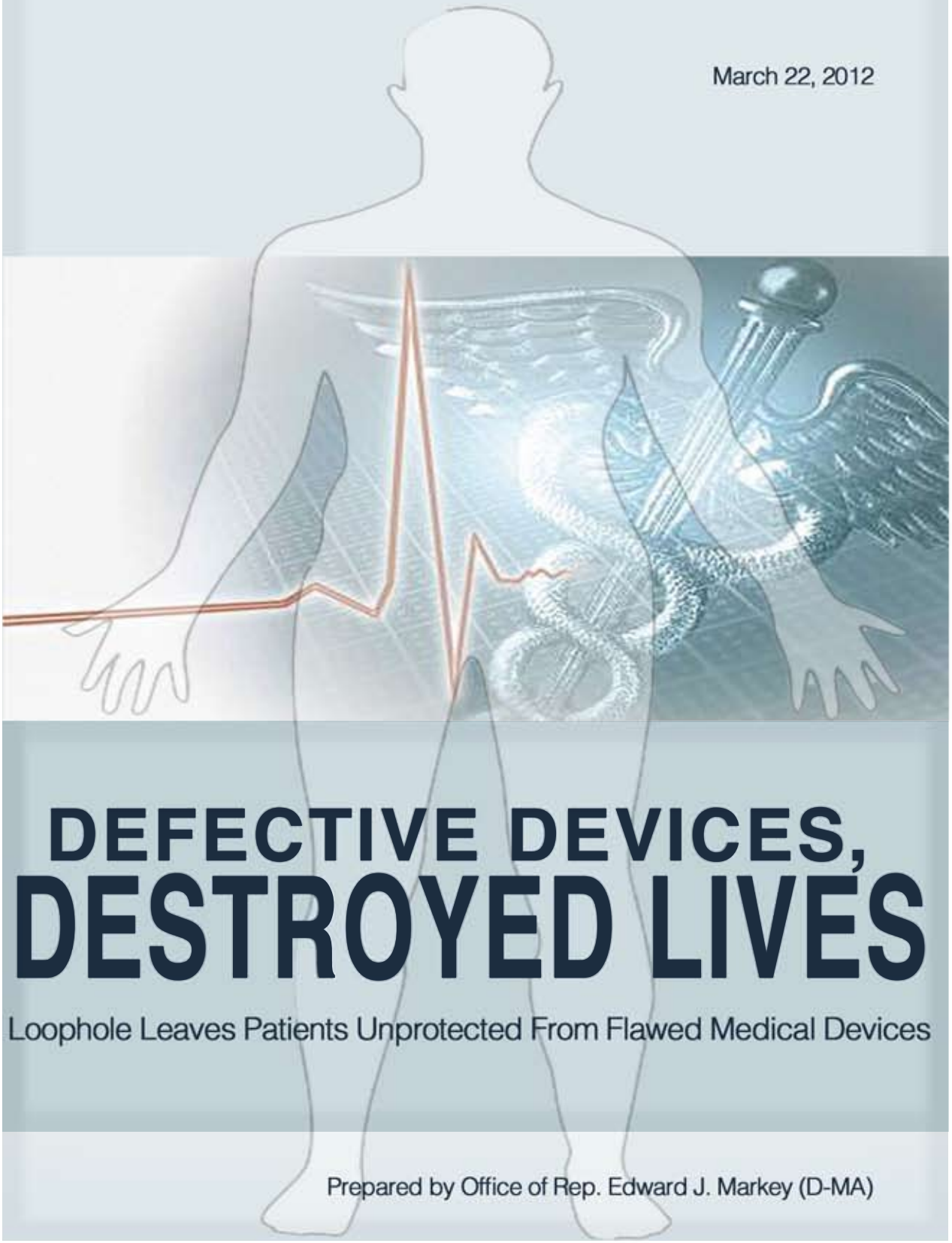
March 22, 2012



DEFECTIVE DEVICES, DESTROYED LIVES

Loophole Leaves Patients Unprotected From Flawed Medical Devices

Prepared by Office of Rep. Edward J. Markey (D-MA)

Table of Contents

Executive Summary…….. 3

I. Background on 510(k) Clearance…… 4

II. A Dangerous Loophole……. 5

III. The Sound Devices Act…….. 7

IV. Consequences for Patients…….. 8
- Transvaginal Mesh Implants…… 8
- Endoscopic Clipping Devices……..... 11
- Cardiovascular Catheters …… 12

V. Patient Stories……. 13

VI. Conclusion……. 15

Appendix A: Congressional Research Service Report
The FDA's Authority with Regard to Substantial Equivalence Determinations

Appendix B: Testimony of Dr. Tom Margolis to Food and Drug Administration on Transvaginal Mesh Implants

Appendix C: Letter from Truth in Medicine and its members

Executive Summary

Patients and clinicians generally assume that when the Food and Drug Administration (FDA) clears a medical device, the device is effective and safe for use in patients. However, a major safety loophole in the current law requires FDA to clear certain medical devices despite the fact that they pose a serious risk of injury or death to patients.

The FDA reviews the vast majority of medical devices through a process commonly known as "510(k)", a reference to its origin in the Food, Drug and Cosmetics Act (Public Law 75-717). The FDA does not require 510(k) devices to undergo clinical testing to demonstrate safety and effectiveness prior to clearing them for commercial sale. Instead, the device manufacturer must show only that the device is similar or "substantially equivalent" in design, technology and use as a previously approved device, known as a "predicate". Once a device receives FDA clearance, manufacturers can use it as a predicate for future devices.

However, the 510(k) process was not designed to evaluate the safety and effectiveness of a device. Rather, a finding of "substantial equivalence" by FDA signifies only what its name implies – that the device is similar in certain respects to a previous predicate device. No determination about risks to safety or effectiveness comes as a result of clearance through the 510(k) process.

These lax standards for device approval reveal a major safety loophole: **The FDA must approve a substantially equivalent 510(k) medical device even in cases where the new product repeats the same flaws of an earlier model that was recalled for major safety problems.**

Already, thousands of patients have been harmed – in some cases grievously and irrevocably – by medical devices that were modeled after recalled devices. Among the most prominent example is that of vaginal mesh implants, used to correct incontinence and weak pelvic organs. Despite the original device's recall in 1999, a number of subsequent meshes – some still on the market and being implanted in patients – trace their FDA approval back to that defective product. Patients with complications from vaginal mesh implants have experienced bleeding, severe pain, infections, and even death.

