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August 30, 2011

Ms. Shanika Craig, MHA, MBA
Designated Federal Officer
Obstetrics and Gynecology Devices Panel
Medical Devices Advisory Committee
U.S. Food and Drug Administration
Center for Devices and Radiological Health
Building 66, Room 1613
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Re: Docket No. FDA–2011–N–0002, September 8-9, 2011 Meeting of the Obstetrics and Gynecology Devices Panel of the Medical Devices Advisory Committee

Dear Ms. Craig:

Cook Group (Cook) is a privately-held multinational medical device manufacturer of products for surgery, gynecology, radiology, cardiology, urology, gastroenterology, wound care, and emergency medicine with more than 10,000 employees worldwide, including 8,000 employees in North America. For nearly 50 years, Cook products have benefited patients by providing physicians with a means of diagnosis and intervention using minimally invasive techniques, as well as by providing innovative products for surgical applications.

For more than 13 years, Cook Biotech Incorporated, a division of Cook Group, has been providing non-crosslinked biologic grafts, including grafts for pelvic organ prolapse (POP) and stress urinary incontinence (SUI). Cook Biodesign® Surgisis® Anterior and Posterior Pelvic Floor Grafts and Biodesign® Surgisis® 4-Layer Tissue Graft have been used in over 10,000 patients for soft tissue repair of pelvic floor defects such as cystocele, rectocele, enterocele, sacrocolpopexy, and intra-operative bladder neck suspension. Given its relevant background in this area, Cook respectfully submits the following comments for consideration by FDA and the Obstetrics and Gynecology Devices Panel regarding the safety and effectiveness of transvaginal surgical mesh products used for repair of POP.

The success of any surgical procedure involving implants depends on at least three factors: assuring that the patient is a suitable candidate, performing the procedure correctly, and choosing the appropriate product. Surgeons have found standard colporrhaphy (plication and suture closure) for POP repair to be less than optimal and

have sought other options for over 10 years, including the use of various synthetic mesh products and biologically derived grafts.

FDA's recent report on surgical mesh products for POP repair[1] raises legitimate concerns about these products. While the report addresses the safety and effectiveness of different procedures (e.g., transvaginal vs. transabdominal, anterior vs. apical vs. posterior), it only briefly acknowledges that there are significantly different types of mesh products and grafts used, i.e., synthetics (both absorbable and non-absorbable) vs. biologics. In addition, it does not discuss the most significant difference between types of biologic grafts, namely, chemically cross-linked vs. non-crosslinked grafts. Finally, it provides only one instance in which consideration is given to the type of biomaterial used in the procedure, stating, "more than half of the women who experienced erosion from non-absorbable synthetic mesh required surgical excision in the operating room."

Cook has conducted a thorough review of the literature on POP repair with respect to type of material used. The literature review is attached for consideration by FDA and the Panel. Briefly, that review can be summarized as follows:

- Non-absorbable synthetic mesh products are permanent implants that elicit a foreign body response. Non-crosslinked biologic grafts remodel into normal host tissue, substantially reducing long-term foreign body response, and do not leave behind a foreign material that may need to be removed at some later time.
- Non-crosslinked biologic grafts have a lower average erosion rate than non-absorbable synthetic mesh products (1.2% vs. 10.0%).
- Non-crosslinked biologic grafts have an acceptably low objective prolapse recurrence rate compared to non-absorbable synthetic mesh products (14.5% vs. 8.2%), especially when compared to standard colporrhaphy (30.0%).
- Important differences exist between non-absorbable synthetic mesh products and non-crosslinked biologic grafts in the management of erosion and recurrence. Erosion associated with non-absorbable synthetic mesh products typically requires one or more surgical operations to remove the mesh, while the natural remodeling associated with non-crosslinked biologic grafts allows for non-surgical management. Recurrence of prolapse associated with a non-absorbable synthetic mesh product requires removing the mesh or attempting another procedure with the mesh still in place, while a non-crosslinked biologic graft will eventually be resorbed.

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[1] Urogynecologic Surgical Mesh: Update on the Safety and Effectiveness of Transvaginal Placement for Pelvic Organ Prolapse. July 2011. Food and Drug Administration Website. Available at: http://www.fda.gov/downloads/MedicalDevices/Safety/AlertsandNotices/UCM262760.pdf. Accessed on July 19, 2011.

In summary, Cook's review shows that the literature strongly suggests that important differences exist between biomaterials in terms of tissue response, risks, and successful clinical outcome. Additionally, it provides strong evidence of the safety of non-crosslinked biologic grafts, such as those provided by Cook and other companies.

Cook urges FDA and the Obstetrics and Gynecology Devices Panel to consider this information when deliberating on possible recommendations concerning the use of synthetic mesh products and biologic grafts to treat pelvic organ prolapse. The data show that non-absorbable synthetic mesh products and non-crosslinked biologic grafts have different risk profiles. Recommendations concerning labeling, post-market studies, and reclassification should be made based on the risk profiles of the different biomaterials.

Thank you for considering our views.

Sincerely,

MED INSTITUTE, INCORPORATED

Daniel J. Dillon, M.S., RAC (US)
Regulatory Scientist

/encl

cc: Mark Bleyer, President, Cook Biotech Incorporated
April Lavender, RAC, Senior Vice-President, Regulatory Affairs, Cook Incorporated

Literature Review:

The Safety and Effectiveness of Pelvic Organ Prolapse Repair Depends on the Type of Biomaterial Used

August 30, 2011

Introduction

FDA's recent report on urogynecologic surgical mesh only briefly acknowledges the existence of different types of mesh product and grafts (i.e., synthetics vs. biologics) and does not distinguish between two important types of biologic grafts (chemically cross-linked vs. non-crosslinked). As a result, Cook has conducted a thorough literature review with respect to material type.

The Importance of Mesh/Graft Biomaterials in POP Repair

A woman's lifetime risk of requiring surgery to correct pelvic organ prolapse (POP) is 11%.[1] At least 200,000 procedures are performed each year in the United States.[2,3] Approximately 30% of these surgeries are for repair following a previous corrective procedure (i.e., recurrence of prolapse).[4] Standard colporrhaphy (plication and suture closure) provides less than optimal results. For example, in recent series, anterior colporrhaphy had success rates of approximately 50%.[5,6]

Recognizing the similarities between the surgical correction of POP and abdominal wall hernia repair, over the past 10 years surgeons have begun to apply the principles employed in hernia repair to POP procedures. These principles include using biomaterials such as synthetic mesh and biologic-derived grafts for reinforcement or repair of soft tissues.[6-9]

FDA's recent report[10] raises legitimate concerns about surgical mesh for POP repair. However, the report groups the different types of materials together and largely fails to acknowledge the significantly different clinical outcomes obtained with different materials. The success of any surgical procedure involving implants depends on at least three factors: assuring that the patient is a suitable candidate, performing the procedure correctly, and choosing the appropriate product. While the report addresses the safety

and effectiveness of different procedures (e.g., transvaginal vs. transabdominal, anterior vs. apical vs. posterior), it only briefly acknowledges that there are significantly different types of mesh and grafts used, i.e., synthetics (both absorbable and non-absorbable) vs. biologics. In addition, it does not discuss the most significant difference between types of biologic grafts, namely, chemically cross-linked vs. non-crosslinked grafts. Likewise, although the review articles referenced in FDA's report differentiate between synthetic and biologic-derived materials, the reviews, such as Foon[11] and Abed,[12] do not differentiate between chemically cross-linked and non-crosslinked biologic grafts when assessing safety and effectiveness. Finally, FDA's report provides only one instance in which consideration is given to the type of biomaterial used in the procedure, stating, "more than half of the women who experienced erosion from non-absorbable synthetic mesh required surgical excision in the operating room."

Cook has conducted a thorough review of the literature on POP repair with respect to the type of material used. Surgical products for POP repair can be divided into four groups:

1. Synthetic, non-absorbable mesh
2. Absorbable synthetic mesh
3. Chemically cross-linked biologic grafts
4. Non-crosslinked biologic grafts

Synthetic mesh materials include non-absorbable polypropylene and absorbable polyglactin. Biologic graft materials include porcine dermis, human dermis, bovine pericardium, and porcine small intestinal submucosa.

