

General and Plastic Surgery Devices Advisory Committee Meeting on Breast Implants

March 25 & 26, 2019

The Panel will be asked to discuss how best to modify and utilize breast implant registries for data generation characterizing longitudinal outcomes to better inform patient care.

1. Please discuss how to utilize breast implant registries for data generation characterizing longitudinal outcomes to better inform BIA-ALCL and BII patient care.
 - a. Please list the highest priority questions to be addressed using breast implant registries.
 - b. Please consider whether modifications to the existing registries are needed to address these questions. If so, what modifications do you recommend?
 - c. Please discuss whether additional policies should be implemented such as mandatory reporting to registries, post-market surveillance requirements, etc. to promote data collection and analysis.
2. Shortcomings cited by some people regarding the PROFILE registry and NBIR include data entry by physicians, limited data access, and data gathered being limited to reoperations. Others consider these shortcomings to be things that promote high quality, consistent data collection.
 - a. In light of the high priority questions identified above to be addressed using breast implant registries, please discuss the extent to which each of the questions requires breadth (e.g. data entry by all, collection of all information) versus depth (e.g. data entry limited to certain individuals, collection of specific information).
 - b. Please make recommendations on what information should be collected to address each of the high priority questions identified above.

The panel will be asked to make recommendations regarding next steps for the characterization of BIA-ALCL incidence and its risk factors

3. Some have identified implant surface texture as one modifiable risk factor for developing BIA-ALCL. While the majority of patients who develop BIA-ALCL have had textured implants, and most cases reported in the literature describe individuals who have had textured implants, there have been reports of BIA-ALCL in patients with smooth-surfaced implants

and many reports do not include the surface texture of the implant at the time of diagnosis. The denominator for the number of textured and smooth implants in the U.S. is also not known to determine whether relatively more cases are observed with one implant type versus another implant type. Please discuss the following issues:

- a. Steps that should be taken to characterize the implant characteristics and patient factors associated with BIA-ALCL risk.
- b. Whether the benefit/risk profile for textured and smooth implants are different.
- c. What information breast implant manufacturers should report regarding number of implants placed in order to assess if there are certain breast implant characteristics affecting BIA-ALCL risk.

The panel will be asked to discuss methods for assessing and addressing breast implant illness symptoms.

4. In preparation for this advisory committee meeting on breast implants, FDA asked each breast implant manufacturer to provide its long-term data regarding a constellation of breast implant illness symptoms. FDA conducted this exercise because while there is not sufficient evidence to show an association between breast implants and connective tissue disease *diagnoses*, there are numerous breast implant patients convening on social media to discuss a wide variety of *symptoms* that they are experiencing, and we have received an increasing number of Voluntary MDRs reporting these symptoms. While FDA doesn't have definitive evidence suggesting breast implants are associated with these conditions, we are looking to gain a full understanding of this issue to communicate risk, minimize harm, and help in the treatment of affected patients. Please discuss the following:
 - a. Steps that should be taken by all stakeholders to characterize implant characteristics and patient factors to better understand the risk of a patient experiencing symptoms consistent with BII.
 - b. Potential basic research questions warranting consideration to determine potential mechanisms of causation or association between breast implants and symptoms of breast implant illness, and, if present, the recommended studies (e.g., genetic, immunological, in situ allergy testing prior to and after implantation).
 - c. How to characterize the relative risk for symptoms of breast implant illness (considering the wide variety of symptoms) in breast implant recipients compared to the general population.
 - d. The work-up and evaluation of patients with breast implants possibly experiencing symptoms of breast implant illness and how this information should be used to inform both individual patient treatment decisions as well as our overall understanding of this issue.

- e. The extent of work-up and factors to be considered when breast implant removal surgery as a treatment for symptoms of breast implant illness is contemplated.
- f. Postoperative information that should be captured regarding patients who undergo breast implant removal surgery for preoperative symptoms of breast implant illness.
- g. Opportunities to leverage existing social media platforms and other technologies, e.g., artificial intelligence, text mining, mobile apps, and digital health, to collect and analyze data on BII symptoms.

The panel will be asked to discuss the evidentiary requirements for assessing the safety/effectiveness and benefit/risk for the implantation of surgical mesh for breast reconstruction and mastopexy procedures.

