FDA Update on the Safety of Silicone Gel-Filled Breast Implants

Executive Summary

Breast implants are medical devices that are used to augment breast size or to reconstruct the breast following mastectomy or to correct a congenital abnormality. Breast implants consist of a silicone outer shell and a filler (most commonly silicone gel or saline). Approximately 5 to10 million women worldwide have breast implants.

According to the American Society of Plastic Surgeons National Clearinghouse of Plastic Surgery Procedural Statistics, there were 296,203 breast augmentation procedures and 93,083 breast reconstruction procedures performed in the United States in 2010. Approximately half the procedures used saline-filled implants and half used silicone gel-filled implants. Figure 1 shows a photograph of woman holding a breast implant.

Figure 1. Photograph of a woman holding a breast implant.

In November 2006, the FDA approved two silicone gel-filled breast implants: the Allergan Natrelle and the Mentor MemoryGel. As conditions of approval, the FDA required each manufacturer to conduct post-approval studies to characterize the long-term performance and safety of the devices.

In June 2011, the FDA issued an Update on the Safety of Silicone Gel-Filled Breast Implants. This report provides a clinical update on the two silicone gel-filled breast implants available in the U.S. It includes:

- Preliminary data from the post-approval studies;
- A summary and analysis of adverse events reported to FDA since approval; and
- A review and analysis of recent clinical publications about the safety and effectiveness of silicone gel-filled breast implants.

The report is not intended to provide a comprehensive clinical update about the safety of saline-filled breast implants. Updated labeling and other information about saline-filled breast implants can be found on the FDA website at www.fda.gov/breastimplants.

Post-Approval Studies (PAS)

As conditions of approval of silicone gel-filled breast implants, the FDA required each manufacturer to conduct six post-approval studies to characterize the long-term performance and safety of the devices. Due to the length of the studies required by the FDA, they have not all been completed. The post-approval studies for silicone gel-filled breast implants included:

(1) *Core Post-Approval Studies (Core Studies)* – To assess long-term clinical performance of breast implants in women that enrolled in studies to support premarket approval applications. These studies were designed to follow women for 10 years after initial implantation.

(2) *Large Post-Approval Studies (Large Studies)* – To assess long-term outcomes and identify rare adverse events by enrolling more than 40,000 silicone gel-filled breast implant patients, following them for 10-years.

(3) *Device Failure Studies (Failure Studies)* – To further characterize the modes and causes of failure of explanted devices over a 10-year period.

(4) *Focus Group Studies* – To improve the format and content of the patient labeling.

(5) *Annual Physician Informed Decision Survey (Informed Decision Study)* – To monitor the process of how patient labeling is distributed to women considering silicone gel-filled breast implants.

(6) *Adjunct Studies* – To provide performance and safety information about silicone gel-filled breast implants provided to U.S. women from 1992-2006, prior to approval, when implants could only be used for reconstruction and replacement of existing implants.

This update focuses primarily on the studies that provided clinical outcomes: the *Core Study* and the *Large Study*. Of these, the most complete data set to date comes from the *Core Studies*.

The Allergan *Core Study* enrolled 715 patients and the Mentor *Core Study* enrolled 1,008 patients. Allergan follow-up rates at 10 years post-implant are 66 percent. Mentor follow-up rates at 8 years post-implant are 58 percent. Longer term follow-up is available for the Allergan *Core Study* participants because the study began enrolling patients approximately 20 months before the Mentor *Core Study*.

Both companies enrolled more than 40,000 women in their *Large Studies*. In these studies, Allergan has collected 2-year data for 60% of participants, and Mentor has collected 3-year data for 21% of participants.

The local complications observed in the silicone gel-filled breast implant post-approval studies are consistent with complications noted at the time of approval. The most common complications and adverse outcomes include capsular contracture, reoperation, and implant removal. Other complications include implant rupture, wrinkling, asymmetry, scarring, pain and infection. The longer a woman has silicone gel-filled breast implants, the more likely she is to experience local complications. As many as one in five primary augmentation patients and one in two primary reconstruction patients require device removal within 10 years of implantation.