Tissue Response to Biomaterials Used for POP Repair

This section discusses the differences in the body's response to the four categories of biomaterials: 1) non-absorbable synthetic mesh, 2) absorbable synthetic mesh, 3) chemically cross-linked biologic grafts, and 4) non-crosslinked biologic grafts.

Non-absorbable Synthetic Mesh. Tissue response to non-absorbable synthetic mesh is partially based on pore structure, classified as Types I-IV. [13,14] The current mesh of choice for POP repair is Type I monofilament polypropylene mesh.[15,16] Type I mesh has a pore size > 75 μm, and thus host cells can infiltrate the mesh. Over time, compact fibrous tissue surrounds the mesh.[13,14] This is postulated to provide a strong mechanical bond between the mesh and adjacent tissue, thereby effecting a long-term repair.[13,14]

However, concerns have been raised that after both acute and chronic inflammatory reactions occur, the ultimate tissue response is that of a foreign body reaction with the formation of granulation tissue, limited neovascularization, and eventual fibrosis (i.e., encapsulation).[17] Mesh with smaller pores (Types II-IV) are even more susceptible to encapsulation and risk of infection with associated clinical consequences.[14,15,16,18]

Absorbable Synthetic Mesh. Absorbable synthetic mesh materials (e.g., polyglactin) have not been reviewed extensively in the literature. The initial inflammatory response to these multifilament materials is similar to the response to the non-absorbable mesh. Unfortunately, absorbable synthetic mesh was found not to provide long-term mechanical support, because the incorporation of the host cells at the implantation site hastens the degradation of the mesh. For example, Polyglactin 910 has been found to retain only 25% of its original strength at 21 days *in vivo*.[5]

Chemically Cross-linked Biologic Grafts. The primary structural component of biologic grafts is collagen fibrils derived from extracellular matrix. Chemical cross-linking agents are used to modify the structure of collagen to inhibit its rate of degradation. As a consequence, cellular infiltration into the graft (a crucial part of the body's remodeling process) is significantly decreased.[14,19-22] Based on studies in humans, inflammation gradually gives way to a foreign body reaction and eventual encapsulation of the graft (dense fibroconnective tissue with limited neovascularization) without beneficial fibroblast infiltration.[20] In addition, cross-linking makes the graft stiffer. The stiffness (i.e., pliability) of a graft affects the ability of the host cells to differentiate – another key part of the remodeling process[23] and may result in an increased propensity for erosion. Thus, the chemically cross-linked graft material behaves much like a synthetic mesh in that, rather than facilitating the body's natural remodeling processes, it elicits an early tissue response characterized by mixed inflammation, followed potentially by encapsulation.

Non-crosslinked Biologic Grafts. Like chemically cross-linked biologic grafts, the non-crosslinked biologic grafts are comprised of acellular extracellular matrices, derived primarily from dermis (human, bovine, or porcine) or porcine small intestinal submucosa. However, because they are not chemically cross-linked, they permit cellular infiltration, proliferation, and remodeling of host tissue.[19,24-26] Over time, the collagen scaffold is gradually repopulated by a mixture of host cells. Structural proteins in the graft are gradually replaced by patient-derived collagen. Several months after placement of the

graft, the implant site is characterized by well-organized connective tissue with collagen bundles oriented into the pattern of parallel arrays typical of true ligaments and aponeuroses.[27,28] Moreover, a normal vascular supply has been re-established, and any inflammation is localized in regions where small remnants of the synthetic suture used to affix the graft remain. Non-crosslinked grafts remodel into normal host tissue[29] and thus, substantially reduce the long-term foreign body response.

Review of Clinical Literature

PubMed® was searched for relevant articles in which biologic grafts were used to reinforce anterior, posterior, or apical prolapse repair. Articles were limited to clinical use, English language, transvaginal access, and to those published from January 1, 1996 to August 2, 2011. Search terms and results may be found in Appendix A. Relevant articles were identified, sorted by type of graft (cross-linked or non-crosslinked biologic), and then reviewed for incidences of erosion, pain, and infection, as well as persistence or recurrence of the original defect. These adverse events were chosen as they were referenced as the three most common complications in FDA's report.[10] The safety and effectiveness of synthetic mesh products were also reviewed for the same factors as biologic grafts (e.g., erosion, recurrence) by examining the references cited in FDA's report. Given the longer history of synthetic mesh products and FDA's reliance on these references for its report, review of additional citations was deemed unnecessary. In addition, multiple systematic reviews used colporrhaphy as a comparison group and thus, the associated complications and recurrence for this procedure were also evaluated for the sake of comparison to the products under consideration.

Appendix B (Tables 1-5) presents the results of the literature reviews for each of the five procedural categories:

Table	Material/Procedure
B-1	Synthetic, non-absorbable mesh
B-2	Absorbable synthetic mesh
B-3	Chemically cross-linked biologic grafts
B-4	Non-crosslinked biologic grafts
B-5	Standard colporrhaphy (plication and suture)

For all tables, the data are further summarized with non-weighted averages across all studies for erosion, pain, infection, and recurrence rates. The following definitions were used when comparing studies:

- Erosion: Includes exposure, extrusion, and protrusion
- Pain: Refers to graft-related pain, including dyspareunia
- Objective Recurrence: Includes both recurrence and persistence, as measured by prolapse quantification/International Continence Society (POP-Q/ICS) guidelines (author-defined, but typically POP-Q of Stage 2 or higher), or Baden-Walker Scale
- Symptomatic Recurrence: Includes both recurrence and persistence, as reported by the patient (i.e., subjective recurrence)

A bibliography for all studies referenced in the tables is provided after the tables.

The literature review is summarized in Table 1.

Table 1. Average incidence of various complications by type of biomaterial.

Type of Biomaterial	Number of Studies Reviewed	Average Incidence (%)				
		Erosion	Pain	Infection	Objective Recurrence	Symptomatic Recurrence
Non-absorbable Synthetic Mesh	20	10.0%	11.6%	4.3%	8.2%	13.9%
Absorbable Synthetic Mesh	3	0.2%	8.0%	0.0%	21.7%	24.1%
Cross-linked Biologic Grafts	22	6.2%	21.6%	2.3%	24.0%	8.5%
Non-crosslinked Biologic Grafts	10	1.2%	15.4%	1.3%	14.5%	15.1%
Standard Colporrhaphy	25	*not applicable*	21.5%	4.0%	30.0%	20.3%

With respect to erosion, absorbable synthetic mesh products and non-crosslinked biologic grafts had very low average erosion rates (0.2% and 1.2%, respectively) compared to cross-linked biologic grafts (6.2%) and non-absorbable synthetic mesh products (10.0%). With respect to pain, absorbable synthetic mesh products had the lowest rate (8.0%), followed by non-absorbable synthetic mesh products (11.6%) and non-crosslinked biologic grafts (15.4%). The average rate for cross-linked biologic grafts (21.6%) was slightly higher than standard colporrhaphy (21.5%). The infection rates for absorbable

synthetic mesh products, non-crosslinked biologic grafts, and cross-linked biologic grafts were below standard colporrhaphy rates (0%, 1.3%, and 2.3%, respectively). The average rate for non-absorbable synthetic mesh products (4.3%) was slightly higher than standard colporrhaphy (4.0%). With respect to objective recurrence, all four types of materials had lower rates than standard colporrhaphy (30%). With respect to symptomatic recurrence, cross-linked biologic grafts (8.5%) had the lowest rate, followed by non-absorbable synthetic mesh products (13.9%) and non-crosslinked biologic grafts (15.1%). The average rate for absorbable synthetic mesh products (24.1%) was higher than standard colporrhaphy (20.3%).

