

April 9, 2004

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

From: Barbara A. Brenner, Executive Director
Jane S. Zones, Recent Past Chair, Board of Directors
Breast Cancer Action

Re: Docket Number 2004D-002 "New Draft Guidance Document for Breast Implants"

Breast Cancer Action is an independent national grassroots organization carrying the voices of those affected by breast cancer to implement institutional and societal changes that will lead to elimination of this disease. Unlike most other breast cancer consumer advocacy organizations, BCA does not accept donations from any group that might represent a conflict of interest.

We were delighted by FDA's decision earlier this year to deny Inamed Corporation's application to market their silicone gel-filled breast implants. Our review of their data raised great concerns about their safety for women with breast cancer who use the devices for reconstruction after mastectomy. Your action was an indication to us of your commitment to assure the long-term safety of these implants for women with breast cancer.

Thank you also for proposing changes in the guidelines for breast implant manufacturers. In general, we appreciate the many ways in which the Draft Guidance Document suggests more stringent testing and review prior to submission of pre-market approval requests for these devices. We are particularly pleased that the FDA has included recommendations that materials testing methods be adjusted to be more predictive of clinical outcomes and that assessments of silicone gel bleed be measured under conditions that simulate those found in the body.

Our review of the Draft Guidance Document suggests several changes that would improve the likelihood that reconstruction with implants is a safe alternative.

Long-Term Safety Data. Since the FDA began reviewing silicone breast implant safety nearly 25 years ago, it was clear that we lacked information about the long-term effects of the devices. The industry and the plastic surgery community have had ample time and counsel to conduct prospective studies that follow women over a long period of use. It is apparent that problems develop in number and severity over time, including asymptomatic rupture and leakage, gel migration, and possible reactions to exposure to materials used in the production of the implants. Accordingly, we recommend that the Guidance Document ask manufacturers for the following prior to submission of a PMA:

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- increased length of time patients are followed, to evaluate the true lifespan and health effects of the implants;
- inclusion of a large enough sample of women who have breast cancer to calculate the independent effects of various forms of cancer treatments upon the safety and effectiveness of the implants;
- expansion of the MRI study to more accurately assess asymptomatic rupture, leakage and gel migration; and
- employment of independent research entities to improve the likelihood of unbiased investigation.

We recognize that it is not politically feasible to require PMA-submitting manufacturers to provide the 15 to 20 years of prospective data that would be necessary to truly understand the ramifications of silicone gel-filled implants for women who are living with breast cancer. However, we think it is reasonable to ask manufacturers to follow women for at least half that period, the time during which it seems that implant rupture becomes increasingly common. Manufacturers need to be held accountable for their products' long-term safety. They should be expected to continue to follow women with the implants indefinitely, particularly as they continue to develop their products and submit further requests for approval of new products.

Mammography. There is evidence that silicone gel-filled breast implants decrease ability to correctly interpret mammograms in women whose breasts have been augmented.¹ We are concerned about the risks of false negative results, which delay breast cancer diagnosis, as well as false positive results, which lead to unnecessary biopsy and possible scarring that would further obscure mammographic results. We highly recommend asking manufacturers to include mammography follow-up as an element of long-term studies. The effects of capsular contracture should be a variable in analysis of implant effects on mammography readings.

¹ Diana L. Miglioretti, et al. "Effects of Breast Augmentation on the Accuracy of Mammography and Cancer Characteristics," *JAMA* 291(4), January 28, 2004, pp.442-450.