Massachusetts Congressman Edward J. Markey recently introduced H.R. 3847, the Safety of Untested and New Devices (SOUND Devices) Act. The SOUND Devices Act will close the loophole that currently hamstrings FDA's efforts to protect patient safety and ensure the quality and reliability of medical devices. The SOUND Devices Act, originally co-sponsored by Representatives Henry A. Waxman (D-Calif.), Jan Schakowsky (D-Ill.) and Rosa DeLauro (D-Conn.), injects common sense into this device approval process by giving FDA the authority to reject a 510(k) application if it repeats the flaws that caused its predicate to be recalled. Rep. Markey's legislation seeks to protect patients by giving FDA the flexibility to prevent a device from entering the market if reviewers recognize that the new device contains the same dangerous or defective flaw that led its predicate device to be removed from the market.

Background on 510(k) Clearance

The Food and Drug Administration (FDA) reviews the vast majority of medical devices through a process known as "510(k)", a reference to its origin in the Federal Food, Drug and Cosmetic Act (Public Law 75-717). The FDA does not require 510(k) devices to undergo clinical testing in patients to demonstrate safety and effectiveness prior to clearing them for commercial sale. Instead, the device manufacturer must show only that the device is "substantially equivalent" to a device (or multiple devices) that previously received FDA clearance, known as the "predicate".

FDA determines that a device is "substantially equivalent" if:

- **the device has the same intended use and technological characteristics as the cited predicate, and**

- **the device is as safe and effective as its legally-marketed predicate (i.e., it poses no new safety or efficacy concerns).**

Once the FDA determines that a device meets the threshold for substantial equivalence, the device may be sold on the market and manufacturers may use the device as a predicate for future 510(k) applications indefinitely.

The 510(k) program looks far different today than it did when Congress created the program in 1976. Congress originally intended the process to be used only for a limited number of low-risk devices. Each generation of surgical drapes, for example, should not be required to undergo clinical testing. However, use of the 510(k)

pathway has grown dramatically since its inception. Companies now rely on the 510(k) pathway to clear more than 90 percent of devices, including such high-risk devices as brain stents, implantable cardiac defibrillators, artificial hip implants, and other implantable devices.

"The 510(k) process was not designed to evaluate safety and effectiveness."

The expansion of this process to include such varied and high-risk devices poses a number of safety risks to patients. Patients and clinicians generally assume that the FDA's "stamp of approval" means that a device is safe. However, the 510(k) process was not designed to evaluate safety and effectiveness.
Therefore, a finding of "substantial equivalence" is not a statement by the FDA as to the safety or effectiveness of the device. It signifies only what its name implies – that the device is similar in certain respects to a previous product.

Furthermore, many predicate devices cited in support of 510(k) applications have themselves been cleared through the 510(k) process, rather than through the full Pre-Market Approval (PMA) process, and thus have not necessarily undergone clinical testing in humans prior to entering the market.

A Dangerous Loophole

A major loophole exists in what already is a process rife with problems. Current law does not permit the FDA to reject a 510(k) device based on a recalled predicate provided that it meets the threshold for substantial equivalence. In other words, the FDA *must* approve a substantially equivalent 510(k) device even in cases where the new product repeats the identical flaws as an earlier model – the predicate – that was pulled from the shelves. Device manufacturers can also continue using a voluntarily-recalled[1] device as a predicate, even if the recall was triggered by a defect causing serious injury or death. According to FDA:

> **"When the intended use and technological characteristics – including any design flaw shared by the predicate and the device under review – are the same, FDA cannot deny clearance based on an independent determination of the safety and effectiveness of the device under review."[2]**

FDA, healthcare providers, and numerous patient and consumer organizations have issued warnings regarding this major loophole in the 510(k) process, which many argue is already fundamentally flawed. This potentially deadly gap in FDA's authority stems from the ability of manufacturers to cite predicate devices that have either been withdrawn from the market or recalled because of safety issues. A device's status as a valid predicate is nullified only if the FDA issues a mandatory recall, which occurs in the rare instances where the device manufacturer fails to voluntarily recall a product that poses a health risk. In these instances, it can no longer be used as a model for future devices. However, the vast majority of recalls are not mandatory; rather, device companies carry them out voluntarily upon learning of significant adverse events. The most recent comprehensive look at device recalls found that between 2005 and 2009, there were approximately 700 voluntary recalls per year and zero mandatory FDA recalls.[3]

The FDA's 510(k) working group, which finished an internal evaluation of the 510(k) program in 2010, identified this loophole as one of several weaknesses in the program. The working group expressed concern that "allowing a device to be used as a predicate after it has been removed from the market due to safety problems would place patients at risk."[4] The report concluded that the FDA's current process allows manufacturers to rely on inappropriate or unsafe predicate devices.[5] Inappropriate predicate selection represents a significant area of concern because the predicate

[1] For the remainder of the report, unless otherwise specified, references to a "recall" or a "recalled device" will refer to voluntary recalls initiated by the device manufacturer or sponsor.

[2] Communications between FDA staff and Representative Markey staff March 7, 2012.

[3] FDA Should Enhance Its Oversight of Recalls. GAO Report: 11-468. June 14, 2011.

[4] U.S. Food and Drug Administration. CDRH. *510(k) and Science Report Recommendations*. Jan. 2011. See: http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDRH/CDRHReports/UCM239449.pdf

[5] CDRH Preliminary Internal Evaluations-Volume I. 510(k) Working Group, Preliminary Report and Recommendations. August 2010. See: http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDRH/CDRHReports/UCM220784.pdf

device chosen by a manufacturer serves as the benchmark for FDA's substantial equivalence determination. As long as the product meets that benchmark, FDA is obligated to allow the device to be sold for commercial use. That device can subsequently serve as a predicate for future applications indefinitely.

The medical device industry has argued that "FDA already has abundant authority to carry out its mandate" to ensure safety and effectiveness of devices and "can deny the substantial equivalence claim and deny 510(k) clearance if there are unaddressed questions on safety and effectiveness"[6].