Discussion

Non-absorbable Synthetic Mesh. Cook's literature review confirms FDA's finding that non-absorbable synthetic mesh products have a relatively high rate of erosion (10.0% vs. 10% reported by FDA[10]), a complication not associated with standard colporrhaphy, while offering a lower rate of recurrence, a lower rate of pain, and a similar rate of infection compared to standard colporrhaphy.

Absorbable Synthetic Mesh. Absorbable synthetic mesh products have the lowest rate of erosion and low rates of pain and infection. However, the recurrence rates associated with absorbable synthetic mesh products are similar to those of standard colporrhaphy. It should be noted that absorbable synthetic mesh products are not widely used in clinical practice for POP repair, likely due to the high recurrence rates and that the products lose strength relatively quickly compared to other types of biomaterials.

Chemically Cross-linked Biologic Grafts. Chemically cross-linked biologic grafts have a high rate of erosion, and rates of pain and objective recurrence that are higher than non-absorbable synthetic mesh products. The high rate of erosion is consistent with histological findings in humans that cross-linked biologic grafts exhibit a foreign body response similar to non-absorbable synthetic mesh products. In addition, although cross-linked biologic grafts have the lowest rate of symptomatic recurrence (in apparent contradiction to their high objective recurrence rate), it should be noted that:
1) symptomatic recurrence is less frequently reported than objective recurrence (e.g., $n = 8$ for cross-linked biologic grafts and $n = 5$ for non-absorbable synthetic mesh products) and 2) the use of objective measures of recurrence (e.g., POP-Q) allows for a more straightforward comparison of study results.

Non-crosslinked Biologic Grafts. Non-crosslinked biologic grafts have a low average erosion rate (1.2%). While the average objective recurrence rate is higher than non-absorbable synthetic mesh products (14.5% vs. 8.2%), its rate is still well below the recurrence rate for standard colporrhaphy. Furthermore, its average symptomatic recurrence rate is similar to non-absorbable synthetic mesh products (15.1% vs. 13.9%).

When comparing different types of materials, objective measures (erosion, infection, and objective recurrence) allow for a more standardized comparison than subjective measures (pain, symptomatic recurrence). Figures 1 to 3 display these three objective measures for each of the three widely-used materials. (Absorbable synthetic mesh is not included because it is not widely used for POP repair.)

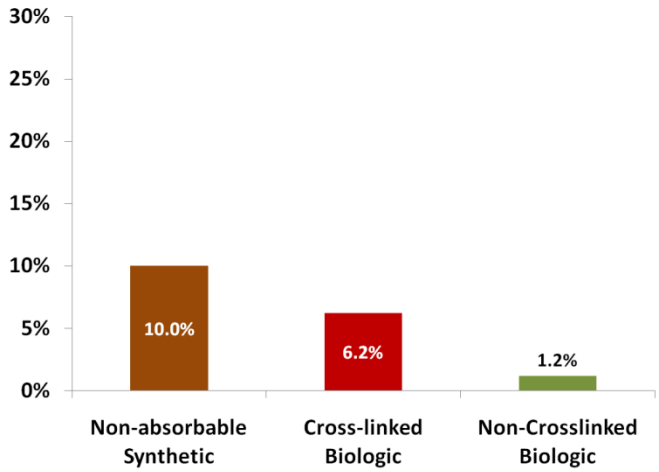

Figure 1. Average rates of erosion by type of biomaterial.

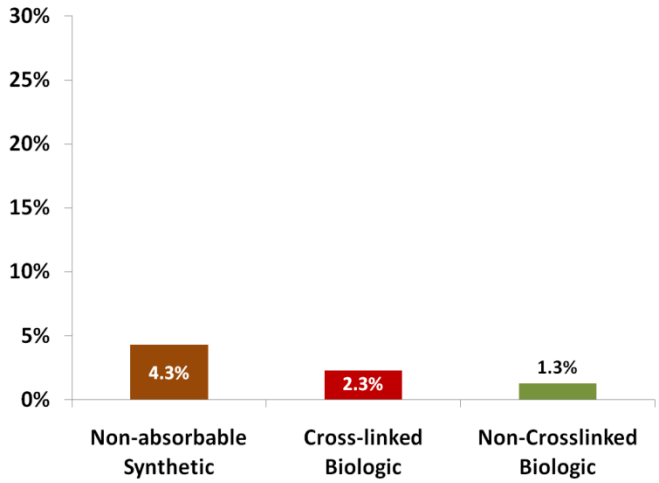

Figure 2. Average rates of infection by type of biomaterial.

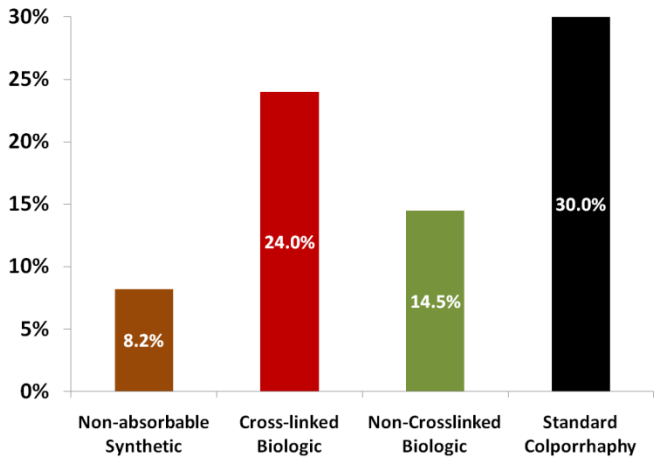

Figure 3. Average rates of objective recurrence by type of biomaterial.

The differences in clinical outcomes between biomaterials are not surprising, given the body's tissue response. As summarized earlier, the body's response to a chemically cross-linked biologic graft is more similar to that of a synthetic mesh (i.e., foreign body reaction) than to the more natural incorporation of a non-crosslinked biologic graft. As stated by Birch[8] with respect to erosion, "[e]rosion of material is a more chronic process, which is secondary to the properties of the prosthesis and its long-term interaction at the tissue interface." In fact, biologic-derived grafts were initially introduced, in part, to mitigate the complications associated with synthetic mesh.[14]

Furthermore, biologic graft erosions can be managed conservatively with topical estrogen and/or antibiotic cream as in Drake et al.[30] However, non-absorbable synthetic mesh erosions typically require one or more operative revisions. As stated in FDA's report,[10] "More than half of the women who experienced erosion from non-absorbable synthetic mesh required surgical excision in the operating room. Some women required two to three additional surgeries." Thus, not only is the risk of erosion higher with non-absorbable synthetic mesh products, the treatment often requires at least one partial excision of the mesh and potentially multiple excisions to remove the entire mesh. Use of a non-crosslinked biologic graft mitigates this long-term risk because the graft remodels into host tissue and thus, is not present long-term in the body.

With respect to recurrence, treatment options vary as a function of material type. For instance, surgical options following use of non-absorbable synthetic mesh products include the use of biologic grafts and standard colporrhaphy. Repair options following

use of a non-crosslinked biologic graft include standard colporrhaphy, biologic graft, and synthetic mesh. Thus, the small increase in recurrence associated with non-crosslinked biologic grafts compared to non-absorbable synthetic mesh products is more than offset by the lower erosion rate.

Conclusion

FDA's recent report on urogynecologic surgical mesh products raises legitimate concerns about synthetic mesh products and biologic grafts for POP repair. However, the report only briefly acknowledges the existence of different types of mesh products and grafts (i.e., synthetics vs. biologics) and does not distinguish between two important types of biologic grafts (chemically cross-linked vs. non-crosslinked). Yet significant differences exist in terms of how the body responds to these different types of biomaterials and the subsequent clinical outcome. As a result, Cook has conducted a thorough literature review with respect to material type.

