



April 19, 2005

Chairman Michael Enzi and Ranking Member Edward Kennedy
Senate Health, Education, Labor and Pensions Committee
428 Dirksen Senate Office Building
Washington, DC 20510-6300

Dear Chairman Enzi and Senator Kennedy,

We are writing to request a Congressional oversight investigation into the FDA's April 11-13, 2005 General and Plastic Surgery Devices Advisory Panel meeting on silicone breast implants for general use.

Background

On April 13, the Advisory Panel voted to recommend that the FDA put Mentor Corporation's silicone gel breast implants back on the market with nine conditions, after rejecting Inamed's application the day before. In the medical reviews prepared prior to the meeting, FDA scientific staff clearly stated that the applications from both companies had serious weaknesses, finding that the data in both applications was of limited value for responding to questions set out in the guidance for industry that the FDA issued in 2004.

Issues for Investigation

- Susan Bond, who is Director of Scientific Policy in the Office of the FDA Commissioner, circulated an email (see attachment) to Dr. Daniel Shultz, Director of the Center for Devices and Radiological Health, and to Acting Commissioner Crawford with an attached document, titled, "Backgrounder for Crawford..." Bond's email explains that this document was written by an "outsider who is interested in seeing us come out ok on the b.i [silicone breast implant] issue." Since the document is a biased summary of breast implant research that clearly advocates for FDA approval, this email implies the FDA had a pre-determined interest in approval even before the FDA advisory panel met. Sending a document from an unidentified outsider, rather than specifying the source of information on either the email or the document itself, is especially questionable. Who was the "outsider" who created this document? Did this "outsider," through Susan Bond, exert inappropriate influence over the agency to act in the interest of industry?

- Given the clear assessment by FDA scientific staff that the companies had not yet collected adequate data to meet the standard set out in the draft guidance, why did the FDA convene the panel rather than simply informing the companies that the data were inadequate to support approval?
- The Guidance Document regarding breast implant research, which was issued by the FDA in January 2004, requested platinum and other toxicology analysis on tissue samples. Neither company provided this. Did the FDA tell the manufacturers that they did not have to comply with that element of the guidance? Why wasn't an expert on platinum appointed to the Advisory Panel?
- What was the FDA's process for determining the members of the panel, and why did the agency issue a conflict of interest waiver that allowed the participation and vote of Dr. Michael Miller? Dr. Miller had a grant from one of the sponsors which he used to create a promotional/educational CD-ROM for the product he was being asked to evaluate. In the CD-ROM, Dr. Miller reassures patients that silicone breast implants are safe, creating a very clear intellectual conflict of interest, in addition to the financial conflict.
- Why were independent scientific experts inside and outside the FDA not invited to present their data? Why were offers to present scientific information, made by several independent experts, rebuffed? Why was FDA's own research on breast implant rupture, which includes the largest published sample of women with leaking silicone implants, not provided to the panel or discussed in either the written reviews or oral presentations?
- Why did the FDA approve the design of Mentor's Core study, despite the fact that it eliminated the data from women whose implants were removed and not replaced? The women who had their implants removed without replacement are among the most likely to have experienced rupture, complications, or symptoms from the devices. These are the women who should have been a focus of the research, but Mentor systematically excluded the data on those problems. The rationale given, lack of consent to gather information from women whose implants were removed, is inconsistent with accepted procedures for clinical trials and apparently inconsistent with the analysis conducted by the other implant maker.
- Why did the FDA accept Mentor's PMA for implant styles 4000 and 8000 even though these models were not included in the company's Core study, the primary clinical data set for the PMA? Mentor provided some data on Style 4000 from its Adjunct study, but FDA's PMA reviewers pointed out that the Adjunct study was fundamentally flawed because it lost 90% of its patients in follow-up. Furthermore, they pointed out that the Adjunct study "data are of no value in determining the rupture rate" due to the absence of an MRI cohort. Style 8000 was not examined in either the Core or the Adjunct studies. In essence, there was no reliable data for 4 of the 6 implant models the Panel recommended for approval.

Now that the Panel has issued this split decision, it is up to the FDA to decide whether to follow the panel recommendations. It is essential that an investigation take place as quickly as possible, so that these questions can be answered before the FDA issues a final decision on the applications from

Mentor and Inamed, which is expected in the coming weeks. We would like to meet with you to provide additional background and documentation to support our request for an oversight investigation. Michelle Nawar will call to follow-up on this request or you can reach her at 202-223-4000 for more information.

Sincerely,

Command Trust Network
In the Know
Our Bodies Ourselves
National Organization for Women
National Research Center for Women & Families
National Women's Health Network

Cc: The Honorable Judd Gregg
The Honorable Bill Frist
The Honorable Lamar Alexander
The Honorable Richard Burr
The Honorable Johnny Isakson
The Honorable Mike DeWine
The Honorable John Ensign
The Honorable Orrin Hatch
The Honorable Jeff Sessions
The Honorable Pat Roberts
The Honorable Christopher Dodd
The Honorable Tom Harkin
The Honorable Barbara Mikulski
The Honorable James Jeffords
The Honorable Jeff Bingaman
The Honorable Patty Murray
The Honorable Jack Reed
The Honorable Hillary Rodham Clinton
Claude Allen, Assistant to the President for Domestic Policy
Lester Crawford, Acting FDA Commissioner
Daniel Schultz, Director, FDA Center for Devices and Radiological Health
Theresa Toigo, Associate Commissioner, FDA Office of Special Health Issues
Peggy Miller, Science Program Manager, FDA Office on Women's Health

Bond, Susan

From: Bond, Susan
Sent: Monday, March 07, 2005 4:13 PM
To: Schultz, Daniel
Cc: Crawford, Lester, D.V.M.
Subject: breast implants



Backgrounder for
Crawford on A...