However, an independent review of FDA's legal authority by the Congressional Research Service (CRS) concluded:

> **"The FFDCA [Federal Food, Drug and Cosmetic Act] does not appear to grant the FDA the explicit authority to find that a new device is not substantially equivalent to a 'faulty' predicate device based upon the existence of safety or other issues with the predicate device. Nor does the statute specify that the FDA is required to find that a new device is not substantially equivalent due to safety issues associated with the predicate device. Therefore, it would not appear that the FDA would be able to deny a § 510(k) clearance based on a predicate device that has been recalled for safety or other reasons…"** (see Appendix A)

In fact, under the Federal Food, Drug and Cosmetic Act "FDA reviewers should only ask for information necessary to establish substantial equivalence"[7] and may do so only after considering "the least burdensome" means for doing so.[8] Asking for information about a design flaw shared by the device under review and its predicate would be contrary to this principle.

The FDA can employ certain regulatory tools to mitigate the risk posed by these flawed devices, such as requiring stronger warning labels. However, none of these tools involve the ability to reject outright a device that would result in known defective devices being used in patients. If a device is substantially equivalent, FDA *must* allow it to be introduced into commercial distribution, even if the agency is aware that it repeats dangerous design flaws. Legislation is needed to close this loophole.

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[6] Communications between Avamed staff and Representative Markey staff March 6, 2010.

[7] 21 U.S.C. § 360c(i)(1)(D) and Communications between FDA staff and Representative Markey staff March 7, 2012.

[8] 21 U.S.C. § 360c(i)(1)(D); *see* Benjamin A. Goldberger, *The Evolution of Substantial Equivalence in FDA's Premarket Review of Medical Devices*, 56 FOOD & DRUG L.J. 317, 328 (2001)(stating that "[i]nformation not related directly to substantial equivalence, such as information about the absolute safety and effectiveness of a device, may not be requested").

The Sound Devices Act

H.R. 3847, the Safety of Untested and New Devices (SOUND Devices) Act, injects common sense into the device approval process by giving FDA the authority to reject a 510(k) application if it repeats the intrinsic design flaws that caused its predicate to be recalled from the market. The legislation seeks to protect patients by giving FDA the flexibility to prevent a device from entering the market if reviewers recognize that the new device contains the same dangerous or defective flaw that led its predicate device to be recalled from the market.

Additionally, because one flawed device could provide the model for a number of future devices, this legislation enables FDA to request information about a device's "predicate lineage". While the new device's immediate predicate may not have been recalled, devices approved prior to that through the 510(k) process may have been removed from the market. It is vital that FDA is aware of any earlier problems to ensure that the new device does not repeat a deadly flaw found in a previous model.

The legislation also strengthens reporting requirements for companies following a voluntary recall, so that the public has reliable and accessible information that explains why the recall occurred. This information is also helpful for device companies, providing them complete and timely data about which predicates – or which component of a predicate – is invalid. Access to this information at the beginning of the device development process will allow the company to avoid wasting time and resources repeating mistakes that have resulted in devices harming patients. Often this information can be difficult to obtain, and access to it will vastly improve the quality and reliability of devices cleared through the 510(k) process in the future.

Finally, the legislation instructs the FDA to review the safety of high-risk devices that are already on the market if their predicate undergoes a recall. This allows FDA to proactively identify potential problems with already-marketed devices rather then waiting for problems to occur. For example, there are three hypothetical hip implants on the market. Hip implant manufacturer recalls Product A because it determines the material used is not stable when implanted in patients. FDA would then review Product B and Product C, which relied on Product A as their predicate, to determine whether the later devices repeat Product A's flaw in material choice. FDA would have the ability to identify defects in the later devices before they harm patients.

The SOUND Devices Act:

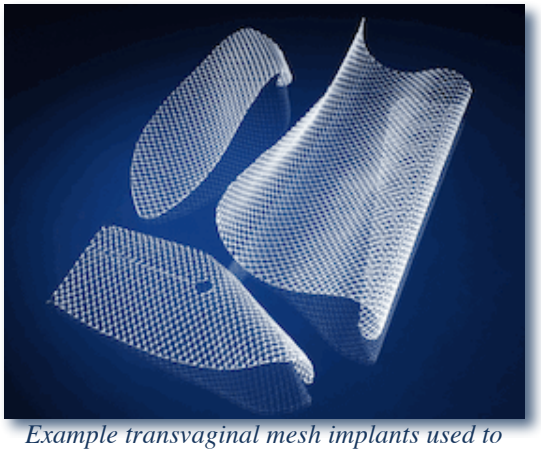
- Gives FDA the ability to reject a device based on a predicate that has been recalled
- Requires companies to inform FDA if products in a device's lineage have caused harm
- Instructs FDA to maintain a publicly accessible database that companies can use to determine whether a device can be used as a predicate
- Calls for FDA to review high-risk devices if a product in their lineage has been recalled

Consequences for Patients

Already tens of thousands of patients have been harmed – in some cases grievously and irrevocably – by devices on the market today that trace their design back to products recalled in the past due to major safety flaws. In other cases, devices remain available to be used as "predicates" for future devices despite the fact that they have been recalled. These instances caused unsuspecting patients to be injured by devices that contained foreseeable and avoidable defects, and they contradict industry claims that FDA already has ample authority to ensure the safety and effectiveness of 510(k) devices. Below are three examples highlighting devices that have slipped through the 510(k) loophole and of the harm caused to patients.

Transvaginal Mesh Implants

The scope and severity of injuries caused by vaginal mesh implants have made this device a prominent example of the loophole in the 510(k) process. The vaginal mesh implant is used in women to treat urinary incontinence or to repair pelvic organ prolapse. Pelvic organ prolapse occurs when the tissues that hold the pelvic organs in place become weak or stretched, generally due to age or childbirth. Internal organs collapse into the vagina, causing pain, bleeding, and urinary incontinence. Surgeons implant the hammock-shaped mesh sling to reinforce the weakened tissue and keep a woman's internal organs in place.



Example transvaginal mesh implants used to urinary treat incontinence

Despite the recall, several vaginal mesh products continue to trace their lineage back to ProtoGen.

