

1. Given the status of the current clinical post-approval studies (Core and Large) and the challenges that have been encountered in both enrollment and long-term follow-up, please discuss:
  - a. Do you agree with FDA's future considerations regarding the current studies?
  - b. What changes, if any, do you think should be made in the current PAS studies?
  - c. Is it appropriate to assume a loss to follow-up rate of 35% over 10 years?
  
2. In future Post-Approval Studies for silicone gel-filled breast implants, please discuss:
  - a. Is it necessary to assess long-term effectiveness?
  - b. If so, how should it be measured (e.g. device survival, patient satisfaction, etc)?
  
3. In future Post-Approval Studies to evaluate the long-term safety of silicone gel-filled breast implants, please discuss which long-term safety endpoints that should be assessed.
  
4. When considering the design of future Post-Approval Studies to evaluate the long-term postmarket safety and effectiveness of silicone gel-filled breast implants, please discuss:
  - a. The strengths and weaknesses of different study designs (e.g., new prospective cohorts, registry, use of administrative databases, case-control designs (prospective or retrospective), Bayesian methods) considering:
    1. Safety endpoints to be evaluated and whether the design should vary by endpoint;
    2. The optimal data sources for collecting safety data;
    3. Duration of follow-up necessary;
    4. Control/comparison groups;
    5. Inclusion of specific patient populations;
    6. Outcomes that can be assessed by aggregating data across manufacturers and across breast implant types (not specific to a particular brand or implant);
    7. Outcomes that can be assessed for a given manufacturer by aggregating data across breast implant styles.
  - b. When considering both current and future post approval study designs for silicone gel-filled breast implants, please discuss methodologies and strategies that will increase compliance with:
    1. Enrollment;
    2. Follow-up clinic visits;
    3. Annual questionnaires;
    4. MRI screening.

5. Please comment on the current scientific data available regarding recommendations about MRI screening for silent rupture in the approved product labeling.
6. Please discuss whether the following conditions of approval, in addition to clinical studies, are recommended to evaluate the postmarket safety and effectiveness of new devices in future post-approval studies:
  - a. Informed Decision Process studies;
  - b. Device Failure studies;
  - c. Focus Group.
7. In future Post-Approval Studies of other breast implants that utilize the same technology as implants already approved, please discuss:
  - a. What postmarket evaluation is needed for newly approved breast implants that are similar to currently approved implants?
  - b. How should new styles/procedural techniques of the same technology be incorporated into ongoing, mandated post-approval studies?
  - c. What are the most appropriate comparators, if any, for nth generation breast implants of the same technology?
8. Please discuss the unique 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