Surgical Mesh for Transvaginal Repair of Pelvic Organ Prolapse in the Anterior Vaginal Compartment

Panel Questions

Obstetrics and Gynecology Devices Panel

February 12, 2019

Discussion Questions

Effectiveness

Question 1

1. In light of its increased risks compared to native tissue repair, to demonstrate reasonable assurance of effectiveness, FDA believes that surgical mesh used in the anterior or anterior/apical vaginal compartment for transvaginal prolapse repair should be superior to native tissue repair. Does the Panel agree?
    a. If yes, at what timepoint should superiority be demonstrated, e.g., 12, 24, 36 months, or longer?
    b. If no, how should the effectiveness of mesh compare to native tissue repair and at what timepoint should the effectiveness be assessed?
    c. Does the Panel have additional comments related to the mesh material (e.g., polypropylene or non-crosslinked biologic) or other mesh characteristics?

Question 2

2. The FDA literature review identified that while anatomic/objective outcomes generally favor mesh, subjective outcomes demonstrate similar effectiveness for mesh and native tissue repair. FDA believes that both anatomic/objective and subjective outcomes should be used to assess the effectiveness of transvaginal anterior or anterior/apical mesh repair compared to native tissue repair.
    a. Does the Panel agree that both objective and subject outcomes should be used to assess the effectiveness of mesh compared to native tissue repair?
    b. If the Panel agrees that both anatomic/objective and subjective outcomes should be used to assess effectiveness, should improvement in both outcomes be required to consider a patient to be a success? Why or why not?
    c. Should the assessment of anatomic/objective outcomes be completed by a blinded evaluator?

Question 2 - continued

d. FDA believes improvement or resolution of patient symptoms are an important component in demonstrating effectiveness of a mesh versus native tissue repair. Please address the following:
   i. How should symptoms be measured (e.g., validated questionnaire)?
   ii. How should we assess if a patient has a meaningful/significant improvement (e.g., what if a patient has symptoms but is not bothered by the symptoms)?
   iii. How is a patient's assessment of her symptoms affected by sexual activity (or other patient factors) (e.g., would a patient who is not sexually active find her prolapse less bothersome compared to a sexually active patient)?
   iv. When patients are not blinded to their treatment (mesh or native tissue repair), how might that affect their assessment of symptoms?

e. Does the Panel have additional comments related to the mesh material or other mesh characteristics?

Safety

Question 3

3. The following adverse events have been associated with mesh and/or native tissue repair and are being collected in the 522 studies:

   a. Pelvic pain
   b. Erosion/exposure
   c. Dyspareunia
   d. De novo voiding dysfunction (e.g., incontinence)
   e. Infection
   f. Vaginal shortening
   g. Atypical vaginal discharge
   h. Neuromuscular problems
   i. Vaginal scarring
   j. De novo vaginal bleeding
   k. Fistula formation

   Please discuss these adverse events and consider their importance, potential to be debilitating, how they should be assessed, when they should be assessed, and key considerations related to the mesh material or other mesh characteristics. Please also comment on any important adverse events that may be missing.

Question 4

4. To demonstrate reasonable assurance of safety, FDA believes the adverse event profile for mesh placed in the anterior or anterior/apical vaginal compartment should be comparable to native tissue repair, or any increase in risk should be offset by a corresponding improvement in effectiveness. FDA also believes that all adverse events (not just those adjudicated as device or procedure related adverse events or serious adverse events) should be considered, along with their severity/seriousness, timing, resolution, and relatedness to the device and/or procedure should be used to evaluate the safety of mesh compared to native tissue repair.
    a. Does the Panel agree with this approach?
    b. What are the effectiveness scenarios where an increased safety risk may be acceptable (e.g., patient with recurrent prolapse)?
    c. At what timepoint should comparable safety (or increase in risk offset by a corresponding improvement in effectiveness) be demonstrated, e.g., 12, 24, 36 months, or longer?
    d. Does the Panel have additional comments related to the mesh material or other mesh characteristics?

Patient Population

Question 5

5. The FDA literature review identified concomitant procedures (hysterectomy and sling placement) and surgical/medical history (age, obesity, current level of sexual activity, parity, premenopausal estrogen therapy, diabetes, and smoking) that may affect the safety or effectiveness outcomes of an anterior or anterior/apical mesh or native tissue repair.
    a. Does the Panel agree that the identified concomitant procedures and surgical/medical history may affect the safety or effectiveness of a mesh or native tissue repair?
    b. Which additional concomitant procedures or surgical/medical history could affect the safety or effectiveness outcomes of mesh or native tissue repair in the target compartment?
    c. How should FDA factor concomitant procedures and surgical/medical history in its interpretation/evaluation of study results (e.g., balance of these characteristics between study arms, assessment of adverse events associated with concomitant procedure versus primary procedure)?

Question 6

6. In non-randomized studies, selection bias can influence safety and effectiveness outcomes. FDA believes the following factors may determine whether a patient undergoes a mesh versus native tissue repair.
    - Patient (e.g., recurrent prolapse, severity of prolapse, age, obesity, sexual activity, parity, other surgical/medical history)
    - Procedure (e.g., need for a concomitant procedure)
    - Clinical Site (e.g., whether site offers only mesh versus native tissue repair, whether the site is a specialty center for one type of repair)
    - Surgeon (e.g., experience with mesh versus native tissue repair, surgeon preference based on individual patient characteristics)

    Please discuss how these factors or any additional factors may bias the safety and effectiveness outcomes of a native tissue or mesh repair.

Training

Question 7

7. The FDA literature review indicated that surgeon experience may affect safety and effectiveness outcomes of a mesh or native tissue repair.
   a. Please comment on how a physician's level of training and experience affects safety and effectiveness outcomes for mesh versus native tissue repair.
   b. How should FDA incorporate the level of training and experience of investigators in a clinical study in its interpretation/evaluation of study results (e.g., need for comparable experience between study arms, clinical study results may not reflect real world results)?

Benefit/Risk

Question 8

8. Surgical mesh for transvaginal repair of pelvic organ prolapse in the anterior or anterior/apical compartment is an implant, and its benefit/risk profile may change over time.
    a. What is the appropriate expectation for the durability of a mesh repair and native tissue repair (e.g., remainder of the patient's lifetime)?
    b. How quickly should the data demonstrate the benefit of a mesh repair versus a native tissue repair?

Question 8 - continued

c. In broad terms, a device subject to PMA is approved for marketing when the benefit/risk profile is favorable for its proposed indications for use, with a reasonable assurance of safety and effectiveness. In light of this regulatory framework, what is the most appropriate time point to assess benefit/risk to support a marketing application, e.g., 12, 24, 36 months, or longer?

d. What is the appropriate duration of follow up needed to support marketing approval versus the follow up needed postmarket? What data should be collected postmarket? Please consider rare adverse events, long-term durability, and use of real world evidence to collect safety and effectiveness outcomes.

e. Does the Panel have additional comments related to the mesh material or other mesh characteristics?