Boston Scientific Corporation (BSC) released the ProteGen bladder sling for urinary incontinence in 1997, relying a 90-day study conducted with rats and the fact that the mesh was being used in cardiovascular – though not urological – operations. FDA deemed the device "substantially equivalent" to an earlier mesh product. The results, according to the American Journal of Obstetrics and Gynecology, were disastrous.[9] After receiving the implants, hundreds of women reported experiencing severe pain, life-threatening infections and neurological complications that required multiple additional surgeries. BSC recalled

[9] Wall LL, Brown D. The perils of commercially driven surgical innovation. Am J 0bstet Gynecol [20]10;202:30.e1 - 4.

ProteGen in 1999 after learning of the harm it was causing patients.

Despite the recall, several vaginal mesh products continue to trace their lineage back to ProtoGen. Gynecare TVT, a product made by Ethicon, a subsidiary to Johnson & Johnson, remains on the market today despite naming ProteGen as its predicate. FDA cleared Gynecare TVT in 1998, just prior to ProteGen's recall.

Additionally, in 2003, FDA cleared a vaginal mesh product, the Obtape Vaginal Sling, made by Mentor Corporation, another Johnson & Johnson subsidiary. Obtape, which also traces its predicate lineage back to ProteGen, remained on the shelves until 2006, when the company pulled the product after receiving reports of women suffering erosion of vaginal tissue, pain, and other injuries.

FDA released a public health notification in 2011 that warned doctors and patients that serious injuries associated with vaginal mesh devices were not uncommon despite being initially thought to be infrequent. From 2005 through 2010, the FDA received approximately 4,000 reports of serious complications stemming from the mesh. According to the agency alert, the most frequent complications reported to the FDA include:

> **"Mesh erosion through the vagina…pain, infection, bleeding, pain during sexual intercourse (dyspareunia), organ perforation, and urinary problems. There were also reports of recurrent organ prolapse, neuro-muscular problems, vaginal scarring/shrinkage, and emotional problems. Many of these complications require additional intervention, including medical or surgical treatment and hospitalization."**[10]

Mesh complications have resulted in at least seven deaths.[11]

The FDA's alert noted that the complications of mesh, including erosion, could require multiple surgeries – a painful and potentially debilitating prospect for women. In some cases, it says, "even multiple surgeries will not resolve the problem".

Trying to remove mesh is "like trying to get gum out of your hair."

Lana Keeton, a 64 year-old woman from Austin, has suffered several of these devastating consequences from vaginal mesh for more than a decade. After triggering a life-threatening infection in Lana, the mesh began to slice through her bladder. To date, she has undergone sixteen surgeries in an attempt to remove as much of the mesh as possible, but trying to remove mesh is "like trying to get gum out of your hair. You're never able to remove it all." (See report section "Patient Stories")

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[10] FDA Safety Communication: UPDATE on Serious Complications Associated with Transvaginal Placement of Surgical Mesh for Pelvic Organ Prolapse." *Alerts and Notices (Medical Devices)*. Food and Drug Administration, 13 July 2011.

[11] Food and Drug Administration. Obstetrics and Gynecology Devices Advisory Committee. *Surgical Mesh for Treatment of Women with Pelvic Organ Prolapse and Stress Urinary Incontinence*. 8-9 Sept 2011.

The FDA also stated that these injuries were not uncommon. The alert stated that "serious complications associated with surgical mesh for transvaginal repair of POP [pelvic organ prolapse] are not rare".[12]

Despite the clear risks posed by surgical mesh, the FDA concluded that there is "no evidence that transvaginal repair of POP [pelvic organ prolapse] provides any added benefit compared to traditional surgery without mesh."[13] As pelvic surgeon Dr. Tom Margolis stated in his 2011 testimony to FDA on the topic (see Appendix B), "synthetic mesh for prolapse and SUI [stress urinary incontinence] produces an unacceptably high and clearly avoidable plethora of life ruining surgical complications in women and there are numerous safer surgical alternatives with superior success rates."[14]

A 2011 report by FDA's Obstetrics and Gynecology Devices Advisory Committee stated that the problems with the vaginal mesh are inherent to the devices and are not a result of poor doctor training or incorrect surgical placement. The report noted that in many of the randomized controlled studies with high reported rates of mesh erosion, the procedure was performed by skilled surgeons with advanced training and experience with the mesh product. The doctors concluded:

> **"The FDA does not believe that the problems associated with mesh procedures can be attributed exclusively to surgical still/training. Restricting use of mesh to surgeons with a specified level of experience and training would not eliminate mesh-related complications. The FDA believes that vaginal placement of surgical mesh for POP [pelvic organ prolapse] repair inherently introduces risks of complications that are unique to the mesh itself."[15]**

"These deadly devices are copycat killers"

In an open letter from Truth in Medicine, a group dedicated to raising awareness and supporting the patients harmed by vaginal mesh implants, the members write that FDA must have the flexibility to reject devices like mesh that are based on recalled products. "These deadly devices are copycat killers," it reads, "ending lives and hopes and dreams." (see Appendix C).

The SOUND Devices Act instructs FDA to determine whether a new 510(k) device repeats the flaws that led to a recall of a device in its predicate history and gives the agency authority to reject clearance of a device if it shares these flaws. If FDA had the authority provided by the SOUND Device Act, the agency may have prevented unsafe vaginal meshes from making it to the market, saving lives and countless women from chronic lifelong debilitation.

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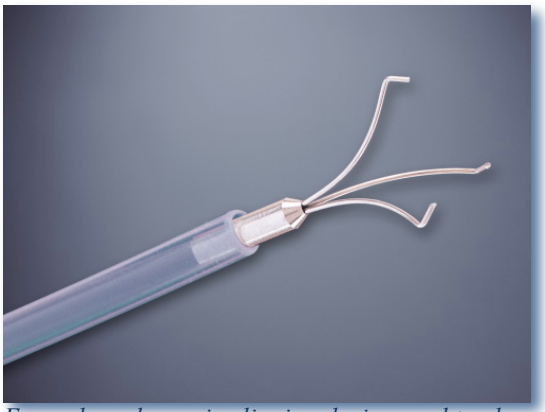
[12] Ibid.
[13] Ibid.
[14] FDA Testimony of Dr. Tom Margolis on Transvaginal Mesh Implants, 8 Sept 2011.