The literature review shows that important differences exist between the safety and effectiveness of different types of biomaterials:

- Non-absorbable synthetic mesh products are permanent implants that elicit a foreign body response. Non-crosslinked biologic grafts remodel into normal host tissue, substantially reducing long-term foreign body response, and do not leave behind a foreign material that may need to be removed at some later time.
- Non-crosslinked biologic grafts have a lower average erosion rate than non-absorbable synthetic mesh products (1.2% vs. 10.0%).
- Non-crosslinked biologic grafts have an acceptably low objective prolapse recurrence rate compared to non-absorbable synthetic mesh products (14.5% vs. 8.2%), especially when compared to standard colporrhaphy (30.0%).
- Important differences exist between non-absorbable synthetic mesh products and non-crosslinked biologic grafts in the management of erosion and recurrence. Erosion associated with non-absorbable synthetic mesh products typically requires one or more surgical operations to remove the mesh, while the natural remodeling associated with non-crosslinked biologic grafts allows for non-surgical management. Recurrence of prolapse associated with a non-absorbable synthetic mesh product requires removing the mesh or attempting another

procedure with the mesh still in place, while a non-crosslinked biologic graft will eventually be resorbed.

Any literature review has limitations, as FDA's own report acknowledges when presenting its results. However, Cook's review shows that the literature strongly suggests that important differences exist between biomaterials in terms of tissue response, risks, and successful clinical outcome. Additionally, it provides strong evidence of the safety of non-crosslinked biologic grafts, such as those provided by Cook and other companies.

Cook urges FDA and the Obstetrics and Gynecology Devices Panel to consider this information when deliberating on possible recommendations concerning the use of synthetic mesh products and biologic grafts to treat pelvic organ prolapse. The data show that non-absorbable synthetic mesh products and non-crosslinked biologic grafts have different risk profiles. Recommendations concerning labeling, post-market studies, and reclassification should be made based on the risk profiles of the different biomaterials.

References

1. Olsen AL, Smith VJ, Bergstrom JO, et al. Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. Obstet Gynecol 1997;89:501-506.
2. Boyles SH, Weber AM, Meyn L. Procedures for pelvic organ prolapse in the United States, 1979-1997. Am J Obstet Gynecol 2003;188:108-115.
3. Luft J. Pelvic organ prolapse: current state of knowledge about this common condition. J Nurse Pract 2006;2:170-177.
4. DeLancey JOL. The hidden epidemic of pelvic floor dysfunction: achievable goals for improved prevention and treatment. Am J Obstet Gynecol 2005;192:1488-1495.
5. Sand PK, Koduri S, Lobel RW, et al. Prospective randomized trial of polyglactin 910 mesh to prevent recurrence of cystoceles and rectoceles. Am J Obstet Gynecol 2001;184:1357-1364.
6. Birch C, Fynes MM. The role of synthetic and biological prostheses in reconstructive pelvic floor surgery. Curr Opin Obstet Gynecol 2002;14:527-535.
7. Huebner M, Hsu Y, Fenner DE. The use of graft materials in vaginal pelvic floor surgery. Int J Gynaecol Obstet 2006;92:279-288.
8. Birch C. The use of prosthetics in pelvic reconstructive surgery. Best Pract Res Clin Obstet Gynaecol 2005;19:979-991.
9. Le TH, Kon L, Bhatia NN, Ostergard DR. Update on the utilization of grafts in pelvic reconstruction surgeries. Curr Opin Obstet Gynecol 2007;19:480-489.
10. Urogynecologic Surgical Mesh: Update on the Safety and Effectiveness of Transvaginal Placement for Pelvic Organ Prolapse. July 2011. Food and Drug Administration Website. Available at: http://www.fda.gov/downloads/MedicalDevices/Safety/AlertsandNotices/UCM262760.pdf. Accessed July 19, 2011.
11. Foon R, Toozs-Hobson P, Latthe PM. Adjuvant materials in anterior vaginal wall prolapse surgery: a systematic review of effectiveness and complications. Int Urogynecol J Pelvic Floor Dysfunct 2008;19:1697-1706.
12. Abed H, Rahn DD, Lowenstein L, et al. For the Systematic Review Group of the Society of Gynecologic Surgeons. Incidence and management of graft erosion, wound granulation, and dyspareunia following vaginal prolapse repair with graft materials: a systematic review. Int Urogynecol J Pelvic Floor Dysfunct 2011;22:789-798.
13. Murphy M. Use of mesh and materials in pelvic floor surgery. Obstet Gynecol Clin North Am 2009;36:615-635.
14. Trabuco EC, Klingele CJ, Gebhart JB. Xenograft use in reconstructive pelvic surgery: a review of the literature. Int Urogynecol J Pelvic Floor Dysfunct 2007;18:555-563.
15. Baessler K, Maher CF. Mesh augmentation during pelvic-floor reconstructive surgery: risks and benefits. Curr Opin Obstet Gynecol 2006;18:560-566.
16. Rardin CR, Washington BB. New considerations in the use of vaginal mesh for prolapse repair. J Minim Invasive Gynecol 2009;16:360-364.
17. Mistrangelo E, Mancuso S, Nadalini C, et al. Rising use of synthetic mesh in transvaginal pelvic reconstructive surgery: a review of the risk of vaginal erosion. J Minim Invasive Gynecol 2007;14:564-569.
18. Falagas ME, Velakoulis S, Iavazzo C, Athanasiou S. Mesh-related infections after pelvic organ prolapse repair surgery. Eur J Obstet Gynecol Reprod Biol 2007;134:147-156.
19. Badylak SF. The extracellular matrix as a scaffold for tissue reconstruction. Sem Cell Dev Biol 2002;13:377-383.
20. Gandhi S, Kubba LM, Abramov Y, et al. Histopathologic changes of porcine dermis xenografts for transvaginal suburethral slings. Am J Obstet Gynecol 2005;192:1643-1648.
21. Jarmin-Smith ML, Bodamyali R, Stevens C, et al. Porcine collagen crosslinking, degradation and its capability for fibroblast adhesion and proliferation. J Mater Sci Mater Med 2004;15:925-932.
22. Kimuli M, Eardley I, Southgate J. In vitro assessment of decellularized porcine dermis as a matrix for urinary tract reconstruction. BJU Int 2004;94:859-866.
23. Buxboim A, Ivanovska IL, Discher DE. Matrix elasticity, cytoskeletal forces and physics of the nucleus: how deeply do cells “feel” outside and in? J Cell Sci 2010;123:297-308.
24. Hodde J. Extracellular matrix as a bioactive material for soft tissue reconstruction. ANZ J Surg 2006;76:1096-1100.
25. Badylak SF, Record R, Lindberg K, et al. Small intestinal submucosa: a substrate for in vitro cell growth. J Biomater Sci Poly Ed 1998;9:863-878.
26. Badylak SF, Park K, Peppas N, et al. Marrow-derived cells populate scaffolds composed of xenogeneic extracellular matrix. Exp Hematol 2001;29:1310-1318.
27. Wiedemann A, Otto M. Small intestinal submucosa for pubourethral sling suspension for the treatment of stress incontinence: first histopathological results in humans. J Urol 2004;172:215-218.
28. Woo SL, Takakura Y, Liang R, et al. Treatment with bioscaffold enhances the the [sic] fibril morphology and the collagen composition of healing medial collateral ligament in rabbits. Tissue Eng 2006;12:159-166.
29. Badylak S, Kokini K, Tullius B, et al. Morphologic study of small intestinal submucosa as a body wall repair device. J Surg Res 2002;103:190-202.
30. Drake NL, Weidner AC, Webster GD, Amundsen CL. Patient characteristics and management of dermal allograft extrusions. Int Urogynecol J Pelvic Floor Dysfunct 2005;16:375-377.

APPENDIX A

LITERATURE SEARCH TERMS AND RESULTS

Literature Search Terms and Results

The searches listed below were conducted on PubMed® between July 20, 2011 and August 2, 2011 and limited to articles published in English since January 1, 1996 (the same date limit used to support FDA's report). Articles were then excluded if they:

1. Did not pertain to transvaginal access,
2. Described devices not approved for use in the United States,
3. Reported data on only 1 or 2 patients,
4. Did not involve a biomaterial, the type of biomaterial was not identified, or involved a synthetic mesh, or
5. Could not be readily obtained through Cook's corporate copyright license (n = 2; in one case, partial information could be obtained through the abstract).

