BEFORE THE JUDICIAL PANEL ON MULTIDISTRICT LITIGATION

In re Cook Medical, Inc.
Products Liability Litigation

MDL-_____

BRIEF IN SUPPORT OF PLAINTIFFS' MOTION FOR TRANSFER TO THE SOUTHERN DISTRICT OF WEST VIRGINIA PURSUANT TO 28 U.S.C. § 1407

COME NOW the Plaintiffs in certain pending constituent civil actions listed in the attached Schedule of Actions, and file their Motion to Transfer to the Southern District of West Virginia pursuant to 28 U.S.C. § 1407 as follows:

I. BACKGROUND

This product liability litigation involves the women's pelvic floor repair products sold by Cook Medical Inc., Cook, Incorporated, Cook Biotech, Inc., Cook Urological Incorporated, Cook Group, Inc., Cook (Canada), Inc., William A. Cook Austrailia Pty. Ltd., and Cook Ireland Limited (hereinafter "Cook defendants"). The products at issue in these cases are implantable biologic surgical meshes sold for use in the female pelvic region to support and reinforce the body's pelvic organs and natural tissues for pelvic organ prolapse repair and/or for stress urinary incontinence. The plaintiffs in the constituent civil actions are women suffering from pelvic organ prolapse and/or incontinence who received implants of these products, and where applicable their spouses. All of the plaintiffs herein claim that the devices implanted in their bodies were defectively designed, manufactured and marketed, and that the defendants failed to provide appropriate warnings and instructions regarding the dangers posed by these devices.

The plaintiffs herein suffered serious and permanent physical injuries from the implantation of the implantation of the Surgisis Biodesign Tension-Free Urethral Sling, Surgisis Biodesign Anterior Pelvic Floor Graft, Surgisis Biodesign Posterior Pelvic Floor Graft, Cook

Urological Stratasis Urethral Sling, Stratasis Tension Free Urethral Sling Kit in their bodies, often requiring additional surgeries, additional medical expenses and unresolved complications for which the devices were implanted.

The common defendants in these cases are Cook Medical Inc. and Cook Group, Inc.. In accordance with 28 U.S.C. § 1407, the undersigned are seeking the transfer of all federal cases involving the Cook women's pelvic repair products to the same Court for coordinated and/or consolidated proceedings. Contemporaneously with the instant motion, the undersigned are filing separate motions to transfer cases involving the Cook women's pelvic repair products to the same Court for overall coordination and management of all of these related product liability litigations.

Federal government action regarding transvaginal mesh products and industry's response

Transvaginal mesh devices pose serious national public health concerns. In light of common alleged defects and problems associated with these products in general, these products are particularly appropriate for coordination before a single federal court.

The Cook Medical, Inc. transvaginal mesh devices that are the subject of this motion are among a number of similar products manufactured and sold by several companies in this country that have been linked by the United States Food and Drug Administration ("FDA") to complications that are unacceptably frequent and severe.

On July 13, 2011, the FDA took the extraordinary step of issuing a Safety Communication addressed to doctors and patients entitled "UPDATE on Serious Complications Associated with Transvaginal Placement of Surgical Mesh for Pelvic Organ Prolapse." (A copy of the 7/13/11 Safety Communication is attached hereto as "**Exhibit 1**").[1] In this Safety

[1] An FDA Safety Communication, such as that issued with respect to transvaginal mesh devices in July of 2011, is an extraordinary action by the government – the FDA has only issued 37

Communication, the FDA explained to doctors and patients that it "is issuing this update to inform you that serious complications associated with surgical mesh for transvaginal repair of [pelvic organ prolapse] are **not rare**. This is a change from what the FDA previously reported [in its prior Public Health Notification] on Oct. 20, 2008. Furthermore, it is not clear that transvaginal POP repair with mesh is more effective than traditional non-mesh repair in all patients with POP and it may expose patients to greater risk." (Emphasis in original).[2]

In association with the July 13, 2011 Safety Communication, the FDA also released a detailed white paper entitled "Urogynecologic Surgical Mesh: Update on the Safety and Effectiveness of Transvaginal Placement for Pelvic Organ Prolapse." (A copy of the July 2011 white paper is attached hereto as "**Exhibit 2**"). The FDA observes in this white paper that "[t]he number of [medical device reports for adverse events] associated with POP repairs [from January 1, 2008 to December 31, 2010] increased by 5-fold compared to the number of reports received in the previous three years (January 1, 2005 – December 31, 2007)." (Id., p. 7). The FDA also conducted its own review of the peer-reviewed scientific literature relating to these products. (Id., pp. 7-8).[3] Summarizing its findings from its review of the adverse event reports and

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Safety Communications since 2001.
http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm181502.htm

[2] On October 20, 2008, the FDA issued a Public Health Notification entitled "Serious Complications Associated with Transvaginal Placement of Surgical Mesh in Repair of Pelvic Organ Prolapse and Stress Urinary Incontinence" wherein it stated that it had received over 1,000 complaints involving mesh-related complications, and that "*although rare*, these complications [associated with transvaginal mesh] can have serious consequences."
http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/PublicHealthNotifications/ucm061976.htm
The 7/13/11 Safety Communication states that the FDA was wrong in its 2008 notification because these serious complications associated with these devices are, in fact, "*not rare*." (**Exhibit 1**).