[15] Food and Drug Administration. Obstetrics and Gynecology Devices Advisory Committee. *Surgical Mesh for Treatment of Women with Pelvic Organ Prolapse and Stress Urinary Incontinence*. 8-9 Sept 2011.

Endoscopic Clipping Devices

An endoscopic clipping device, the Resolution II Clip manufactured by Boston Scientific Corporation (BSC), provides another example of a device that FDA cleared for commercial sale based on its substantial equivalence to a recalled device. An endoscopic clip is a metallic clip used to close two disjointed surfaces inside the body, without the need for surgery and suturing. Its function is similar to a suture, but the clip can be applied through the channel of an endoscope using a catheter under direct visualization. Doctors often use these devices to close off ulcers, gastrointestinal bleeding or other bleeding lesions.

In 2009, BSC recalled an earlier iteration of its endoscopic clip, the Resolution Homeostasis Clipping Device, because of a flaw that caused the deployed clip to remain anchored to the clip's catheter delivery system.[16] The patient's tissue would tear when doctors attempted to remove the endoscope and clip delivery system from the patient's body.



Example endoscopic clipping device used to close disjointed surfaces inside the body

In 2010, BSC submitted an application for another endoscopic clip, the Resolution II clip, which named the Homeostasis device as its predicate.[17] The FDA reviewed patient injuries and other adverse events. Despite the known recall of the Homeostasis clip, the FDA found that there were "no changes in the safety or effectiveness of the proposed device". Thus, the agency had no legal authority to deny the Resolution II clearance under the "substantial equivalence" standard.

To mitigate foreseeable issues with this second device, the FDA requested a stronger warning on the label that the manufacturer agreed to include. However, despite the additional warning labels, BSC recalled the Resolution II clip in August 2011 after patients reported tissue trauma and increased bleeding due to the fact that the deployed clip remained attached to the catheter during withdrawal of the system – the same problem patients experienced with the predicate. This second device was recalled because it repeated the same flaw identified in the first recalled device. Unfortunately, it took additional patient injuries to trigger the device's removal from the market.

This situation could have been avoided if the FDA had the authority to reject a 510(k) application when the agency became aware that the device shared a flaw with a previously recalled device. The SOUND Devices Act grants FDA this authority so that additional patients do not need to be injured by a foreseeable problem with a device.

[16] FDA Enforcement Report for October 7, 2009. Food and Drug Administration website, 7 Oct 2009.

[17] BSC 510(k) for Resolution II Clip, http://www.accessdata.fda.gov/cdrh_docs/pdf10/K102764.pdf

Cardiovascular Catheters

Two cardiovascular catheters were recalled in 2004 and 2005 due to defective sheaths, or "sleeves" that are used to insert a catheter into the heart or artery. The first device, SafeSheath, was recalled by Thomas Medical Products, Inc. because the sheaths were degrading when exposed to fluorescent light.[18]

According to FDA's adverse event reporting database, the device broke off inside patients during surgery, requiring additional surgery to remove the fragmented sheath from the patient. In another instance, the surgeon reported that while the sheath was being inserted, "it started to crumble and break" causing a loss of blood in the patient. The surgeon obtained a second sheath and it "broke in half while trying to remove it from the package."[19]

The second device, sheaths manufactured by B. Braun Medical, were recalled in 2005 after the company received reports that the devices had cracked handles and were peeling during operations.[20]

Unfortunately, these two catheter devices served as predicates for a later device, Oscor Inc.'s Adelante Luer-Lock Peel Away Introducer Set, which is used as a tube to introduce diagnostic or therapeutic devices into the body. Oscor's 510(k) application for the Adelante Introducer Set failed to include information on the recall of either recalled predicate device. The FDA reviewer, following the substantial equivalence standard, found the device to be substantially equivalent in 2007,[21] three years after the first predicate device was recalled. Oscor subsequently recalled the Adelante Introducer Set in 2008 after discovering the devices also malfunctioned and prevented doctors from safely inserting catheters during surgery.[22]

The SOUND Devices Act requires manufacturers of a device to inform FDA if any products in their new device's predicate lineage have caused serious harm and to explain how their new device avoids defects in the predicate device. Device manufacturers largely do this research during their product development, but there are no requirements that this information be provided to the FDA. If the new device has avoided the identified flaw in the first device, FDA would be allowed to clear this device for market. However, if the possibly dangerous flaw was repeated, FDA would have the authority to deny the new device clearance, protecting patients from potentially devastating and deadly consequences.

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18 http://www.fda.gov/Safety/Recalls/EnforcementReports/2004/ucm120323.htm

19 http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfmaude/detail.cfm?mdrfoi__id=591380

20 http://www.fda.gov/Safety/Recalls/EnforcementReports/2005/ucm120366.htm

21 http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=26282

22 http://www.fda.gov/Safety/Recalls/EnforcementReports/2008/ucm120530.htm

LANA KEETON - a 64 year-old woman living in Austin, Texas, has suffered from more than a decade because of the loophole in the 510(k) process. In 2001, she entered the hospital for a hysterectomy to remove benign tumors on her uterus that were causing cramping and bleeding. She had also been experiencing minor urine leakage that occurred when she coughed or sneezed. After mentioning this to her doctor, she was told that the incontinence could easily be fixed during the hysterectomy surgery by implanting a mesh sling to hold up her bladder. Her vaginal mesh had been cleared by FDA due to its similarity to the recalled ProteGen.

Days after the surgery, Lana began experiencing searing pain in her abdomen caused by a raging infection, a known side effect of mesh. She was rushed to the hospital for emergency surgery to cut away tissue being attacked by flesh-eating bacteria known as necrotizing fasciitis. Lana was hospitalized for more than two weeks and bed ridden for months.

After fending off this life-threatening infection, Lana's mesh implant began to erode through the wall of her bladder, shredding the tissue. She has since undergone 16 surgeries to remove the parts of the mesh that could be cut out and repair the damage. "It's like getting gum out of your hair," Lana explains. "Doctors will never be able to remove it all."
Once a successful steel broker, Lana lost her job and her home. Facing a mountain of medical bills, she was forced to declare bankruptcy.

In 2008, Lana founded Truth in Medicine, and organization dedicated to raising awareness and supporting patients harmed by vaginal mesh implants.

