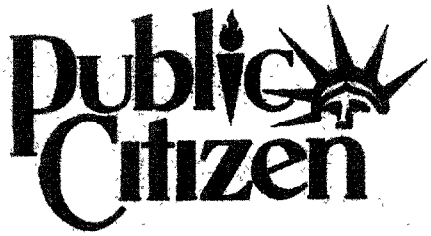
2005-6042



Buyers Up • Congress Watch • Critical Mass • Global Trade Watch • Health Research Group • Litigation Group
Joan Claybrook, President

September 14, 2005

Daniel Schultz, M.D.
Director, Center for Devices and Radiologic Health
Food and Drug Administration
9200 Corporate Boulevard
Rockville, MD 20850

Dear Dr. Schultz:

On behalf of Public Citizen, a nationwide consumer organization with 135,000 members, we are petitioning the Food and Drug Administration (FDA) to establish tighter regulations governing the process by which medical devices are reviewed and recalled. This issue has been brought to light recently in news reports about a series of Guidant defibrillators that continued to be implanted even after improvements had been made to newer models to correct what was known to be a potentially fatal malfunction.[1] In both that case and the case that is the subject of this letter, the manufacturer knew that its product was potentially defective but did not promptly remove that product from the market or notify doctors or patients. As a result, patients were implanted with devices that were known to be potentially defective even when newer, improved devices were available from the same company.

Until this week, the focus had been on Guidant itself, but a story in the *New York Times*[2] revealed that the FDA had been informed about the problem months before, but took no action until the *Times* investigation. We report still another case, involving a pacemaker, in which the FDA was complicit in a company's inaction. The agency was aware of the problems with the device but did not ensure that older, potentially defective models were expeditiously removed from the market, even as that agency approved a safer device for marketing by the same company. In this case, the manufacturer appears to have used a more formal process to alter its device than in the Guidant case, making the FDA's inaction all the more unacceptable. A minimum of 180 devices were surgically removed from patients, all with potentially lethal premature battery depletion.

We were contacted by one patient, [redacted], who was given a replacement St. Jude Medical pacemaker after another pacemaker, also made by St. Jude, had failed prematurely. At the time of the replacement he did not know that St. Jude and the FDA had known that the pacemaker he received as a replacement was inferior to another St. Jude device. Several months prior to his implantation, St. Jude had received permission from the FDA to market this substitute pacemaker with the problem corrected. At the time that [redacted] received his replacement pacemaker, St. Jude had already been distributing the corrected version for six weeks. St. Jude initially failed to recall the older device (even though the company

1600 20th Street NW • Washington, DC 20009-1001 • (202) 588-1000 • www.citizen.org

CP1

2005P-0453

believed it was problematic enough to require redesign), but eventually the company was compelled to do so as cases of pacemaker failure predictably accumulated.

The current system does not provide for automatic, mandatory review of older devices as newer ones, with improved safety and/or efficacy, are brought to market. Instead, companies are permitted to delay (or even prevent) the removal from the market of a flawed device as physicians continue to use the remaining inventory. The company can then manufacture and distribute the improved version to its field representatives who introduce the physicians to the new model as the older model is slowly phased out. One benefit to the manufacturer is that the company can wait until the new device has an established market before it recalls the older version, all the time depleting its inventory of older, inferior devices. Although this practice benefits the manufacturers and distributors, the patients who receive these inferior products are potentially placed in grave danger.

ACTION REQUESTED

This petition asks the agency to promulgate a new regulation that enables the FDA to withdraw approval for an approved medical device that has caused patients harm, or that raises a substantial likelihood of causing harm, when another device is on the market that is equally or more effective for the same use, but poses less risk. Such a regulation should also facilitate a recall of such a problematic device.

CASE HISTORY

[redacted] who had his third pacemaker, a St. Jude pulse generator Trilogy 2364L, implanted in February 1998. One year later, in February 1999, the atrial portion of the new pacemaker failed. [redacted] is pacemaker-dependent; his heart rate can become life-threateningly low, at which point his pacemaker is supposed to automatically keep his heart beating. Fortunately, the pacemaker failure was detected by his physician, and [redacted] underwent surgery on March 1, 1999. The defective pacemaker was replaced with another St. Jude Trilogy 2364L.

[redacted] was curious why the pacemaker battery had failed in only one year because pacemaker batteries are expected to last five-to-six years. When a pacemaker fails prematurely, it is routinely sent back to the company for evaluation and the company sends the explanting physician a "failure analysis report" explaining what went wrong. [redacted] got a copy of this report from his doctor, and it revealed that there had been a

> loss of output and telemetry capabilities which resulted from a depleted battery ... Invasive examination revealed foreign material contamination, producing an electrical short circuit from the battery case (+) to its (-) terminal.[3]

St. Jude found that metallic weld spatter between the battery pin and the battery case caused a dangerous electrical connection between the positive and negative terminals of the battery, causing the battery to short-circuit and therefore deplete prematurely. The FDA-approved fix

solved this problem by creating an insulating ring around the negative pin of the battery so that it was not possible to form a connection between it and the positive end of the battery.