The post-approval studies to date do not show evidence that silicone gel-filled breast implants cause connective tissue disease, reproductive problems, or breast cancer.

Low follow-up rates and other study limitations may limit interpretation of the data and preclude the detection of very rare complications.

Post-market Surveillance of Adverse Events

As part of the FDA's ongoing surveillance of silicone gel-filled breast implants, it collects and analyzes adverse event information from a variety of sources. Allergan and Mentor must submit adverse event reports on silicone gel-filled breast implants received after November 2006 through one of two reporting methods:

- Medical Device Reports (MDR) for deaths and unusual, unique or uncommon adverse events, or
- Postmarket Spreadsheet Reports (PSR) for serious injuries and malfunctions that are well-known or expected to occur.

Health care professionals, patients, and other concerned individuals who do not have a mandatory reporting obligation, can submit reports voluntarily to the FDA through MedWatch, FDA's safety information and adverse event reporting program.

The FDA designed the PSR program specifically to monitor the postmarket performance of approved silicone gel-filled breast implants. In addition to information about serious injuries and malfunctions, the PSR reports include details about the patient's race/ethnicity, whether the patient is enrolled in the *Large Study*, the reason for implanting the device, whether a reoperation was performed as a result of the adverse event, and the reason for implant removal. Collection of these data will help characterize the known breast implant-related problems and improve data analysis.

Overall, the adverse event reports submitted to the FDA are consistent with the results from the premarket and post-approval studies. No new outcomes or complications were reported through December 2010, except for rare reports of Anaplastic Large Cell Lymphoma (ALCL).

Literature Review

This report summarizes the epidemiologic literature published in peer-reviewed journals since 2005 on the clinical safety and effectiveness of silicone gel-filled breast implants. It focuses on

outcomes that have not been addressed to date in post-approval studies.

Most women reported high levels of satisfaction with their body image and the shape, feel and size of their implants. There is no apparent association between connective tissue disease and silicone gel-filled breast implants, although most of the available studies have limitations. Silicone gel-filled breast implants are not associated with an increased risk of breast cancer. There is no evidence that suggests untoward effects of silicone gel-filled breast implants on pregnancy or fertility. Furthermore, current evidence does not support an association between mothers with breast implants and difficulty with breast feeding or adverse health events in their children.

Recent case reports have suggested that women with breast implants may be more likely to be diagnosed with anaplastic large cell lymphoma (ALCL). See Anaplastic Large Cell Lymphoma (ALCL) In Women with Breast Implants: Preliminary FDA Findings and Analyses.

Summary of Key Findings

1. Based on the totality of the evidence, the FDA believes that silicone gel-filled breast implants have a reasonable assurance of safety and effectiveness when used as labeled. Despite frequent local complications and adverse outcomes, the benefits and risks of breast implants are sufficiently well understood for women to make informed decisions about their use.

2. The longer a woman has breast implants, the more likely she is to experience local complications or adverse outcomes. Women with breast implants will need to monitor their breasts for local complications for the rest of their lives.

3. The most frequent complications and adverse outcomes experienced by breast implant patients include capsular contracture, reoperation, and implant removal (with or without replacement). Other frequent complications include implant rupture, wrinkling, asymmetry, scarring, pain, and infection, among others. These observations are consistent with the local complications and adverse outcomes that were known at the time of approval.

4. Women with breast implants may have a very small but increased likelihood of being diagnosed with anaplastic large cell lymphoma.

5. In the post-approval *Core Studies,* between 20 to 40 percent of augmentation patients and 40 to 70 percent of reconstruction patients had reoperations during the first 8 to 10 years after they received their implants. Although routine replacement is not necessary, many women will need additional surgery to modify, remove, or replace their implants.

6. There is no apparent association between silicone gel-filled breast implants and connective tissue disease, breast cancer, or reproductive problems. Associations that are very rare or that take many years to manifest may not be detected using currently

available data.

