



Brief Summary of the General and Plastic Surgery Devices Panel – August 30 & 31, 2011

Introduction:

The General and Plastic Surgery Devices Panel of the Medical Devices Advisory Committee to the Food and Drug Administration met on August 30 and 31, 2011 to discuss and make recommendations on postmarketing issues related to silicone gel-filled breast implants or SGBIs. This meeting updated the advisory panel on the status of ongoing Post-Approval Studies (PAS) and discussed strategies for current and potential future studies that would evaluate the real-world and long-term performance of silicone gel-filled breast implants. Additionally, this meeting was held to provide transparency and a public forum for discussion of the PAS SGBI data and to provide an opportunity for stakeholder input and perspectives.

Open Public Hearing:

Over 50 open public speakers presented during the OPH session over the course of both days. The presenters consisted of patients, patient advocacy groups, women's health groups, surgeons, surgical and professional societies and consumer groups. The OPH was very diverse, discussing both real-world positive and negative reactions to Silicone Gel-filled Breast Implants, discussion of new methods of data collection, adverse events related to SGBIs, methods to increase patient follow-up and PAS methods and ways that FDA could collaborate with external stakeholder for these studies.

Panel Deliberations/FDA questions:

The Panel generally agreed that a loss to follow-up rate of 35% over 10 years is an appropriate assumption in for SGBI post-approval studies given the challenges that have been encountered in both enrollment and long-term follow-up. The questionnaires should be re-written to be more easily understood and completed by the study participants. Follow-up rates in subgroups of participants should be evaluated considering including economic and racial and ethnic groups. The Panel believed that more onus should be placed on the sponsors and physicians in order to improve follow-up rates and that appropriate incentives for physicians and patients should be identified to raise the participation/follow-up rate. It would be worthwhile to reach out to the 80% who missed follow-ups in Mentor's loss and explore if they are willing to come in for one more follow-up (data point) to see if they had they had any complications. Another point of discussion was obtaining better data with fewer patients or conducting a number of studies to address different endpoints, rather than one large study.

The Panel discussed future Post-Approval Studies for silicone gel-filled breast implants; the panel agreed that it is necessary to assess long-term effectiveness in terms of the failure rate of the implant. The panel discussed the definition of long-term effectiveness and what is the reasonable expectation for the life of these devices, a consensus of a reasonable time frame of 15 years was agreed upon.

The Panel agreed that the line between long-term Safety and Effectiveness is blurred; however, the effectiveness of this device can be measured by following the original cohort out to 10 years.

The Panel discussed the selection of long-term safety endpoints for future PASs should take into account the current Post Approval Studies for future PMAs and refocus the endpoints to gather data on unanswered questions (e.g. family history, autoimmune disease etc.) and other questions not answered by the premarket studies for the new PMA.

Well-publicized, sufficiently inclusive registries will collect a great amount of data in order to capture the rare endpoints, such as connective tissue disease. It would be possible to address study endpoints with different subsets of the registry patients. The pooling of data from databases would also be useful in finding rare endpoints. Smaller cohort studies will capture more common endpoints.

The Panel agreed that aggregate data across manufacturers and across breast implant types (not specific to a particular brand or implant) would be useful in discovering outcomes. The Panel discussed that a comparison group could consist of women who considered breast implants but decided against them or compare saline vs silicone; or women who had other breast surgeries, breast cancer vs. breast cancer with implants. Pooling the data between sponsors would work only if the sponsors worked out the details prior to implementation of the PAS.

When considering both current and future post approval study designs for silicone gel-filled breast implants, the panel discussed methodologies and strategies that could increase compliance with follow up. These included a web-based questionnaire that is easier to use for the patient, with incentives for the patient. The panel agreed that the paper questionnaire is laborious and its length may discourage women from participating in the PAS. Confidentiality is also important to the patient; the panel discussed that giving the patient options to speak with the company at their leisure and empowering the patients with notion that they are helping the research aspect for women's health. As discussed in a number of questions about methods and data collection, the panel felt that a breast implant registry of all women who receive the device may provide a means to answering many of the longer term and real world questions, in particular the questions related possible association with rare adverse events.

The panel commented on the current scientific data available regarding recommendations about MRI screening for silent rupture in the approved product labeling and questioned whether much was gained by this recommendation. There is a concern expressed about cost to patients and mentioned, false-positive findings and whether information about a silent rupture would change practice (such as decisions about removal of the device). One of the panel's radiology specialist indicatee that high resolution ultrasound had limitations of only able to detect ruptures on the front half of implants and not all sites have high resolution ultrasound. It was also noted that MRI was able to detect silent ruptures of the entire breast implant surface.

The Panel agreed that Device Failure studies would be a good way to evaluate why these devices are failing. It is important that explanted devices be returned to manufacturers so they can further evaluate the reasons for failure.

The panel recommended that Focus groups be continued because the information they provide can be used to improve labeling. These studies are relatively inexpensive and are a useful way of engaging stakeholders.

The panel discussed that future Post-Approval Studies of other breast implants that utilize the same technology as implants already approved, need to be combined with the marketed SGBIs to answer any outstanding questions. The data should be set up in order to allow for pooling the data and comparisons can be made. A post approval registry should be created in order to capture all breast implants including new generation implants. The newer generation implants should be compared to the marketed implants.

The panel discussed potential contributions that groups other than FDA can make to implement and maintain improvement strategies for current and future post approval studies of silicone gel-filled breast implants by pooling data and working together to improve patient follow up and registry enrollment. A

broad based stakeholder analysis was recommended and would help to guide the collection of data to give patients the information they need. Academic, professional societies and other non-government organizations could act as a third party to assist sponsors in enrolling patients into the PAS.

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