[redacted] filed a complaint with the FDA to find out more about why his pacemaker had failed. The complaint was assigned to James Fleckenstein, an FDA investigator in the Los Angeles District office. Mr. Fleckenstein explained in his report that "[I]t seems clear from my review of the management controls within the quality system that top management [at St. Jude] was aware of the premature battery problem in 1997 and monitored it until July 1999."[4] In 1997, according to Fleckenstein, St. Jude

> initiated Product Improvement report 97-001 to study and correct the problem. By October 1998, St. Jude understood the problem and had validated a fix for it. They submitted this fix as supplement 56 to PMA P880086. FDA approved the supplement on 11/3/98. St Jude's formal change control program implemented the fix into production on 1/6/99 ... The first unit built with the fix was reportedly released on or about 2/3/99.[4]

However, [redacted] received his replacement pacemaker (another Trilogy 2364L from the potentially defective series) on March 1, 1999, and it did not did not contain the FDA-approved fix. According to Mr. Fleckenstein, [redacted] new pacemaker was

> reported to have begun top level production on 12/8/98 and was released to finished goods on 1/11/99. It was shipped on 2/22/99 to the St. Jude field representative, who is believed to have hand delivered it to the hospital shortly thereafter.[4]

Despite the fact that, at the time of his surgery, corrected units had been available for almost a month, [redacted] received an older unit manufactured after the new units began production. The report explains that

> St Jude did not rework or retrieve the [older] pacers in its possession prior to 01/06/99. Those pacers already built or in process with the potential for premature battery failure were distributed to the field. At the time, St. Jude believed the subject failure rate did not warrant such an action.[4]

St. Jude not only failed to remove its potentially defective pacemakers from the market but also continued to manufacture the problematic pacemakers (for at least five days) and distribute them (for at least six weeks) *after* it began distributing the improved version. As a result, it was possible for a patient to receive a pacemaker that would fail prematurely, potentially costing someone his or her life, even though an undeniably safer device was already being distributed. Ironically, a patient could even receive one of the defective pacemaker models as the replacement for another defective pacemaker, as was the case for [redacted]. Fortunately, his pacemaker has continued to function adequately.

It was not until July 17, 1999, that St. Jude alerted the medical community (via a medical news release, a technical bulletin, and a physicians' alert) to the problems with the Trilogy

pacemakers. The FDA classified the firm's actions as a Class II recall.[5] The FDA recall classification report notes eight Trilogy models that the FDA considers

> to be adulterated in that [they] may exhibit premature battery depletion caused by a current leakage path that could be created during the laser welding process to attach the battery to the device hybrid. The device defect presents a moderate risk of serious adverse health consequence including death.[6]

In the end, out of the 163,000 devices manufactured, 2,393 were retrieved as a result of the recall.[7] There had been 88 explants for premature battery failure at the time of the recall, a number that had climbed to 180 as of September 18, 2000.[4]

Mr. Fleckenstein's report concludes with the statement that St. Jude was informed that

> the complainant was very disappointed that [he] received a replacement pacer that has the same potential for failure as the one that was explanted ... This disappointment is compounded in that St. Jude was aware of the problem for two years before the replacement surgery.

Mr. Fleckenstein continues that while St. Jude understood the complaint, the company "stands by [its] actions."[4]

There were many points where St. Jude could have taken proactive steps to protect public safety. St. Jude executives could have recalled the pacemakers as soon as they realized that they contained a design flaw that would lead to premature battery depletion (1997). They could have recalled the pacemakers once they knew exactly what the problem was and how to fix it (October 1998). They could have ordered a recall when the FDA approved the Premarket Approval (PMA) Supplement allowing St. Jude to correct the problem (November 1998). And, at a minimum, it could have initiated a recall when they began to distribute the corrected models (January 1999). Instead, the company chose to wait until July 1999, six months after the new pacemakers were on the market, before it initiated a recall or informed patients and doctors. During this period, some fraction of the remaining inventory was used (i.e., implanted in unsuspecting patients) while the company had time to establish its improved pacemaker in the marketplace. The inappropriateness of this is obvious when examined from the patient's point of view. No patient, if given the choice, would choose a pacemaker from a series that contains a significant percentage of dangerous pacemakers when a safer alternative was available.

