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Division of Dockets Management (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, MD 20852

**Docket Number 2004D-0002 "New Draft Guidance Document for Breast Implants"**  
**Document number: 1239**

Dear Sir or Madam:

I was pleased to learn of the decision by the Food and Drug Administration (FDA) in January not to approve silicone breast implants until basic safety questions could be addressed. My experience with silicone breast implants began in the early 1980s when after battling breast cancer and enduring a double mastectomy I was implanted with silicone gel-filled breast implants. At the time I considered my decision an "informed" one, given that the information and research at the time was very limited and sadly remains the case today. As my experience makes clear, no woman will truly have an informed choice until we understand why ruptures occur and assess the short- and long-term health consequences of rupture and silicone gel migration.

The members of the General and Plastic Surgery Advisory Panel who met in October 2003 to make recommendations on the approval of one manufacturer's silicone breast implant product expressed serious reservations that the clinical trials did not adequately determine safety. Throughout the two-day meeting, members of the panel provided recommendations on strengthening the current clinical trials to address the basic questions of device function (and failure), the clinical consequence of failure, the risks to women of childbearing age and second generation effects. I am submitting the following recommendations on the draft guidance document for breast implants based in part on the comments made by the FDA advisory panel members as well as my extensive experience with silicone breast implants as a breast cancer survivor.

- 1. Increase the length of time patients are followed in the clinical trial prior to applying for and achieving FDA approval of the device for market to the general population.** The previous (and new draft) guidance calls for a minimum of 10 years of prospective patient follow-up but it does not stipulate the amount of follow-up necessary prior to approval. To make an assessment of safety we must have a full understanding of the risk of device failure and the clinical consequence of that failure over the expected lifetime of the device. Furthermore, if it is decided that the preemptive explantation (that is to say explantation prior to

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device rupture) should be standard, we must also have a clear understanding of the timeframe in which the majority of the implants rupture.

Considering that these devices have been available in both an unrestricted and restricted capacity for several decades, it is unfathomable that the manufacturers have not undertaken the long-term surveillance necessary to understand the true risks of these devices.

A number of the adverse events under consideration in the most recent application by Inamed Corporation (including rupture, silent rupture, CTD signs and symptoms, local complication and reoperations) increased substantially over just a few years. Clinical trials need to collect more long-term data prior to approval in order to more fully examine this trend.

- 2. Expand the MRI study to include all patients in the Core clinical trial and continue MRI evaluations as part of the clinical trials throughout the lifetime of the device to obtain an accurate assessment of the risk of silent (asymptomatic) rupture.**

By the time my ruptured silicone breast implants were removed, silicone gel had migrated into the surrounding capsular tissue. I later found that silicone had migrated and deposited in distant organs, including my uterus. The health consequences of this gel migration remain unknown.

The advisory panel that met in October was concerned about the occurrence of silent rupture and the potential clinical consequences of undetected rupture. A clear understanding of the prevalence of silent rupture is necessary if we hope to fully evaluate the risk of device failure and leakage in the absence of detectable rupture, the migration of gel into surrounding breast tissue, the potential for gel migration beyond the fibrous capsule and the health consequences of short- and long-term exposure to silicone gel.

- 3. Evaluate and provide an explanation for any differences in complications and reoperation rates between the augmentation and reconstruction cohorts.**

The short-term clinical data presented by Inamed Corporation in October of 2003 demonstrated significantly higher rates of complications (including rupture) and reoperations for the reconstruction cohort. The panel agreed that this trend should be rigorously evaluated over time and that it was necessary for the manufacturer to understand the mechanism responsible for a higher rupture rate in the augmentation group.

- 4. Follow women in childbearing years and collect information on pregnancy including the outcome of pregnancies in terms of live births, total number of children born, and any complications with the pregnancy or the delivery.**

5. **Collect information on breastfeeding complications. Part of this analysis should include sampling of breast milk.** If a woman experiences a breastfeeding complication she should be evaluated by MRI to determine the nature of the complication, including any evidence of rupture or gel migration.
6. **Children born to mothers with silicone breast implants should be followed. Any health or developmental problems of the child should be evaluated. Correlations between implants status during pregnancy and health and developmental problems should be evaluated (e.g., whether the implant was ruptured during pregnancy or breast feeding, status of gel migration, etc.)**

Dr. Ruth Lawrence, a FDA advisory panel member, recommended:

- An evaluation of the potential exposure levels during pregnancy;
- Collecting blood cords because exposure is considered greater transplacentally than through breast milk; and
- Following children born to mothers with silicone breast implants for a minimum of 10 years.

7. **The evaluation of rupture should focus on identifying the mode and clinical consequence of failure.**

Dr. Michael Choti, a FDA advisory panel member, commented that the importance of understanding rupture goes beyond developing an accurate risk versus benefit analysis. He stressed that understanding failure is critical if we are ever to improve the design or manufacturing processes of the devices. “In the absence of a clinical test to demonstrate [the mechanism of failure],” he stated, “how will we ever believe the next implant will, in fact, be more rupture resistant?” (*Excerpt from page 213, October 15, 2003 transcripts of the General and Plastic Surgery Devices Panel*)

8. **The evaluation of the clinical consequences of rupture and gel migration must include laboratory parameters to evaluate the safety of short- and long-term exposure to silicone gel.**

Whether an exposure to silicone gel is the cause of or related to systemic illness has been highly debated for decades. Women who have received silicone breast implants have experienced similar health complications following rupture and gel migration though little research has been conducted to evaluate a potential relationship. Manufacturers conducting clinical trials have access to a patient population that can be assessed for laboratory tests prior to implantation and at intervals post-implantation that will help elucidate the long-term physiological implications for this exposure.

For the following tests, a baseline should be established prior to implantation and routine laboratory tests should be conducted at each follow-up examination:

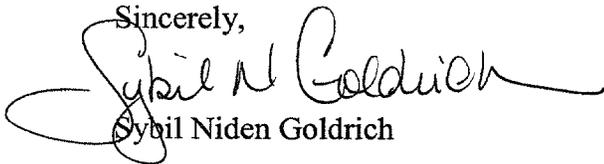
- a. Anti-nuclear antibodies (full screen)
- b. Markers for inflammation such as Erythrocyte Sedimentation Rate (ESR) and C-Reactive Proteins (CRP)
- c. Total immunoglobulin levels
- d. Screen for monoclonal gammopathies
- e. Combined blood counts (CBC)
- f. Natural Killer cell counts
- g. Rheumatoid factors
- h. Anti-polymer antibodies

Finally, I want to close by reminding the agency of its responsibility to provide appropriate education to the advisory panel members as to the regulatory responsibility and limitations of the agency when it comes to postapproval conditions. In turn, the advisory panel members must be fully informed of their responsibility to provide recommendations on approval based solely on the merits of the clinical data collected through a premarket approval (PMA) application and not based on the expectation of post-market surveillance and post-approval conditions.

The manufacturers have had decades to evaluate the risks of silicone breast implants and make improvements to the design and function of these devices. I was shocked to learn at the advisory panel meeting in October of 2003 that the manufacturers had not made any significant improvements on the devices in the last ten years. For this reason, the FDA must demand that clinical trials are conducted in a manner that fully examines the short- and long-term risks of these devices.

I appreciate the opportunity to provide comments and recommendations on the FDA's draft guidance to the breast implant industry. The safety of silicone breast implants has been an ongoing public health concern for decades. We have the opportunity to better our understanding of the short- and long-term safety of silicone breast implants through tighter controlled, longer-term clinical trials. It is only through this process that women will have access to safe devices and the ability to make informed decisions.

Sincerely,



Sybil Niden Goldrich