[3] In 2010, approximately 300,000 women had POP repair surgery, approximately one-third of those involved the use of mesh products. (**Exhibit 2**, p. 6). From its review of this published

applicable literature, the FDA stated that it "has NOT seen conclusive evidence that using transvaginally placed mesh in POP repair improves clinical outcomes any more than traditional POP repair that does not use mesh, and it may expose patients to greater risk." (Id., pp. 9-10).

In its July 2011 Safety Communication, the FDA did not differentiate between manufacturers or specific products. Instead, its warnings related to all manufacturers of these devices and all products. Plaintiffs submit that this lack of differentiation is due to the fact that many of the problems associated with transvaginal mesh products are inherent in the use of mesh in the female pelvic region, and thus are not limited to any one product or material.

In September 2011, the FDA convened a two-day hearing before the Obstetrics & Gynecology Devices Advisory Committee to discuss the use of surgical mesh for treatment of pelvic organ prolapse (POP) and stress urinary incontinence (SUI). (See, Excerpt of Transcript of FDA hearing attached hereto as "**Exhibit 3**," p. 132).Cook Medical made its own presentation touting the unique characteristics and qualities of its own product, attempting to contrast its products with those of its competitors.

As a result of the hearing, the Advisory Committee concluded that there is insufficient scientific data to establish the safety or efficacy of the pelvic organ prolapse products now on the market. Based thereon, the Advisory Committee recommended to the FDA the institution of studies to assess the risks and benefits for transvaginal mesh for both POP and SUI, as well as expanded post-market monitoring of the performance of these devices. The Advisory

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scientific literature, the FDA observed that approximately 10 percent of women undergoing POP mesh repair experienced erosion within 12 months of surgery, and further that complications associated with transvaginal mesh "can be life altering for some women," and that "[s]equelae (e.g., pain) may continue despite mesh removal." (**Exhibit 2**, p. 8). The FDA noted that the literature demonstrates that "[p]atients who undergo POP repair with mesh are subject to mesh-related complications that are not experienced by patients who undergo traditional surgery without mesh." (Id.).

Committee also recommended that surgical mesh for treatment of POP be reclassified from a Class II, which are marketed by way of the FDA's 510(k) "substantial equivalence" process, to a Class III under which each manufacturer would be required to go through the "premarket approval" process to prove the safety and efficacy of their products. The Supreme Court explained the marked difference between the 510(k) process and the more rigorous "premarket approval" process in Medtronic, Inc. v. Lohr, 518 U.S. 470, 478-79 (1996), observing:

> If the FDA concludes on the basis of the [manufacturer's] § 510(k) notification that the device is 'substantially equivalent' to a pre-existing device, it can be marketed without further regulatory analysis.... The § 510(k) notification process is by no means comparable to the [premarket approval] process; in contrast to the 1,200 hours necessary to complete a PMA review, the § 510(k) review is completed in an average of only 20 hours.... Section 510(k) notification requires little information, rarely elicits a negative response from the FDA, and gets processed very quickly.

The Supreme Court in Lohr observed that "the 510(k) process is focused on *equivalence*, not safety. As a result, substantial equivalence determinations provide little protection to the public.... [T]he design of...'substantially equivalent' devices [such as the products at issue in this motion] has never been formally reviewed...for safety or efficacy." Id. at 493 (Emphasis in original). The Cook women's pelvic repair products at issue herein, and the women's pelvic repair products in general, were all marketed through the FDA's 510(k) "equivalence" process, and none of them have been formally reviewed for safety or efficacy.

While the findings of the Advisory Committee were somewhat different for the mesh products used for SUI treatment compared with the mesh products used to treat POP, Plaintiffs submit that there are many similarities. These products are generally manufactured from the same materials, often implanted by the same basic surgical route and generally by the same physicians at the same time as POP mesh who are taught by the same manufacturers how to perform these implant procedures. The scientific literature is replete with examples of injuries

associated with SUI mesh products. Perhaps most significantly, women implanted with mesh to treat SUI have suffered injuries similar to those caused by mesh used to treat POP. Many of the women who have been implanted with POP mesh have also been implanted with SUI mesh, and have likewise suffered through multiple repair surgeries necessitated by the failures of their defective mesh products. Additionally, the other five MDLs pending in the Southern District of West Virginia encompass both POP and SUI devices for these reasons.[4]

Actions involving multiple products

Many women who undergo mesh surgery for treatment of POP or SUI are implanted with more than one product, and often with products manufactured and sold by different companies. This "multi-product/multi-defendant" phenomenon makes these cases particularly appropriate for coordination before a single federal judge.