A total of 32 articles were found that met these criteria.

Search Term(s) and Limits

1. Pelvic floor prolapse AND mesh
2. Transvaginal repair AND mesh
3. Transvaginal repair AND graft
4. Transvaginal repair AND augmentation
5. Anterior colporrhaphy AND mesh
6. Anterior colporrhaphy AND graft
7. Posterior colporrhaphy AND mesh
8. Cystocele AND mesh
9. Cystocele AND graft
10. Rectocele AND mesh NOT rectopexy
11. Rectocele AND graft NOT rectopexy
12. Pelvic AND small intestinal submucosa
13. Pelvic AND Surgisis
14. Pelvic AND Biodesign
15. Repliform
16. Xenform
17. Pelvicol
18. Pelvic AND porcine dermis
19. InteXen
20. Pelvic AND human dermis
21. Pelvic AND fetal bovine
22. Vagina AND fetal bovine AND graft
23. Pelvic AND surgical AND mesh AND transvaginal
24. Vagina AND mesh AND complications NOT laparoscopic NOT rectopexy NOT slings NOT sacrocolpopexy
25. Transvaginal AND erosion NOT sling NOT sacrocolpopexy
26. Pelvic AND mesh AND morbidity (limit: Title)
27. Biologic AND prolapse (limit: Human)

APPENDIX B

TABULAR RESULTS AND BIBLIOGRAPHY

BY TYPE OF BIOMATERIALS

Table B-1. Non-absorbable synthetic mesh.

FDA Ref. No.*	Study	Base Procedure	No. of Patients	Postoperative Complications			Objective Recurrence	Symptomatic Recurrence
				Erosion	Pain	Infection		
6	Carey (2009)	Anterior colporrhaphy	63	6.3% (4/63)	40.0% (12/30)	-**	19.0% (12/63)	-
7	Iglesia (2010)	Anterior colporrhaphy	32	15.6% (5/32)	-	0.0% (0/32)	-	-
8	Withagen (2011)	Anterior colporrhaphy	93	16.9% (14/83)	10.1% (8/79)	-	9.6% (8/83)	20.0% (16/80)
9	Nieminen K (2010)	Anterior colporrhaphy	105	19.0% (20/105)	-	-	13.3% (14/105)	8.7% (9/105)
10	Sivaslioglu (2008)	Anterior colporrhaphy	43	7.0% (3/43)	4.7% (2/43)	-	9.3% (4/43)	-
11	Nguyen (2008)	Anterior colporrhaphy	37	5.4% (2/37)	8.7% (2/23)	10.8% (4/37)	10.8% (4/37)	-
12	Altman (2011)	Anterior colporrhaphy	186	3.2% (6/186)	2.7% (5/186)	-	12.4% (24/194)	39.2% (69/176)
13	Caquant (2008)	Anterior colporrhaphy	108	8.3% (9/108)	-	-	7.4% (8/108)	-
		Posterior colporrhaphy	101	1.0% (1/101)	-	-	4.0% (4/101)	-
		Both	475	7.6% (36/475)	-	-	5.1% (24/475)	-
14	Aungst (2009)	Anterior and/or posterior colporrhaphy	290	3.8% (11/290)	18.3% (53/290)	-	5.2% (15/290)	-
16	Miller (2011)	Anterior and/or posterior colporrhaphy	66	18.8% (16/85)	11.1% (3/27)	-	22.7% (15/66)	-
18	Jia (2008)	Anterior colporrhaphy	-	10.2% (68/666)	36.4% (4/11)	2.0% (11/558)	8.8% (48/548)	1.8% (1/55)
		Posterior colporrhaphy	-	6.5% (2/31)	-	3.8% (4/106)	6.5% (2/31)	-
		Both	-	5.5% (62/1119)	7.1% (3/42)	5.0% (33/661)	6.4% (41/645)	0.0% (0/148)
19	Foon (2008)	Anterior colporrhaphy	31	-	6.5% (2/31)	-	3.2% (1/31)	-
20	Diwadkar (2009)	Anterior colporrhaphy	3425	5.8% (198/3425)	-	-	8.5% (291/3425)	-
21	Feiner (2009)	Anterior colporrhaphy	525	10.7% (56/525)	2.7% (14/525)	-	5.0% (26/525)	-
		Anterior colporrhaphy	1295	5.7% (74/1295)	2.1% (27/1295)	-	13.0% (168/1295)	-
		Anterior colporrhaphy	178	4.5% (8/178)	5.6% (10/178)	-	7.9% (14/178)	-
22	Maher (2010)	Anterior colporrhaphy	-	10.2% (30/293)	-	-	-	-
23	Abed (2011)	Anterior and posterior colporrhaphy	-	8.6% (897/10440)	6.2% (284/4566)	-	-	-

FDA Ref. No.*	Study	Base Procedure	No. of Patients	Postoperative Complications			Objective Recurrence	Symptomatic Recurrence
				Erosion	Pain	Infection		
Cited in 24	Hiltunen (2007)	Anterior colporrhaphy	104	17.3% (18/104)	-	-	6.7% (7/104)	-
Cited in 24	Julian (1996)	Anterior colporrhaphy	12	-	-	-	0.0% (0/12)	-
Cited in 24	Bai (2007)	Anterior colporrhaphy	28	-	-	-	0.0% (0/28)	-
Cited in 24	Deffieux (2007)	Anterior colporrhaphy	89	16.9% (15/89)	-	-	3.4% (3/89)	-
			49	24.5% (12/49)	-	-	8.2% (4/49)	-
Average Incidence				**10.0%**	**11.6%**	**4.3%**	**8.2%**	**13.9%**

*FDA Ref. No. refers to the reference given in FDA's *Urogynecologic Surgical Mesh: Update on the Safety and Effectiveness of Transvaginal Placement for Pelvic Organ Prolapse.* July 2011.
**Cells marked with a dash indicate that the reference did not report this value.

Table B-2. Absorbable synthetic mesh.

FDA Ref. No.*	Study	Base Procedure	No. of Patients	Postoperative Complications			Objective Recurrence	Symptomatic Recurrence
				Erosion	Pain	Infection		
5	Sand (2001)	Anterior colporrhaphy	73	0.0% (0/73)	0.0% (0/49)	0.0% (0/73)	24.7% (18/73)	-**
		Posterior colporrhaphy	73	0.0% (0/73)	-	0.0% (0/73)	8.2% (6/73)	-
18	Jia (2008)	Anterior colporrhaphy	273	0.7% (1/147)	-	0.0% (0/112)	23.1% (63/273)	4.5% (5/112)
		Posterior colporrhaphy	70	-	16.0% (4/25)	0.0% (0/5)	8.6% (6/70)	-
		Both	32	-	-	-	7.7% (2/26)	43.8% (14/32)
Cited in 22	Weber (2001)	Anterior colporrhaphy	26	-	-	-	57.7% (15/26)	-
Average Incidence				**0.2%**	**8.0%**	**0.0%**	**21.7%**	**24.1%**

*FDA Ref. No. refers to the reference given in FDA's *Urogynecologic Surgical Mesh: Update on the Safety and Effectiveness of Transvaginal Placement for Pelvic Organ Prolapse.* July 2011.
**Cells marked with a dash indicate that the reference did not report this value.

Table B-3. Cross-linked biologic grafts.