7. MRI continues to be the most effective method of detecting silent (asymptomatic) rupture of silicone gel-filled breast implants.

8. Interpretation of the data from the silicone gel-filled breast implant post-approval studies may be limited by low follow-up rates.

Recommendations for Patients Who Have or Who Are Considering Breast Implants

- Be aware that breast implants are associated with significant local complications, and the longer the devices remain implanted, the more likely you are to experience a complication. Local complications and adverse outcomes include capsular contracture, reoperation, removal, and implant rupture. Many women also experience breast pain, wrinkling, asymmetry, scarring, and infection.

- Continue to receive routine follow-up with your physician. This includes having periodic MRI exams to detect "silent rupture" of the implant.

- Notify your health care provider if you develop any unusual signs or symptoms including pain, asymmetry, hardness or swelling.

- Recognize that breast implants are not lifetime devices. The longer you have your implants, the more likely it will be for you to have them removed.

- If you have enrolled in an Allergan or Mentor post-approval study, continue to participate. These studies are the best way to collect information about the long-term rates of complications.

- Continue routine screening mammography for breast cancer at intervals recommended by your health care provider based on your age and risk factors.

Recommendations for Health Care Providers

- Provide women with copies of patient brochures and informed consent so that they have access to the critical information needed to make informed decisions about receiving and caring for breast implants. Labeling for Approved Breast Implants for patients and for physicians is available on FDA's breast implant website.

- Maintain medical vigilance through follow-up and post-approval studies so that the long-term effects of silicone gel-filled breast implants can be better understood. Your contributions provide data that are used to evaluate how new surgical techniques, patient characteristics, and implant characteristics influence the cosmetic and health outcomes of

patients undergoing breast implantation.

- Screen for silent rupture using MRI. Women with silicone gel-filled breast implants should undergo MRI screening for silent implant ruptures at 3 years post-implantation, and every 2 years thereafter.

- Report breast implant associated adverse events and deaths to FDA via MedWatch.

FDA Activities

The FDA activities surrounding silicone gel-filled breast implants focus on three key goals:

- Fostering the collection of data about implant performance;
- Improving the follow-up rates in current and future post-approval studies; and
- Communicating new safety information when it becomes available so that women can make informed decisions about their healthcare.

To accomplish these goals, the FDA:

- Closely monitors the status and conduct of the on-going required post-approval studies so that data is collected, validated scientifically and disseminated widely;

- Actively encourages and facilitates adverse event reporting by the manufacturers, patients, healthcare providers, and health care facilities;

- Is collaborating with the American Society of Plastic Surgeons (ASPS) and other experts in the clinical and scientific community to develop a registry of women with breast implants and anaplastic large cell lymphoma (ALCL) to better understand the nature and possible factors contributing to their association;

- Will hold a meeting of its Medical Device Advisory Committee in the summer of 2011 to seek input on issues related to postmarket surveillance of silicone breast implants including study design, patient enrollment and follow-up, and data analysis;

- Released, in June 2011, a newly updated breast implant website (www.fda.gov/breastimplants). Key sections of this website describe the risks of breast implants, the questions women should ask their doctors before getting breast implants, and what women should expect during the surgical procedure and recovery.

- Developed a new Breast Implants Complications Booklet for patients. The booklet includes the latest information from the post-approval studies. It is available on the FDA website.

- Requires silicone gel-filled breast implant manufacturers to update their labeling each time the data is reanalyzed. The most current Labeling for Approved Breast Implants is

available on the FDA website.

Conclusion

Based on the totality of the evidence, the FDA believes that silicone gel-filled breast implants have a reasonable assurance of safety and effectiveness when used as labeled. Despite frequent local complications and adverse outcomes, the benefits and risks of breast implants are sufficiently well understood for women to make informed decisions about their use. Manufacturers and physicians should continue to provide balanced and up-to-date information to women considering breast implants to help inform their decisions.