COMPARISONS TO THE GUIDANT CASE

This past March, a 21-year-old student died when his Guidant defibrillator short-circuited. In this case, the company had been aware of the electrical flaw that was responsible for the short-circuit for years, and three years previously had changed the way it manufactured the device to eliminate the flaw. The FDA appears to have been notified of the manufacturing change in an annual report. However, neither patients nor physicians were made aware of the potential problems with the defibrillators manufactured prior to the fix. The potentially defective

defibrillators were left on the market until this summer when the company issued a recall only after this situation was made public.[8]

As they were in the Guidant case, the FDA was made aware of the problem in the St. Jude case, although apparently much more formally. St. Jude requested permission from the FDA (by applying for a Supplement to its PMA) to alter the pacemaker design to prevent early battery depletion. The St. Jude pacemakers underwent an expedited review process because the fix was judged to qualify for "Real-Time" review. Real-Time review requires that the company demonstrate that the fix involves "a minor change to the design of the device, software, manufacturing, sterilization, or labeling." Furthermore, a Real-Time review is permitted only when the FDA feels that no clinical data or inspection are needed.[9]

The criteria for pacemakers to qualify for Real-Time review are specific.[10] If the FDA agrees that an expedited review is appropriate, the company provides the FDA with "a detailed description of the proposed change, a complete assessment of the impact of the change on the safety and effectiveness of the device, and a summary of the data from testing which is intended to support the change and demonstrate a reasonable assurance of safety and effectiveness." A decision is made within five days of a phone conversation between the company and the FDA.[11] While this mechanism requires that the company demonstrate the safety of the fix, there is no built-in guarantee that the company, or the FDA, will take any action regarding any devices known to be defective that are still on the market. In the St. Jude case, the FDA took no immediate action to have the potentially defective products removed from the market. Like the Guidant case, Mr. Gleeson's exposes both company greed and the failure of the FDA to protect the public from the profit motives of device companies.

LEGAL BACKGROUND

The agency has the authority to require the removal of less safe and/or effective models from the market. As enacted in 1976, the Medical Device Amendments ("MDA") to the Food, Drug, and Cosmetic Act, 21 U.S.C. 360c et seq., give the agency authority to order a device manufacturer to notify device users and health professionals of devices that pose unreasonable risks. 21 U.S.C. 360h(a). Before ordering notification, the FDA must determine that the device presents "an unreasonable risk of substantial harm to the public health" and that "notification ... is necessary to eliminate the unreasonable risk of such harm and no more practical means is available ... to eliminate such risk." Id. § 360h(a)(1)-(2). Under that provision, the FDA is authorized to notify patients, doctors, and health care facilities that certain potentially risky devices should not be used in light of the fact that equally effective, but safer alternatives are on the market.

The 1976 Act also gave the agency authority to order manufacturers to repair, replace, or refund the purchase price of faulty devices. Id. § 360h(b). When used in conjunction with the notification remedy, that provision in effect gives the agency the power to recall devices in certain circumstances. To exercise this power, however, the FDA is required to find that "there are reasonable grounds to believe that the device was not properly designed and manufactured with reference to the state of the art as it existed at the time of its design and manufacture ..." Id. § 360h(b)(a)(A)(ii).

In 1990, Congress amended the Act to provide an additional remedy — explicit recall authority for medical devices. Under 21 U.S.C. 360h(e), the FDA may, after an opportunity for a prompt, informal hearing, recall a device if it "finds that there is a reasonable probability that [the] device ... would cause serious, adverse health consequences or death ..." In issuing a recall order, the agency may require a manufacturer, distributor, or retailer to immediately cease distribution of an offending device and/or notify health professionals and health care facilities to cease use of the device.

In circumstances where an approved device has harmed patients or has the potential to harm patients, the MDA's notification, replacement, and recall provisions all ensure that the FDA can act promptly to minimize or eliminate the risk of future harm. It should use that authority when a device known to have a design or manufacturing defect remains on the market despite the existence of equally effective, safer alternatives.

With respect to devices with PMAs, the FDA has additional authority. The FDA may withdraw premarket approval when it is shown that the device is not, in fact, safe and effective, or, on the basis of new information, that there is a lack of evidence showing that the device is safe and effective. See 21 U.S.C. 360e(e). Once again, in circumstances where it can be shown that an approved device has harmed patients, or has a potential to do so, *and* there is an equally effective, safer alternative, it cannot be said that the product is safe and effective for its intended use. That is true because safety and efficacy are relative terms; a product's value can only be evaluated against its alternatives, which is why the MDA asks whether a device provides a "reasonable assurance" of safety and effectiveness. 21 U.S.C. 360e(d)(A)&(B). When a product is approved and marketed, but is thereafter shown to have a potential to cause serious harm, the agency must ask whether the device continues to provide a "reasonable assurance" of safety and efficacy in light of safer, equally effective alternatives on the market. If there are safer, equally effective alternatives in those circumstances, the agency should withdraw the device's approval.