- 5. The use of an implanted surgical mesh in breast surgery has potential risks, including: infection, seroma, capsular contracture, explantation, reconstructive failure, implant rupture, alteration of breast physiology and interference with imaging. Some surgeons, however, will not perform pre-pectoral (above the pectoralis muscle) placement of a breast implant without the use of surgical mesh. FDA has not evaluated the safety and effectiveness, and the benefits and risks, of surgical mesh in any breast surgery and has not cleared or approved any surgical mesh for use in breast surgery/reconstruction.
 - a. FDA has advised manufacturers seeking to justify claims of mesh use with breast implants to achieve reconstruction that the data provided should include the following (i-vii below). Please discuss if this is appropriate or if there are additional considerations.
 - i) A comparison of patients treated with the subject device to a breast reconstruction control group that does not receive mesh.
 - ii) Inclusion and evaluation of relevant adverse events for both the treatment and control arms.
 - iii) Assessment of the effectiveness of the surgical mesh device for breast reconstruction compared to the no-mesh control in at least one effectiveness outcome assessing patient benefit. The outcome measure chosen should be clinically relevant and unbiased.
 - iv) Pre-specified statistical analysis accounting for reasonably obtainable relevant confounding variables including: radiation, chemotherapy, patient demographics and medical history, type of reconstruction, type of mastectomy, type of breast implant, etc. This analysis would also potentially allow identification of specific patient populations or methods for use that result in a favorable benefit-risk profile.
 - v) An analysis comparing treatment and control on both a per-breast and per-patient basis, where feasible and appropriate.

- vi) Premarket clinical follow-up to a minimum of 12 months post-implantation. If time to mesh resorption or time to quiescence of the inflammatory response of the tissue surrounding the mesh exceeds 12 months, then longer duration follow-up may be necessary.
 - vii) Evidence of a favorable benefit-risk profile for breast reconstruction with the subject device compared to breast reconstruction without the use of mesh.
- b. Considering the number of combinations of different surgical mesh, breast implant, surgical reconstruction procedures (e.g., prepectoral, submuscular, direct to implant, tissue expander to implant) possible, please discuss the extent to which each combination should be studied separately. Should all prepectoral and submuscular implantation, or direct-to-implant and tissue expander-to-implant reconstructions, be considered comparable in terms of assessing device benefit/risk, or should each mesh/breast implant/procedure require independent clinical data to assess benefits and risks? For prepectoral breast reconstruction specifically, current clinical practice is to generally use mesh with a breast implant; this makes it challenging to have a prepectoral implantation control arm without mesh. For prepectoral breast reconstruction with mesh, could the control arm be subpectoral implantation without mesh?
 - c. Given that implantation of mesh for breast reconstruction involves the implantation of 2 devices i.e., surgical mesh and breast implant, please discuss if it is possible to consider benefit versus risk for the mesh and breast implant separately or if a single benefit risk assessment should be made for the combination of the mesh and breast implant together as a unit.
 - d. Please discuss how benefits, should be assessed with respect to risks. As you consider this issue please comment on the appropriate duration of time for patient follow-up, both in premarket and in postmarket studies, to characterize benefit/risk and safety/effectiveness over time.
 - e. Please discuss whether a registry for characterizing benefit/risk for breast implant reconstruction involving mesh may be necessary and, if so, how it should be structured and potentially interface with existing breast implant registries.

The panel will be asked to discuss the MRI screening recommendations for silent silicone gel-filled breast implant rupture.

- 6. The FDA currently recommends that patients have their silicone gel implants evaluated for silent rupture by MRI, beginning at 3 years post implantation and every 2 years after that. American College of Radiology currently recommends the following: *For asymptomatic women (any age) with silicone implants, no imaging is recommended for implant evaluation.* Issues related to health insurance reimbursement have been reported, and data from implant manufacturer studies indicates low compliance with this recommendation. Please discuss the following:

- a. Should the FDA continue to recommend MRI screening for silent rupture of silicone gel-filled breast implants?
- b. If FDA should continue to recommend MRI screening, what level of evidence for clinical benefit would be required to support screening?
- c. What is the clinical benefit of continued screening, and what is the risk of not screening?
- d. Are there alternative screening methods that should be used?

The panel will be asked to discuss the role and responsibility of all stakeholders for communicating breast implant related risks and benefits to patients.

7. Choosing to obtain a breast implant, whether for augmentation or reconstruction, is a deeply personal choice and should be discussed between a patient and their provider in a transparent and balanced way with clear information about the benefits and risks of breast implants and the procedure. Please discuss the following issues related to communication of risks associated with breast implants:
 - a. What additional steps can FDA take to ensure that patients are better informed about the risks of breast implants?
 - b. Please discuss what additional steps providers and patients can take to ensure that patients are better informed about the risks of breast implants both at the time of breast implant surgery and longitudinally.
 - c. Breast implant patient labeling contains information on the risks and benefits of breast implants, results from clinical studies, a checklist of pertinent information and additional resources. Please discuss how to inform patients on how to best request and review breast implant patient labeling before surgery.
 - d. Please discuss what BIA-ALCL information should be communicated to patients who are considering breast implants and are concerned about the risk of developing BIA-ALCL.
 - e. Please discuss what information about possible systemic symptoms should be communicated to patients considering breast implants and to patients that have breast implants.
 - f. Are there opportunities to leverage existing social media platforms and other technologies to communicate benefit and risks associated with breast implants when deciding to obtain breast implants, and to stay informed on breast implant safety after receiving breast implants?
8. In closing, please comment on whether there are additional actions, not otherwise raised over the course of these two days, that the FDA should consider taking.