Dan, I got this from an outsider who is interested in seeing us come out okay on the b.i. issue and has intel that it will likely be raised at the confirmation hearings. can you take a look at this and tell me your thoughts?

Background and Update on Silicone Gel Breast Implants

Background:

An FDA Advisory Committee meeting will be held on April 11-13, 2005 to consider two premarket approval ("PMA") applications for silicone gel breast implants. As you know, these products have generated considerable controversy in the past, and continue to do so, despite continual reaffirmations of safety.

As the April meeting approaches, a small number of vocal opposition groups are actively advancing their negative views regarding these products on Capitol Hill and elsewhere. As part of their message, these groups have mischaracterized the science behind these products; therefore, it is important to set the record straight. The scientific data and evidence support the safe use of these products. While opponents seek to focus public attention on anecdotes and junk science, it is the role of the Advisory Committee and FDA to base their decisions on sound science.

Facts:

- Breast implants have been marketed and available in the U.S. for over 30 years, providing profound benefits for many women. Following anecdotal reports of connections between silicone breast implants and autoimmune diseases, and rising product liability litigation, FDA called for a voluntary moratorium on these products in January 1992. This moratorium was lifted in April 1992. Since then, silicone gel breast implants have been available to mastectomy patients for reconstruction or revision, pursuant to an "adjunct study" initiated in 1992 at the recommendation of an FDA Advisory Committee, and supported by the breast cancer community, to continue access. Over 125,000 patients have participated in this adjunct study; these women have had their implants for up to 12 ½ years.
- FDA's actions on silicone breast implants have been widely misunderstood and mischaracterized. In October 2003, an FDA Advisory Committee voted to recommend approval of silicone breast implants, with certain conditions to further ensure patient and physician education, patient follow-up and data-gathering. In January 2004, FDA concluded that additional scientific data was necessary before proceeding. FDA issued a Draft Guidance for Industry, requesting additional scientific data be submitted to address questions raised by the Advisory Committee and "to provide a reasonable assurance of safety, and to allow women and physicians to make informed decisions about silicone implants." Opposition groups characterize FDA's January 2004 actions as a denial of approval or a "ban," which was not the case.
- Opponents allege that it is too soon for FDA to again consider PMA applications for these devices, without providing sufficient time for manufacturers to conduct long-term safety studies. In fact, FDA's January 2004 Draft Guidance on silicone gel breast implants does not require manufacturers to initiate new studies; the Guidance acknowledges the value of existing data, literature and information sources, from the U.S. and other countries. Numerous epidemiologic studies have been conducted and have not found a link between breast implants and long-term

3/4/2005

health effects. Several recent studies have followed women with implants for an average of 10 years, and up to 30 years.

- The Institute of Medicine (“IOM”) concluded in 1999 that medical evidence does *not* support an association between implants and either breast cancer or systemic disorders such as connective tissue disease. This was recently reconfirmed in an NCI study published in 2004. While some breast-implant patients (silicone and saline) do experience localized problems after their surgeries; these effects are well-known and are described on the product’s labeling, but are not systemic or life-threatening.
- It is also our understanding that opposition efforts (as fueled by trial lawyer interests), are on Capital Hill trying to make the case that breast implants are an example of the need for more FDA oversight on medical devices, and are also comparing silicone breast implants to Vioxx. In fact, silicone breast implants have been the subject of more scrutiny and oversight by FDA than virtually any other device.

Recent Scientific Developments:

In addition to the long history of use and evidence of long-term safety of silicone breast implants demonstrated in the 1999 IOM report, recent studies have reaffirmed these conclusions.

- In a very large study, the NCI recently found no conclusive evidence that breast implants affect development of connective tissue disorders. *American Journal of Epidemiology. Brinton, Risk of Connective Tissue Disease Among Breast Implant Patients, Am. J. Epidemiol. 2004;160:619.*
- Numerous analytic epidemiological studies have studied the long-term effects and found no link between breast implants and long term health effects. *McLaughlin, Long-Term Follow-Up of Women with Cosmetic Breast Implants: How Long is Long Enough?, Plast. Recon. Surg., 114(3):801-3.*
- The prognostic characteristics of tumors are not affected by augmentation; breast cancer is diagnosed at a similar stage and status with or without breast implants. *Migloretti, Effect of Breast Augmentation on the Accuracy of Mammography and Cancer Characteristics, JAMA, January 28, 2004.*
- For modern [third generation] silicone breast implants intact three years after implantation, 98% are estimated to be rupture-free at five years, and 83% are rupture-free at 10 years. Further, 90% of intracapsular and 84% of extracapsular ruptures remain relatively stable over 2-3 years. *Holmich et al., Incidence of Silicone Breast Implant Rupture. Arch. Surg. 138:801-6.*
- There is no survival disadvantage for mastectomy patients with breast implants; in fact, women with breast implants “experienced better survival than women without implants.” *Le, Breast Implants Following Mastectomy in Women with Early-Stage Breast Cancer: Prevalence and Impact on Survival, Breast Cancer Res. 2005, 7:R184-R193 (D01 10.11861/bcr974).*

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3/4/2005

Unlike most products undergoing FDA review, silicone gel breast implants have been used in patients for many years, providing a significant amount of long-term data for review. These data and the published literature provide a substantial database of scientific evidence that supports use of these products for both reconstruction and augmentation patients.