

OBSTETRICS & GYNECOLOGY DEVICES PANEL

September 8-9, 2011

Summary Day-1 Surgical Mesh for Repair of Pelvic Organ Prolapse (POP)

Open Public Hearing (OPH)

Twenty-two persons presented during the OPH session. The panel heard presentations from individual patients, patient and women's advocacy groups, individual clinicians, and clinical organizations, including ACOG, AUGS, SGS, AUA, SUFU, and AAGL. Presentations included a range of views, both summaries of individual experiences (mostly adverse events) as well as overall reviews of clinical data. The views expressed ranged from requests that mesh for POP repair be banned due to safety concerns to arguments that POP repair without mesh would be a disservice to women.

Industry Presentation

The open public hearing was followed by presentations by manufacturers of surgical mesh and tissue-derived grafts. AdvaMed, a trade association that formed a Transvaginal Mesh Industry Working Group, presented a collaborative industry view. The industry working group cited scientific literature to support its view that the benefits outweigh the risks for surgical mesh used for POP repair. The industry group was supportive of premarket clinical studies for new mesh products and postmarket studies to evaluate the long term safety and effectiveness of mesh for POP repair, but did not believe reclassification to Class III (Premarket Approval) is necessary.

In a separate presentation, Cook Medical reviewed its marketing experience and the scientific literature on the Surgisis® graft, an absorbable, porcine-derived, non-crosslinked collagen product used for POP repair. Cook argued that non-crosslinked grafts like the Surgisis® graft result in much lower vaginal erosion rates compared to synthetic surgical mesh and cross-linked biological grafts. Consequently, Cook believes these products have a better risk-benefit profile than other types of surgical mesh.

FDA Presentation

The FDA review team presented an overview of safety and effectiveness data on surgical mesh used for POP repair, including a review of findings from the FDA MAUDE database, an epidemiological review of the published literature, and the FDA's clinical perspective on the risk-benefit profile of mesh for POP repair based on scientific literature. The FDA concluded that vaginal mesh for POP repair poses risks that are unique to mesh, e.g., vaginal erosion, and that the clinical benefit of mesh compared to surgical repair of POP without mesh is questionable. The FDA recommended that additional premarket and postmarket clinical studies are needed to fully evaluate the risk/benefit profile of vaginal mesh intended for surgical POP repair. The FDA also recommended that these devices be reclassified from the current Class II (Special Controls) to Class III (Premarket Approval). Reclassification would ensure that the FDA could require appropriately designed clinical trials, i.e., with a control arm of women undergoing POP repair using traditional technique without

mesh. FDA also stated its belief that 522 postmarket studies should be implemented to evaluate currently marketed vaginal mesh used for POP repair.

Panel Deliberations/FDA Questions

The Panel considered four discussion questions prepared by the FDA. The Panel's recommendations are summarized below (in italics):

Vaginal Placement of Surgical Mesh for POP Repair

Question 1a (safety), 1b (effectiveness), 1c (risk/benefit)

- *The panel discussed a number of serious adverse events associated with use of vaginal mesh for POP repair. The panel consensus was that the safety of vaginal mesh intended for POP repair is not well-established.*
- *The panel consensus was that, depending on the compartment, vaginal placement of mesh for POP repair may not be more effective than traditional 'native-tissue' repair without mesh.*
- *The panel consensus was that the risk/ benefit of vaginal placement of mesh for POP repair is not well-established.*

Question 2a (premarket evaluation), 2b (adequacy of Class II special controls), 2c (reclassification)

- *The panel consensus was that clinical studies are needed for premarket evaluation of vaginal mesh for POP repair. The panel recommended that these studies be conducted with a control arm of women receiving traditional 'native-tissue' repair without mesh. The panel also emphasized that endpoints for effectiveness should address both anatomic outcomes (e.g., degree of prolapse), as well as patient satisfaction (including re-surgery). The duration of follow-up should be at least one-year, with additional follow-up in a postmarket setting.*
- *The panel re-affirmed that the control arm for such premarket studies should be a group of women undergoing surgical repair of POP without use of mesh. Accordingly, the panel consensus was that Class II special controls would not be sufficient to ensure safety and effectiveness.*
- *The panel consensus was that vaginal mesh for POP repair should be reclassified from Class II to Class III to ensure that the study design can include a non-mesh control arm.*

Question 3 522 postmarket studies

The panel consensus was that manufacturers of vaginal mesh products should conduct postmarket studies of currently marketed mesh products for POP repair, and that such studies should help better explain the risk/ benefit of mesh vs. POP repair without mesh.