Ref. No.*	Study	Base Procedure	No. of Patients	Postoperative Complications			Objective Recurrence	Symptomatic Recurrence
				Erosion	Pain	Infection		
1	Altman (2005)	Posterior colporrhaphy	29	0.0% (0/29)	86.7% (13/15)	-**	10.3% (3/29)	-
2	Altman (2006)	Posterior colporrhaphy	27	0.0% (0/23)	86.7% (13/15)	-	40.7% (11/27)	-
3	Daraï (2009)	Sacrospinous suspension (post.); Paravaginal (ant.)	89	-	3.4% (3/89)	-	18.0% (16/89)	-
4	David-Montefiore (2005)	Anterior or posterior sacrospinous suspension	47	-	4.3% (2/47)	0.0% (0/47)	17.0% (8/47)	6.4% (3/47)
5	De Boer (2010)	Anterior and/or posterior colporrhaphy	71	0.0% (0/71)	1.4% (1/71)	-	25.4% (18/71)	-
6	Gomelsky (2007)	Anterior or posterior colporrhaphy	40	15.0% (6/40)	-	7.5% (3/40)	-	-
7	Guerette (2009)	Anterior colporrhaphy	47	0.0% (0/47)	15.0% (3/20)	0.0% (0/47)	14.3% (5/35)	-
8	Handel (2007)	Anterior colporrhaphy; interposition graft	56	21.4% (12/56)	-	1.8% (1/56)	35.7% (20/56)	-
9	Hviid (2010)	Anterior colporrhaphy (fascia not plicated)	28	-	-	-	7.1% (2/28)	3.6% (1/28)
10	Koutsougeras (2009)	Anterior colporrhaphy	95	3.2% (3/95)	-	-	18.9% (18/95)	-
11	Lebouef (2004)	Anterior four-defect repair	19	0.0% (0/19)	-	0.0% (0/19)	15.8% (3/19)	5.3% (1/19)
12	Leu (2011)	Anterior colporrhaphy; interposition graft	70	-	-	-	12.9% (9/70)	4.3% (3/70)
13	Meschia (2007)	Anterior colpotomy + fascial plication	98	1.0% (1/98)	14.9% (7/47)	1.0% (1/98)	7.1% (7/98)	-
14	Natale (2009)	Tension-free cystocele repair	94	0.0% (0/94)	14.9% (14/94)	0.0% (0/94)	43.6% (41/94)	-
15	Novi (2007)	Site-specific rectocele repair	50	-	8.0% (4/50)	-	-	-
16	Paraiso (2006)	Site-specific rectocele repair	29	-	10.3% (3/29)	10.3% (3/29)	46.2% (12/26)	21.4% (6/28)
17	Ross (2008)	Anterior and/or posterior colporrhaphy	72***	1.2% (1/82)	9.7% (7/72)	-	15.9% (13/82)	7.3% (6/82)
18	Salomon (2004)	Vaginal hysterectomy + anterior wall repair	27	-	3.7% (1/27)	0.0% (0/27)	18.5% (5/27)	3.7% (1/27)
19	Simsiman (2006)	Vaginal paravaginal anterior repair	89	16.9% (15/89)	-	-	23.6% (21/89)	-
20	Singh (2007)	Anterior colporrhaphy	56	21.4% (12/56)	-	-	35.7% (20/56)	-
21	Taylor (2008)	Site-specific rectocele repair	198	13.1% (26/198)	-	-	-	-
22	Wheeler (2006)	Anterior colporrhaphy	35	0.0% (0/35)	-	-	50.0% (14/28)	16.1% (5/31)
Average Incidence				**6.2%**	**21.6%**	**2.3%**	**24.0%**	**8.5%**

*Ref. No. refers to bibliography following Table 5. **Cells marked with a dash indicate that the reference did not report this value. ***82 repairs on 72 patients.

Table B-4. Non-crosslinked biologic grafts.

Ref. No.*	Study	Base Procedure	No. of Patients	Postoperative Complications			Objective Recurrence	Symptomatic Recurrence
				Erosion	Pain	Infection		
23	Botros (2009)	Anterior colporrhaphy (graft arcus anchored)	72	0.0% (0/72)	13.7% (7/51)	-**	19.4% (14/72)	-
24	Chaliha (2006)	Anterior colporrhaphy	14	0.0% (0/14)	-	0.0% (0/14)	-	28.6% (4/14)
25	Chung (2002)	Pubovaginal sling + anterior repair	19	-	-	5.3% (1/19)	15.8% (3/19)	-
26	Drake (2005)	Anterior or posterior colporrhaphy	64	10.9% (7/64)	-	-	-	-
27	Feldner (2010)	Anterior colporrhaphy (graft arcus anchored)	29	0.0% (0/29)	17.2% (5/29)	0.0% (0/29)	13.8% (4/29)	-
28	Goldstein (2010)	Anterior or posterior colporrhaphy	43	0.0% (0/43)	0.0% (0/43)	-	11.6% (5/43)	-
29	Gomelsky (2004)	Anterior colporrhaphy; interposition graft	70	0.0% (0/70)	-	-	12.9% (9/70)	0.0% (0/70)
30	Jeffery (2009)	Anterior and/or posterior colporrhaphy	21	0.0% (0/21)	38.1% (8/21)	-	4.8% (1/21)	28.6% (6/21)
31	Kohli (2003)	Site-specific rectocele repair	30	0.0% (0/30)	0.0% (0/30)	0.0% (0/30)	6.7% (2/30)	-
32	Mouritsen (2010)	Anterior colporrhaphy or site-specific rectocele repair	41	0.0% (0/41)	23.1% (3/13)	-	31.3% (10/32)	3.1% (1/32)
Average Incidence				**1.2%**	**15.4%**	**1.3%**	**14.5%**	**15.1%**

*Ref. No. refers to bibliography following Table 5.
**Cells marked with a dash indicate that the reference did not report this value.

Table B-5. Standard colporrhaphy.

FDA Ref. No.*	Study	Compartment	No. of Patients	Postoperative Complications			Objective Recurrence	Symptomatic Recurrence
				Erosion	Pain	Infection		
5	Sand (2001)	Anterior or Posterior	70	N/A**			52.9% (37/70)	-***
6	Carey (2009)	Anterior or Posterior	61	N/A	39.4% (13/33)	-	34.4% (21/61)	11.3% (7/62)
7	Iglesia (2010)	Anterior and/or Posterior	33	N/A	-	0.0% (0/33)	72.7% (24/33)	-
8	Withagen (2011)	Anterior and/or Posterior	96	N/A	11.8% (10/85)	-	45.2% (38/84)	20.0% (16/80)
9	Nieminen (2010)	Anterior	96	N/A	-	-	41.2% (40/97)	65.0% (26/40)
10	Sivaslioglu (2008)	Anterior	42	N/A	9.5% (4/42)	-	28.6% (12/42)	-
11	Nguyen (2008)	Anterior	37	N/A	15.4% (4/26)	0.0% (0/38)	44.7% (17/38)	-
12	Altman (2011)	Anterior	182	N/A	0.5% (1/189)	-	65.5% (114/174)	37.9% (66/174)
18	Jia (2008)	Anterior	640	N/A	-	2.8% (4/142)	28.8% (184/640)	10.6% (19/179)
		Posterior	142	N/A	-	13.8% (13/94)	12.7% (18/142)	15.0% (9/60)
		Both	109	N/A	-	-	24.8% (27/109)	41.2% (14/34)
19	Foon (2008)	Anterior	229	N/A	9.6% (11/115)	4.1% (4/97)	22.3% (51/229)	12.6% (13/103)
20	Diwadkar (2009)	Anterior	7827	N/A	1.6% (125/7827)	3.5% (274/7827)	-	-
Cited in 22	Meschia (2007)	Anterior	103	N/A	10.4% (5/48)	-	19.4% (20/103)	12.6% (13/103)
Cited in 22	Gandhi (2005)	Anterior	78	N/A	-	-	29.5% (23/78)	10.5% (6/57)
Cited in 22	Colombo (2000)	Anterior	33	N/A	56.5% (13/23)	-	3.0% (1/33)	0.0% (0/33)
Cited in 22	Meschia (2004)	Anterior	25	N/A	-	-	28.0% (7/25)	32.0% (8/25)
		Posterior	25	N/A	-	-	12.0% (3/25)	-
Cited in 22	Colombo (1997)	Anterior	55	N/A	-	-	10.9% (6/55)	-
Cited in 22	Weber (2001)	Anterior	33	N/A	-	-	69.7% (23/33)	-
Cited in 22	Kahn (1999)	Posterior	24	N/A	25.0% (6/24)	-	12.5% (3/24)	12.5% (3/24)
Cited in 22	Nieminen (2004)	Posterior	15	N/A	33.3% (4/12)	-	6.7% (1/15)	6.7% (1/15)
Cited in 22	Paraiso (2006)	Posterior	31	N/A	45.0% (9/20)	-	14.3% (4/28)	16.1% (5/31)