JAY NEVAREZ, a 50 year-old mother of three, lives in constant pain caused by a vaginal mesh implant she received four years ago. Jaye used to work as a truck driver in Colorado, where she earned a good salary and enjoyed playing the drums in a band. She began to suffer urinary incontinence, and in April 2008 Jaye underwent surgery to receive the Gynecare TVT mesh implant.

Upon awaking from the surgery, Jaye says that she felt as if a "razor blade" was running through her. She complained immediately to her doctor but was told that her symptoms were normal for having just undergone surgery. Over the following weeks, however, her pain worsened to the point where she could not sit, stand, or walk. The pain was so searing and so constant that Jaye considered ending her own life.

Three weeks later, an examination revealed that the mesh implant had begun to through her vaginal wall and was slicing into her urethra. Jaye underwent a second surgery so that a surgeon could remove whatever parts of the device he was able to dislodge from her organs. Though nearly four years have passed, Jaye's condition has barely improved. She lives in constant pain and cannot walk without the help of a cane or a walker. The pieces of the implant that remain in her body have led to nerve damage that causes her left leg to collapse frequently.

"I was a tax-paying citizen," Jaye says, recalling her life before her surgery. "I was a truck driver making decent money with a nice house. Now I can't walk. I'm on disability. I'm in debt and they've got liens against my house. Why? All because of a little piece of plastic."

"I was a truck driver making decent money with a nice house. Now I can't walk."

Conclusion

A dangerous loophole exists in the current 510(k) process that puts unsuspecting patients at risk of avoidable and foreseeable injuries from medical devices. Currently, FDA does not have authority to reject a 510(k) medical device application when the company can claim it is similar to an already-approved device, even if that predicate device has fundamental design flaws that resulted in it being recalled from the market.

As a result of this loophole, several medical devices have been able to enter the market, being implanted into patients and causing severe and sometimes life-long debilitating consequences. Many victims of these "copycat killers" have had their lives transformed by these defective devices. Once productive and active members of society, patients have become shells of their former selves, unable to participate in the activities they once enjoyed, and reliant on government support through disability benefits. In some cases, these medical devices even led to death.

The SOUND Devices Act introduced by Congressman Edward J. Markey closes this major loophole by providing FDA with clear authority to reject clearance of a medical device if it repeats flaws found in a previously recalled device. Now is the time to close this lethal loophole.

Appendix A

Congressional Research Service Report
The FDA's Authority with Regard to Substantial Equivalence Determinations

Congressional Research Service

MEMORANDUM March 16, 2012

To: Rep. Edward Markey
Attention: Avenel Joseph, Legislative Assistant

From: Vanessa Burrows, Legislative Attorney, 70831

Subject: **The FDA's Authority with Regard to Substantial Equivalence Determinations**

This memorandum responds to your request for a review of whether the Food and Drug Administration (FDA) has the authority to deny a § 510(k) clearance for a new device based on a predicate device that has been recalled for safety reasons. In other words, this memorandum addresses whether the FDA is required to find that a new device is not substantially equivalent to a "faulty" predicate device based upon the existence of safety or other issues with the predicate device.[1]

Background

Under the Federal Food, Drug, and Cosmetic Act (FFDCA),[2] new medical devices are automatically designated in the highest risk device class and therefore must receive the greatest amount of regulatory oversight and control from FDA—premarket approval—unless the device meets one of Act's exceptions.[3] One of these exceptions is if the new device is "substantially equivalent" to a predicate device that is legally marketed.[4] A device is "substantially equivalent" if the FDA makes such a determination based on a comparison of the new device with a predicate device, which could have been marketed either before or after Congress passed the Medical Device Amendments Act of 1976.[5] An FDA finding of "substantial equivalence" is not a statement by the agency as to the safety or effectiveness of the device.[6]

[1] The Federal Food, Drug, and Cosmetic Act (FFDCA) provides that "[a] device may not be found to be substantially equivalent to a predicate device that has been removed from the market at the initiative of the Secretary or that has been determined to be misbranded or adulterated by judicial order." 21 U.S.C. § 360c(i)(2). This memorandum assumes that "faulty" predicate devices are those other than addressed in this specific statutory provision.

[2] 21 U.S.C. §§ 301 *et seq*.

[3] 21 U.S.C. § 360c(f)(1); 21 U.S.C. § 360e.

[4] 21 U.S.C. § 360c(f)(1)A).

[5] 21 U.S.C. § 360c(f)(1)(A).

[6] As the Supreme Court stated in *Medtronic, Inc. v. Lohr*, "the 510(k) process is focused on *equivalence*, not safety." 518 U.S. 470, 493 (1996)(citation omitted). The Court noted that determinations of substantial equivalence "simply compare a post-1976 device to a pre-1976 device to ascertain whether the later device is no more dangerous and no less effective than the earlier device. If the earlier device poses a severe risk or is ineffective, then the later device may also be risky or ineffective." *Id.* (quoting Robert Adler, *The 1976 Medical Device Amendments: A Step in the Right Direction Needs Another Step in the Right Direction*, 43 FOOD DRUG COSM. L. J. 511, 516 (1988)).

The new device seeking the "substantially equivalent" determination must either have (1) the same intended use as the predicate device and the same technological characteristics as the predicate device, or (2) the same intended use, different technological characteristics,[7] information "that demonstrates that the device is as safe and effective as a legally marketed device," and also must "not raise different questions of safety and effectiveness than the predicate device."[8] If information is requested by the Secretary of Health and Human Services (acting through FDA) "to demonstrate that devices with differing technological characteristics are substantially equivalent," the FFDCA provides that such requests must be for information "necessary to making substantial equivalence determinations" and that requests be made after the Secretary's consideration of "the least burdensome means of demonstrating substantial equivalence."[9] In making determinations of substantial equivalence, the predicate device must not have been "removed from the market at the initiative" of the FDA and must not have "been determined to be misbranded or adulterated by a judicial order."[10]