Question 4 abdominal sacrocolpopexy (ASC)

The panel consensus was that the safety and effectiveness of surgical mesh indicated for ASC is well-established and that reclassification of this group of devices is not necessary. Any new products can be adequately evaluated using the 510(k) premarket notification.

In the course of its Day-1 discussion, the panel also emphasized that additional work should be focused on patient labeling and informed consent, mandatory registering of mesh device placed in each procedure, as well as surgeon training and credentialing. They encouraged the FDA to work with other stakeholders such as clinical organizations and industry to use existing databases as well as new data collection tools (e.g. registries) to develop a meaningful database on postmarket clinical

outcomes from which to evaluate long term safety and effectiveness, optimal patient population, requisite surgeon training, and risk factors for complications, particularly for rare life-altering adverse events.

*Summary Day-2 Surgical Mesh for Surgical Management of Female Stress Urinary
Incontinence (SUI)*

Open Public Hearing

Fourteen persons presented during the OPH session on Day-2. The panel heard presentations from individual patients, patient and women's advocacy groups, individual clinicians, and clinical organizations (including AUGS, AUA, and SUFU). Presentations included a range of views, both summaries of individual experiences (all adverse events) as well as overall reviews of clinical data.

Industry Presentation

The open public hearing was followed by presentations by manufacturers of surgical mesh. AdvaMed presented a collaborative industry view, citing a large body of published studies to support its view that the safety and effectiveness of suburethral slings are well-established. AdvaMed argued that Class II special controls are sufficient and that clinical studies are not necessary for premarket evaluation. AdvaMed also stated that mandatory 522 postmarket studies were not needed for suburethral slings currently on the market because many of these products have already been studied extensively, and studies are being undertaken for products with new features.

FDA Presentation

The FDA review team presented an overview of safety and effectiveness data on mesh suburethral slings used for surgical management of female SUI. The FDA summarized findings from its MAUDE database, presented an epidemiological view on adverse events, and gave a clinical overview of the risk-benefit profile for these devices. The FDA concluded that reclassification was generally not necessary for this type of urogyn mesh product, but asked the panel to comment on the safety and effectiveness of a subset of so-called single-incision mini-slings, as well as the need for long-term safety data.

Panel Deliberations/FDA Questions

The Panel considered two questions prepared by the FDA. The Panel's recommendations are summarized below (in italics):

Question 1 retropubic and transobturator suburethral slings

The panel consensus was that the safety and effectiveness of these devices is well-established. Unless there are significant material changes or changes in the surgical access (including introducer instrumentation), premarket clinical studies would generally not be necessary. The panel consensus was that consideration should be made to better characterize low frequency life-altering adverse events, potentially via collaboration with industry and use of existing large-scale health databases. The panel did not believe that 522 postmarket studies would be an appropriate mechanism for this, and the consensus was that 522 postmarket studies for these devices are not necessary.

Question 2 single-incision mini-slings

The panel consensus was that the safety and effectiveness of mini-slings is not well understood and that premarket evaluation of new mini-slings should be supported by clinical studies. Such studies should have a control arm of women using a retropubic or transobturator sling with a well-understood risk-benefit profile. The panel believed that the FDA could address this using the 510(k) premarket notification pathway. The panel consensus also was that, in this case, 522 postmarket studies should address the safety and effectiveness of currently marketed mini-slings. In such 522 studies, the currently marketed mini-sling should be compared to a conventional retropubic or transobturator sling with either a randomized or rigorous cohort design and a 3-5 year follow-up.

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Clinical Organizations

AAGL	American Association of Gynecologic Laparoscopists
ACOG	American College of Obstetricians and Gynecologists
AUA	American Urological Association
AUGS	American Urogynecologic Society
SGS	Society of Gynecologic Surgeons
SUFU	Society for Urodynamics and Female Urology