FDA Ref. No.*	Study	Compartment	No. of Patients	Postoperative Complications			Objective Recurrence	Symptomatic Recurrence
				Erosion	Pain	Infection		
Cited in 24	Altman (2004)	Posterior	15	N/A	-	-	13.3% (2/15)	-
Cited in 24	Hiltunen (2007)	Anterior	97	N/A	-	-	39.2% (38/97)	-
Cited in 24	Julian (1996)	Anterior	12	N/A	-	-	33.3% (4/12)	-
Cited in 24	Bai (2007)	Anterior	72	N/A	-	-	1.4% (1/72)	-
Cited in 24	Vakili (2005)	Anterior and/or Posterior	214	N/A	-	-	43.0% (92/214)	-
Average Incidence					**21.5%**	**4.0%**	**30.0%**	**20.3%**

*FDA Ref. No. refers to the reference given in FDA's *Urogynecologic Surgical Mesh: Update on the Safety and Effectiveness of Transvaginal Placement for Pelvic Organ Prolapse.* July 2011.

**N/A: Not applicable

***Cells marked with a dash indicate that the reference did not report this value.

Bibliography for All Tables

References for Tables B-1, B-2 and B-5

Note: The reference numbers correspond to the FDA literature review citations found in Urogynecologic Surgical Mesh: Update on the Safety and Effectiveness of Transvaginal Placement for Pelvic Organ Prolapse. July 2011, for the convenience of cross-referencing between this literature review and FDA's report. References 1-4, 15, 17, and 25-27 were not relevant to this literature review and are not listed here.

5. Sand PK, Koduri S, Lobel RW, et al. Prospective randomized trial of polyglactin 910 mesh to prevent recurrence of cystoceles and rectoceles. Am J Obstet Gynecol 2001;184:1357-1364.
6. Carey M, Higgs P, Goh J, et al. Vaginal repair with mesh versus colporrhaphy for prolapse: a randomised controlled trial. BJOG 2009;116:1380-1386.
7. Iglesia CB, Sokol AI, Sokol ER, et al. Vaginal mesh for prolapse: a randomized controlled trial. Obstet Gynecol 2010;116:293-303.
8. Withagen MI, Milani AL, den Boon J, et al. Trocar-guided mesh compared with conventional vaginal repair in recurrent prolapse: a randomized controlled trial. Obstet Gynecol 2011;117:242-250.
9. Nieminen K, Hiltunen K, Takala T, et al. Outcomes after anterior vaginal wall repair with mesh: a randomized, controlled trial with a 3 year follow-up. Am J Obstet Gynecol 2010;203:235e1-8.
10. Sivaslioglu AA, Unlubilgin E, Dolen I. A randomized comparison of polypropylene mesh surgery with site-specific surgery in the treatment of cystocele. Int Urogynecol J Pelvic Floor Dysfunct 2008;19:467-471.
11. Nguyen JN, Burchette RJ. Outcome after anterior vaginal prolapse repair: a randomized controlled trial. Obstet Gynecol 2008;111:891-898.
12. Altman D, Väyrynen T, Engh ME, et al. Anterior colporrhaphy versus transvaginal mesh for pelvic-organ prolapse. N Engl J Med 2011;364:1826-1836.
13. Caquant F, Collinet P, Debodinance P, et al. Safety of trans vaginal mesh procedure: retrospective study of 684 patients. J Obstet Gynaecol Res 2008;34:449-456.
14. Aungst M, Friedman EB, von Pechmann WS, et al. De novo stress incontinence and pelvic muscle symptoms after transvaginal mesh repair. Am J Obstet Gynecol 2009;201:73e1-7.
16. Miller D, Lucente V, Babin E, et al. Prospective clinical assessment of the transvaginal mesh technique for treatment of pelvic organ prolapse - 5-year results. FPMRS 2011;17:139-143.
18. Jia X, Glazener C, Mowatt G, et al. Efficacy and safety of using mesh or grafts in surgery for anterior and/or posterior vaginal wall prolapse: systematic review and meta-analysis. BJOG 2008;115:1350-1361.
19. Foon R, Toozs-Hobson P, Lathe PM. Adjuvant materials in anterior vaginal wall prolapse surgery: a systematic review of effectiveness and complications. Int Urogynecol J Pelvic Floor Dysfunct 2008;19:1697-1706.
20. Diwadkar GB, Barber MD, Feiner B, et al. Complication and reoperation rates after apical vaginal prolapse surgical repair: a systematic review. Obstet Gynecol 2009;113:367-373.
21. Feiner B, Jelovsek JE, Maher C. Efficacy and safety of transvaginal mesh kits in the treatment of prolapse of the vaginal apex: a systematic review. BJOG 2009;116:15-24.
22. Maher C, Feiner B, Baessler K, et al. Surgical management of pelvic organ prolapse in women. Cochrane Database Syst Rev 2010;4:CD004014.

Articles of note referenced in Maher C, Feiner B, Baessler K, et al.:

- Altman D, Mellgren A, Blomgren B, et al. Clinical and histological safety assessment of rectocele repair using collagen mesh. Acta Obstet Gynecol Scand 2004;83:995-1000.
- Colombo M, Maggioni A, Scalambrino S, et al. Surgery for genitourinary prolapse and stress incontinence: a randomized trial of posterior pubourethral ligament plication and Pereyra suspension. Am J Obstet Gynecol 1997;176:337-343.

- Colombo M, Vitobello D, Proietti, et al. Randomised comparison of Burch colposuspension versus anterior colporrhaphy in women with stress urinary incontinence and anterior vaginal wall prolapse. BJOG 2000;107:544-551.
- Gandhi S, Goldberg RP, Kwon C, et al. A prospective randomized trial using solvent dehydrated fascia lata for the prevention of recurrent anterior vaginal wall prolapse. Am J Obstet Gynecol 2005;192:1649-1654.
- Kahn MA, Stanton SL, Kumar D, et al. Posterior colporrhaphy is superior to the transanal repair for treatment of posterior vaginal wall prolapse. Neurourol Urodynamics 1999;18:329-330.
- Meschia M, Pifarotti P, Spennacchio M, et al. A randomized comparison of tension-free vaginal tape and endopelvic fascia plication in women with genital prolapse and occult sress urinary incontinence. Am J Obstet Gynecol 2004;190:609-613.
- Meschia M, Pifarotti P, Bernasconi F, et al. Porcine skin collagen implants to prevent anterior vaginal wall prolapse recurrence: a multicentre, randomized study. J Urol 2007;177:192-195.
- Nieminen K, Hiltunen R, Laitinen J, et al. Transanal or vaginal approach to rectocele repair: a prospective, randomized pilot study. Dis Colon Rectum 2004;47:1636-1642.
- Paraiso M, Barber M, Muir T, et al. Rectocele repair: a randomized trial of three surgical techniques including graft augmentation. Am J Obstet Gynecol 2006;195:1762-1771.
- Weber AM, Walters MD, Piedmonte MR, et al. Anterior colporrhaphy: a randomized trial of three surgical techniques. Am J Obstet Gynecol 2001;185:1299-1304.

23. Abed H, Rahn DD, Lowenstein L, et al. for the Systematic Review Group of the Society of Gynecologic Surgeons. Incidence and management of graft erosion, wound granulation, and dyspareunia following vaginal prolapse repair with graft materials: a systematic review. Int Urogynecol J Pelvic Floor Dysfunct 2011;22:789-798.
24. Sung VW, Rogers RG, Schaffer JI, et al. for the Society of Gynecologic Surgeons Systematic Review Group. Graft use in transvaginal pelvic organ prolapse: a systematic review. Obstet Gynecol 2008;112:1131-1142.

