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Comments to Docket No. 2004N-0423

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**Second Annual Stakeholder Meeting on the
Implementation of the Medical Device User Fee
And Modernization Act of 2002 Provisions**

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In 2003, the FDA considered the Premarket Approval (PMA) application for one manufacturer's silicone gel-filled breast implant devices. The process around the FDA's review of the PMA for these devices raised a number of serious concerns for the public health community.

The manufacturer's clinical data revealed high complication and reoperation rates for all study cohorts (augmentation, revision and reconstruction) and failed to address several critical questions regarding the long-term safety of the devices. The FDA ultimately denied approval, however the manufacturers were given the opportunity to file amendments to their original PMAs. In August 2004, both manufacturers filed amendments signifying that there will be future consideration of silicone gel-filled breast implants. In addition, other silicone breast implant devices, cohesive gel breast implants, are currently under clinical trials at the FDA.

There are two issues of relevance to the FDA's oversight of silicone breast implant devices that are directly impacted by the implementation of the Medical Device User Fee and Modernization Act of 2002.

(1) Modular Review of Silicone Breast Implant Devices

On October 26, 2002, the Medical Device User Fee and Modernization Act amended the Federal Food, Drug and Cosmetic Act to include several new provisions, including the use of a modular review program for premarket approval applications (PMAs). This authorization was inspired by the successful fast track program for drugs and biologics, which permits similar rolling submissions for products treating a serious or life-threatening condition or those that demonstrate the potential to address unmet medical needs.

The original intent of the modular review has been expanded to include all medical devices, including breast implants. In stark contract to the fast tracked drugs and biologics which receive expedited review and more intensive attention from FDA, silicone breast implants do

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not treat serious or life-threatening conditions, address unmet medical needs, represent breakthrough therapy or offer any other meaningful medical value to patients which would warrant FDA review under a streamlined, expedited process like modular review.

While there is value in expediting the review of life saving drugs and biologics, the provision has been inappropriately applied to the PMA review process for breast implant devices and as such should not be considered a suitable process for the review of these devices.

(2) Bundling Multiple Devices in a Single PMA Application

In 2003, the FDA's General and Plastic Surgery Advisory Panel reviewed Inamed Corporation's PMA for silicone gel-filled breast implant devices. The Core Study collected data on silicone gel-filled breast implant Styles 40, 45, 110, 120 and 153. However, Inamed was also seeking approval for silicone gel-filled breast implant Styles 10 and 20, which were not included in the Core Study. Styles 10 and 20 were included in an ongoing Adjunct study, the purpose of which was to provide access to the devices, not to collect clinical data to support approval.

The FDA acknowledged in the Inamed Clinical Summary Memorandum, dated September 12, 2003, that "Styles 10 and 20 were used in a minimal [number] of cases." Further, Inamed Styles 10 and 20 were introduced into the adjunct study in July of 2003, just one month prior to the close of the database in August 2003. Therefore, the adjunct study provided only one month of actual follow-up data for these two styles of devices

Further, the Adjunct Study was not intended to collect data to support approval. Follow-up rates were alarmingly low for this study. The FDA cited follow-up rates for the three cohorts at approximately 50% for 1 year follow-up and 25% for 3 year follow-up.

The FDA should require that all devices contained within a PMA receive at least the minimum standard of evaluation through clinical trials. The aforementioned case of silicone gel-filled breast implants demonstrates the abuse of the system. There is essentially no clinical data to evaluate the safety and effectiveness of Styles 10 and 20. While these styles are similar in nature to the styles evaluated in the Core clinical trial, they differ in important design features such as volume, shell surface, shape and profile. Slight variations between styles of the devices may produce vastly different clinical outcomes. The lack of scrutiny of preclinical mechanical testing in the breast implant clinical trials further adds to the uncertainty of the performance of the devices.

Without clinical trials designed to assess the difference in performance and clinical outcomes, consumers will not have the information they need to make an informed decision – and essentially have access to an unregulated, unstudied medical device.