A finding of "substantial equivalence" is tied to the premarket notification requirement for new devices under the FFDCA § 510(k) clearance process. A premarket notification submission is known as a § 510(k) submission, after the section of the FFDCA that requires it. At least 90 days before an applicant (such as a manufacturer) may market certain new devices, the applicant must submit a premarket notification to the FDA that demonstrates the device is "substantially equivalent" to a legally marketed device that does not require FDA premarket approval.[11] After the FDA reviews a premarket notification submission, the agency may find that the device either is or is not substantially equivalent to a legally marketed predicate device; request more information; withhold a decision pending the submission of certain information; or find that the device does not require premarket notification.[12] If the FDA issues an order finding that the new device is substantially equivalent, then the new device is considered to be "cleared" for marketing. A manufacturer may not market the new device if the FDA finds that a new device is not substantially equivalent to a legally marketed predicate device.[13]

Analysis

As the above explanation of the § 510(k) process indicates, the FFDCA does not appear to grant the FDA the explicit authority to find that a new device is not substantially equivalent to a "faulty" predicate device based upon the existence of safety or other issues with the predicate device. Nor does the statute specify that the FDA is required to find that a new device is not substantially equivalent due to safety issues associated with the predicate device. Therefore, it would not appear that the FDA would be able to deny a § 510(k) clearance based on a predicate device that has been recalled for safety or other reasons, as

[7] " 'Different technological characteristics' means … that there is a significant change in the materials, design, energy source, or other features of the device from those of the predicate device." 21 U.S.C. § 360c(i)(1)(B).

[8] 21 U.S.C. § 360c(i)(1)(A).

[9] 21 U.S.C. § 360c(i)(1)(D); *see* Benjamin A. Goldberger, *The Evolution of Substantial Equivalence in FDA's Premarket Review of Medical Devices*, 56 FOOD & DRUG L.J. 317, 328 (2001)(stating that "[i]nformation not related directly to substantial equivalence, such as information about the absolute safety and effectiveness of a device, may not be requested").

[10] 21 U.S.C. § 360c(i)(2); 21 C.F.R. § 807.100(b)(3).

[11] 21 U.S.C. § 360(k); 21 C.F.R. § 807.81(a); 21 C.F.R. § 807.3(n); 21 C.F.R. § 807.92(a)(3). The submission must contain the information required in 21 C.F.R. § 807, Subpart E. Certain § 510(k) submissions "in which a determination of substantial equivalence is also based on an assessment of performance data" must contain, where applicable, "a discussion of the safety or effectiveness data obtained from the testing, with specific reference to adverse effects and complications … relevant to a determination of substantial equivalence." 21 C.F.R. § 807.92(b)(2); *see also* 21 C.F.R. § 807.87(j)(providing that the FDA may require adverse safety and effectiveness data).

[12] 21 C.F.R. § 807.100(a).

[13] 21 C.F.R. § 807.100(a)(5).

long as that predicate device was not "removed from the market at the initiative" of the FDA.[14] To the extent that the predicate device was "removed from the market at the initiative" of the FDA, the FFDCA does specify that a new device "may not be found to be substantially equivalent" to such a predicate device, and, as a result, the new device would not be cleared for marketing.[15]

If the new device has the same intended use and the same technological characteristics as the predicate device, the FFDCA indicates that this is "substantial equivalence."[16] The statute does not appear to provide for a finding other than substantial equivalence in such a case, based on concerns about the safety of the new or the predicate devices. Therefore, if a new device has the same intended use and the same technological characteristics as a "faulty" predicate device, the FDA would not appear to have the authority to find that the new device is not substantially equivalent to the "faulty" predicate device.

If the new device has the same intended use and different technological characteristics than the predicate device, the FFDCA requires that the new device be "*as safe* and effective as a legally marketed device" and "not raise *different* questions of safety and effectiveness than the predicate device."[17] This language appears to indicate that while the FDA may have concerns about the safety of a predicate device, to the extent that the new device is *as safe* as the predicate device and raises the *same* questions about safety as the predicate device, the FDA could still determine that the new device is "substantially equivalent" to the problematic predicate device. To the extent that the new device appears *less safe* or raises *different* questions of safety than the predicate device, the FDA could request information necessary on this point in order to determine whether the device is as safe as the predicate or whether the questions of safety for the new device are different, and thus make an appropriate substantial equivalence determination.[18]

This conclusion appears to be buttressed by language in another provision of the FFDCA that prohibits the Secretary, acting through the FDA, from withholding a substantial equivalence determination "because of a failure to comply with any provision of this Act unrelated to a substantial equivalence determination."[19] If safety or other problems with a predicate device are seen as "unrelated to a substantial equivalence determination," then the FDA would be prohibited from making a determination of substantial equivalence based on such problems.[20]

[14] 21 C.F.R. § 807.100(b)(3).

[15] 21 C.F.R. § 807.100(b)(3).

[16] 21 U.S.C. § 360c(i)(1)(A)(i).

[17] 21 U.S.C. § 360c(i)(1)(A)(ii) (emphasis added).

[18] 21 U.S.C. § 360c(i)(1)(A), (D).

[19] 21 U.S.C. § 360c(f)(5). This language could be viewed as a catch-all provision for other violations of the FFDCA that are not specifically listed as the reasons for which the FDA may not find a device to be substantially equivalent—the predicate device was removed from the market at the initiative of the Secretary or the predicate device was found by a court to be misbranded or adulterated. 21 U.S.C. § 360c(i)(2).

[20] 21 U.S.C. § 360c(f)(5).

Appendix B

Testimony of Dr. Tom Margolis to Food and Drug Administration on Transvaginal Mesh Implants

9/8/2011

I'd like to thank the FDA for inviting me to speak on the serious issue of transvaginal surgical mesh complications.

My comments pertain only to the transvaginal implantation of synthetic mesh for pelvic organ prolapse and stress incontinence. These comments are based on my knowledge, experience, education and training as a Pelvic Surgeon and on observations made during scores of "salvage" operations I've performed on women who have experienced mesh complications over the last decade.

Transvaginal implantation of synthetic mesh for any reason is a surgical theory and technique that defies core surgical doctrines.