Articles of note referenced in Sung VW, Rogers RG, Schaffer JI, et al.:

- Bai SW, Jung HJ, Jeon MJ, et al. Surgical repair of anterior wall vaginal defects. Int J Gynaecol Obstet 2007;98:147-150.
- Deffieux X, de Tayrac R, Huel C, et al. Vaginal mesh erosion after transvaginal repair of cystocele using Gynemesh or Gynemesh-Soft in 138 women: a comparative study. Int Urogynecol J Pelvic Floor Dysfunct 2007;18:73-79.
- Hiltunen R, Nieminen K, Takala T, et al. Low-weight polypropylene mesh for anterior vaginal wall prolapse: a randomized controlled trial. Obstet Gynecol 2007;110:455-462.
- Julian TM. The efficacy of Marlex mesh in the repair of severe, recurrent vaginal prolapse of the anterior midvaginal wall. Am J Obstet Gynecol 1996;175:1472-1475.
- Valkili B, Huynh T, Loesch H, et al. Outcomes of vaginal reconstructive surgery with and without graft material. Am J Obstet Gynecol 2005;193:2126-2132.

References for Tables B-3 and B-4

1. Altman D, Zetterström J, López A, et al. Functional and anatomic outcome after transvaginal rectocele repair using collagen mesh: a prospective study. Dis Colon Rectum 2005;48:1233-1242.
2. Altman D, Zetterström J, Mellgren A, et al. A three-year prospective assessment of rectocele repair using porcine xenograft. Obstet Gynecol 2006;107:59-65.
3. Daraï E, Coutant C, Rouzier R, et al. Genital prolapse repair using porcine skin implant and bilateral sacrospinous fixation: midterm functional outcome and quality-of-life assessment. Urology 2009;73:245-250.
4. David-Montefiore E, Barranger E, Dubernard G, et al. Treatment of genital prolapse by hammock using porcine skin collagen implant (Pelvicol). Urology 2005;66:1314-1318.
5. de Boer TA, Gietelink DA, Hendriks JCM, et al. Factors influencing success of pelvic organ prolapse repair using porcine dermal implant Pelvicol®. Eur J Obstet Gynecol Reprod Biol 2010;149:112-116.
6. Gomelsky A, Haverkorn RM, Simoneaux WJ, et al. Incidence and management of vaginal extrusion of acellular porcine dermis after incontinence and prolapse surgery. Int Urogynecol J Pelvic Floor Dysfunct 2007;18:1337-1341.
7. Guerette NL, Peterson TV, Aguirre OA, et al. Anterior repair with or without collagen matrix reinforcement. Obstet Gynecol 2009;114:59-65.
8. Handel LN, Frenkl TL, Kim YH. Results of cystocele repair: A comparison of traditional anterior colporrhaphy, polypropylene mesh and porcine dermis. J Urol 2007;178:153-156.
9. Hviid U, Hviid TVF, Rudnicki M. Porcine skin collagen implants for anterior vaginal wall prolapse: a randomised prospective controlled study. Int Urogynecol J Pelvic Floor Dysfunct 2010;21:529-534.
10. Koutsougeras G, Nicolaou P, Karamanidis D, et al. Effectiveness of transvaginal colporrhaphy with porcine acellular collagen matrix in the treatment of moderate to severe cystoceles. Clin Exp Obstet Gynecol 2009;36:179-181.
11. Leboeuf L, Miles RA, Kim SS, et al. Grade 4 cystocele repair using four-defect repair and porcine xenograft acellular matrix (Pelvicol): Outcome measures using SEAPI. Urology 2004;64:282-286.
12. Leu PB, Scarpero HM, Dmochowski RR. Cystocele repair with interpositional grafting. Urol Clin N Am 2011;38:47-53.
13. Meschia M, Pifarotti P, Bernasconi F, et al. Porcine skin collagen implants to prevent anterior vaginal wall prolapse recurrence: a multicenter, randomized study. J Urol 2007;177:192-195.
14. Natale F, La Penna C, Padoa A, et al. A prospective, randomized, controlled study comparing Gynemesh®, a synthetic mesh, and Pelvicol®, a biologic graft, in the surgical treatment of recurrent cystocele. Int Urogynecol J Pelvic Floor Dysfunct 2009;20:75-81.
15. Novi JM, Bradley CS, Mahmoud NN, et al. Sexual function in women after rectocele repair with acellular porcine dermis graft vs site-specific rectovaginal fascia repair. Int Urogynecol J Pelvic Floor Dysfunct 2007;18:1163-1169.
16. Paraiso MFR, Barber MD, Muir TW, et al. Rectocele repair: a randomized trial of three surgical techniques including graft augmentation. Am J Obstet Gynecol 2006;195:1762-1771.
17. Ross JW. Porcine dermal hammock for repair of anterior and posterior vaginal wall prolapse: 5-year outcome. J Minim Invasive Gynecol 2008;15:459-465.
18. Salomon LJ, Detchev R, Barranger E, et al. Treatment of anterior vaginal wall prolapse with porcine skin collagen implant by the transobturator route: preliminary results. Eur Urol 2004;45:219-225.
19. Simsiman AJ, Luber KM, Menefee SA. Vaginal paravaginal repair with porcine dermal reinforcement: correction of advanced anterior vaginal prolapse. Am J Obstet Gynecol 2006;195:1832-1836.
20. Singh P, Gupta M, Srivastava A. A comparison of traditional anterior colporrhaphy, polypropylene mesh and porcine dermis in cystocele repair. Indian J Urol 2007;23:484-485.
21. Taylor GB, Moore RD, Miklos JR, et al. Posterior repair with perforated porcine dermal graft. Int Brazil J Urol 2008;34:84-90.
22. Wheeler II TL, Richter HE, Duke AG, et al. Outcomes with porcine graft placement in the anterior vaginal compartment in patients who undergo high vaginal uterosacral suspension and cystocele repair. Am J Obstet Gynecol 2006;194:1486-1491.

23. Botros SM, Sand PK, Beaumont JL, et al. Arcus-anchored acellular dermal graft compared to anterior colporrhaphy for stage II cystoceles and beyond. Int Urogynecol J Pelvic Floor Dysfunct 2009;20:1265-1271.
24. Chaliha C, Khalid U, Campagna L, et al. SIS graft for anterior vaginal wall prolapse repair - a case-controlled study. Int Urogynecol J Pelvic Floor Dysfunct 2006;17:492-497.
25. Chung SY, Franks M, Smith CP, et al. Technique of combined pubovaginal sling and cystocele repair using a single piece of cadaveric dermal graft. Urology 2002;59:538-541.
26. Drake NL, Weidner AC, Webster GD, et al. Patient characteristics and management of dermal allograft extrusions. Int Urogynecol J Pelvic Floor Dysfunct 2005;16:375-377.
27. Feldner Jr. PC, Castro RA, Cipolotti LA, et al. Anterior vaginal wall prolapse: a randomized controlled trial of SIS graft versus traditional colporrhaphy. Int Urogynecol J Pelvic Floor Dysfunct 2010;21:1057-1063.
28. Goldstein HB, Maccarone J, Naughton MJ, et al. A multicenter prospective trial evaluating fetal bovine dermal graft (Xenform® Matrix) for pelvic reconstructive surgery. BMC Urology 2010;10:21-25.
29. Gomelsky A, Rudy DC, Dmochowski RR. Porcine dermis interposition graft for repair of high grade anterior compartment defects with or without concomitant pelvic organ prolapse procedures. J Urol 2004;171:1581-1584.
30. Jeffery ST, Doumouchtsis SK, Parappallil S, et al. Outcomes, recurrence rates, and postoperative sexual function after secondary vaginal prolapse surgery using the small intestinal submucosa graft. J Pelvic Med Surg 2009;15:151-156.
31. Kohli N, Miklos JR. Dermal graft-augmented rectocele repair. Int Urogynecol J Pelvic Floor Dysfunct 2003;14:146-149.
32. Mouritsen L, Kronschnabl M, Lose G. Long-term results of vaginal repairs with and without xenograft reinforcement. Int Urogynecol J Pelvic Floor Dysfunct 2010;21:467-473.