CONCLUSIONS

As both the St. Jude and Guidant cases demonstrate, the benefits of life-saving technologies such as pacemakers and defibrillators are limited when industry prioritizes market share and product continuity over patient safety, and the FDA does not force patient safety to the forefront. This problem is especially apparent when faulty devices are left on the market. The FDA should do more to evaluate what the approval of a new device, or improvement of an older device, means in terms of the devices that came before it. If a newer device is safer or more effective, whether made by the same company or not, the company should be forced to recall unimplanted versions of the older product. Patients and doctors should be informed so that they can make their own decisions about the wisdom of explantation.

St. Jude may not have been *required* by existing regulations to recall the faulty model, but this example highlights the way in which current FDA policy defies common sense, despite the availability of adequate regulatory authority as argued in this petition. Companies should not be allowed to continue to market defective devices when safer or more effective devices are available. The FDA should be particularly aware of this possibility when a company files a PMA supplement for a design change. The question the FDA should always ask at this point

is what the improvement of the design says about the initial device and whether the firm should be required to recall the original device. The underlying issue here is the failure of the FDA to adequately consider comparative safety and efficacy, given that existing device regulations provide adequate authority to do so.

Yours sincerely,

PL for RR

Rachel Roisman, MD
Research Associate

Peter Lurie

Peter Lurie, MD, MPH
Deputy Director
Public Citizen's Health Research Group

[1] Meier B. Maker of heart device kept flaw from doctors. New York Times, May 24, 2005, p. A1; Meier B. Heart device sold despite flaw, data shows. New York Times, June 2, 2005.
[2] Meier B. F.D.A. had report of short circuit in heart devices. New York Times, September 12, 2005.
3 Memorandum from Rita Brown, Manager, Product Reporting at St. Jude Medical, to Dr. Barry Albert, West Penn Cardiology, regarding Mark Gleeson's cardiac pulse generator model #2364L, July 7, 1999.
4 Fleckenstein JR. Memo to James Kozick: *F/U to consumer complaint LOS-9364*, September 28, 2000.
5 A Class II recall is a situation in which use of or exposure to a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote.
6 Memorandum from Cardiovascular and Neurological Devices Branch, DOE III, Office of Compliance, Center for Devices and Radiological Health, to Scott A. Goff, April 17, 2000.
7 E-mail communication with Harold Pellerite, Assistant to the Director of Compliance, Office of Compliance, Center for Devices and Radiological Health, Food and Drug Administration, April 20, 2002.
8 Meier B. Maker of heart device kept flaw from doctors. New York Times, May 24, 2005, p. A1.
9 See "Assessing User Fees: PMA Supplement Definitions, Modular PMA Fees, BLA and Efficacy Supplement Definitions, Bundling Multiple Devices in a Single Application, and Fees for Combination Products; Guidance for Industry and FDA," February 25, 2003. Available at: http://www.fda.gov/cdrh/mdufma/guidance/1201.html#_Toc33587908.
10 Real-Time review applies only when "all [p]acing and low risk changes…do not affect or impact the primary function or Neurological performance of the device: Devices changes…are based on existing technology, an incremental change made to an existing approved device from the same manufacturer, changes which are intended to correct device flaws that threaten patient safety and do not require substantive review, changes which do not require clinical data, changes which do not require substantial data analysis and/or do not involve new testing requirements." "Real-Time" Review Program for Premarket Approval Application (PMA) Supplements Available at: http://www.fda.gov/cdrh/ode/realtim2.html#Pacing%20and%20Neurological%20Devices%20Group.
[11] See "Real-Time" Review Program for Premarket Approval Application (PMA) Supplements. Available at: http://www.fda.gov/cdrh/ode/realtim2.html#Pacing%20and%20Neurological%20Devices%20Group.

Ortega, Gloria M

From: Peter Lurie [PLURIE@citizen.org]
Sent: Wednesday, November 09, 2005 10:05 AM
To: gortega@oc.fda.gov
Subject: This supplements Public Citizen's petition of 9/14/05

ENVIRONMENTAL IMPACT STATEMENT

Nothing requested in this petition will have an impact on the environment.

CERTIFICATION

We certify that, to the best of our knowledge and belief, this petition includes all information and views on which this petition relies, and that it includes representative data and information known to the petitioners which are unfavorable to the petition.

Peter Lurie, MD, MPH
Deputy Director
Public Citizen's Health Research Group
1600 20th Street, NW
Washington, DC 20009
Phone: (202)588-7781
Fax: (202)588-7796
Email: plurie@citizen.org
Web address: http://www.citizen.org