In 1982, the CDC adopted the American College of Surgeons wound classification system that classifies wounds according to the likelihood and degree of wound contamination during surgery. In this system, vaginal surgery is classified as "clean-contaminated" carrying a risk of wound infection of 3-11% as compared to clean wounds, which carry a risk of infection of 1-5%. (1)

The vagina is classified as "clean-contaminated" because normal vaginal flora cannot be surgically cleansed from the operative field. These normal flora include a diverse array of bacteria including but not limited to Staph., E. coli, Kebsiella, Streptococcus, Peptostreptococcus, and Bacteroides, all of which are found in wound infections. (2)

The implantation of contaminated synthetic mesh through the vagina defies basic surgical tenets because by definition it is not performed in a sterile manner. In fact so-called "mesh erosion", the most common mesh complication, is in reality "mesh infection with chronic wound breakdown". Time does not permit me to expound upon the plethora of other complications associated with transvaginal mesh such as damage to bowel, bladder and blood vessels, vaginal scarring, dyspareunia, need for multiple repairs and destroyed personal lives but the MAUDE database has already begun to do this.

What it's like to remove mesh from the surgeon's perspective can perhaps be appreciated by this analogy. Extirpation of vaginal mesh is akin to taking a hammer and chisel and trying to remove the rebar from a sidewalk while leaving the cement otherwise intact and not damaging the water mains and power lines below. It is difficult if not impossible to remove all the mesh and do it safely.

Nearly 20 years ago FDA Commissioner Kessler wrote, "It is not the culture of U.S. medicine to report adverse events to the FDA". (3) He speculated that only one percent of serious adverse events are reported to the FDA, an estimate consistent with a 1986 survey of hospitals by the Government Accountability Office which found that 99% of problems associated with select medical devices had not been reported to the FDA's post marketing surveillance system. (4) Thus, the recent adverse mesh findings already published by the FDA represent only a small percentage of the total number of women affected.

The counterintuitive surgical technique of vaginal mesh implantation was seemingly invented to accommodate new devices which made it easier for doctors with less surgical training to operate. These doctors were apparently seen as a target rich environment for a marketing campaign which convinced many of them that this inherently risky approach was safe. It's quite possible that some device manufacturers' financially incorporated so called "key opinion leader" surgeons into their promotional endeavors which may have further facilitated the publishing and dissemination of misleading (and sometimes fabricated) clinical data.

On a positive note, there are numerous superior options to the use of synthetic mesh for SUI and prolapse. The MMK (or Burch) is still the Gold Standard surgery for SUI as are the sacrospinous fixation and sacral colpopexy for vault prolapse. It is firmly established in the world's literature that when these procedures are combined with traditional repairs as indicated, their success rates are second to none. Furthermore, with fewer complications than mesh they are simply the best procedures in the repertoire.

In summary, synthetic mesh for prolapse and SUI produces an unacceptably high and clearly avoidable plethora of life ruining surgical complications in women and there are numerous safer surgical alternatives with superior success rates. I hope the FDA will, through firm action, help save others from the painful experiences that thousands of unfortunate women have had to suffer through so far.

Again, I'd like to thank the FDA for inviting me to speak on this important issue.

Michael Thomas Margolis
MD, FACS, FACOG

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Appendix C

Letter from Truth in Medicine and its members
Re: The Safety Of Unused and New Devices (SOUND Devices) Act

To Whom It May Concern:

We write to express our deep frustration and anger about a major loophole in our nation's medical device approval process that has allowed dangerous products onto the market, killing and injuring thousands of patients. The problem stems from a flaw in the 510(k) process, which allows medical devices to be cleared for use without undergoing human clinical trials assuring safety and effectiveness. Instead, the device company must only show that the new device is "substantially equivalent in technology and intended use" to a previous product, known as a "predicate." Under current law, however, FDA is legally obligated to clear a device that meets the current requirements of "substantial equivalence" to an earlier model, even if that model was recalled because of a major defect.

All of the undersigned women underwent surgery to receive mesh implants, whose design traces back to an implant that was voluntarily recalled in 1999 after causing thousands of injuries. The mesh implants are used to repair pelvic organ prolapse (POP) or to treat urinary incontinence. Pelvic organ prolapse, usually caused by age or childbirth, occurs when the tissues that hold the pelvic organs in place become weak or torn. The mesh implants, we were told, would "fix the problem".

We had no idea of the devastating consequences we would face as a result of these surgeries, and none of us deserve what has happened. We do not deserve to live with chronic and life-altering pain, though many of us do. We do not deserve recurring infections, bleeding, painful sexual intercourse, difficulty urinating, or to have our organs perforated by sharp pieces of eroding surgical mesh. We certainly do not deserve to die.

Jaye Nevarez from Colorado deserves the right to her life as she knew it, driving a truck and playing drums in her band. She can no longer work and struggles to pay her bills. Robert Fish's mother deserved the right to life without the intense and incurable pain that caused her to go out in the back yard, wrap herself in a blanket, slit both of her wrists to the bone and then shoot herself in the heart. Robert Fish deserves to have his mother, the woman he loved and admired so much, here on earth with him.

The tragedy of this situation is compounded by the fact that device companies can still use these flawed surgical mesh implants as predicates or models for future devices. And if any new devices are, in fact, substantially equivalent to the older defective devices, FDA must allow the device to be sold. This is true even if the predicate was recalled by the company.

Reports of mesh-related injuries continue to surface. In 2011, FDA announced that it had received more than 3,800 reports of serious complications associated with trans-vaginal surgical

mesh implants, including more than a dozen deaths. Furthermore, it announced that "serious complications associated with surgical mesh…are not rare." Furthermore, FDA stated that treating POP with mesh implants has notshown to be more effective than traditional non-mesh repair though it exposes patients to greater risk.

FDA must be given the ability not to clear for market "substantially equivalent" medical devices based on recalled predicates. These deadly devices are "copycat killers," ending lives and hopes and dreams. That is why Truth in Medicine strongly commends Congressman Ed Markey and the co-sponsors of the Safety Of Unused and New Devices (SOUND Devices), which would allow FDA to reject devices whose design may mirror a major safety flaw found in their predicate.

Most of us will live with the pain of our surgeries for the remainder of our lives. But Congress can protect others from suffering the same fate. Truth in Medicine urges all members of Congress - all Democrats and all Republicans - to support the SOUND Devices Act and give the FDA the ability to protect unsuspecting patients from unsafe, untested, and potentially dangerous medical devices. Please stop the harm!

Yours truly,

The Board of Directors of Truth in Medicine Incorporated
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