In several cases now pending in the United States Federal Courts, a single plaintiff has been implanted with multiple women's pelvic repair products manufactured by different defendants and Cook's products. Without the necessity of listing every such case, suffice it to show hased on the Schedule of Actions that there are other multi-product, multi-defendant cases involving Cook pending in the Federal court system and it is anticipated that there will be many more such cases filed in the coming months.

The cases that involve multiple products and defendants present a unique situation that militates strongly in favor of having mesh pelvic repair products before the same court and judge as the other mesh products. As discussed more fully below, the splitting of these Cook multi-product/multi-defendant cases between two or more Courts would destroy the convenience,

[4] In re: C. R. Bard, Inc., Pelvic Repair System Products Liability Litigation MDL-2187, In re: American Medical Systems, Inc., Pelvic Repair System Products Liability Litigation MDL-2325, In re: Boston Scientific Corporation Pelvic Repair System Products Liability Litigation, MDL 2326, In re: Ethicon, Inc. Pelvic Repair System Products Liability Litigation MDL-2327, and In re: Coloplast Corp. Pelvic Support Systems Products Liability Litigation MDL-2387.

efficiency and economy for which coordinated proceedings are granted pursuant to 28 U.S.C. § 1407. The only way to avoid this antithetical result is for the Cook MDL also to be assigned to Judge Goodwin in the Southern District of West Virginia.

II. THE LOCATION AND STATUS OF THE ACTIONS

To date, 42 women (and, in most instances, their husbands) have filed civil actions arising from the implantation of the women's pelvic repair devices designed, manufactured and sold by the Cook defendants.

There are 42 actions pending in 9 federal districts. The breakdown is: Southern District of West Virginia (29 actions; 29 women/14 spouses); Middle District of Tennessee (3 actions; 3 women/1 spouse); Northern District of Alabama (3 actions; 3 women/2 spouses); District of Montana (1 action; 1 woman/1 spouse); Middle District of Florida (1 action; 1 woman); Middle District of Georgia (1 action 1 woman/1 spouse); Eastern District of Kentucky (1 action; 1 woman/1 spouse); Middle District of Alabama (2 actions; 2 women); District Court of New Jersey (1 action; 1 woman).

It is the expectation of the undersigned that there will be many hundreds of additional cases filed in the very near future dealing with these products.

ARGUMENTS

I. These actions are appropriate for centralization and transfer for coordinated and/or consolidated pretrial treatment under 28 U.S.C. § 1407.

These 42 actions currently pending in 9 separate federal district courts all involve similar product design and manufacturing defect and warnings claims against the manufacturer/seller defendant Cook regarding the women's pelvic repair products that were implanted in these women. The Panel has previously found that product liability actions involving similar claims relating to similar implantable medical devices are proper for centralization under 28 U.S.C. §

1407. See, e.g., In re Protegen Sling and Vesica Systems Prods. Liab. Litig., MDL No. 1387 (J.P.M.L. 2001); In re Mentor Corp. ObTape Transobturator Sling Prods. Liab. Litig., 588 F. Supp. 2d 1374, MDL No. 2004 (J.P.M.L. 2008); In re Avaulta Pelvic Support Systems Prods. Liab. Litig., MDL No. 2187 (J.P.M.L. 2010). In re American Medical Systems, Inc. Product Liability Litigation MDL No. 2325 (J.P.M.L 2012); In re Boston Scientific Corporation Product Liability Litigation MDL No. 2326 (J.P.M.L. 2012); In re Ethicon Product Liability Litigation MDL 2327 (J.P.M.L. 2012); In re Coloplast Corporation Product Liability Litigation MDL 2387 (J.P.M.L. 2012). As set forth above, the undersigned respectfully submit that MDL treatment of all of these similar products is appropriate and that transfer of all of these women's pelvic repair product cases to a single court before one Judge would be the only way to eliminate inconsistency and redundancy and allow for coordination in accordance with 28 U.S.C. § 1407.

II. The Southern District of West Virginia is uniquely situated to serve as the proper forum for coordinated and/or consolidated pretrial proceedings of these actions.

Transfer of these Cook women's pelvic repair product cases to a single Court before a single judge for purposes of pre-trial discovery and coordination is the only effective means to efficiently manage this litigation. From a practical standpoint, the Southern District of West Virginia is uniquely situated as the appropriate forum to handle these cases because that Court is already handling related litigation that could be coordinated with the product actions involving other manufacturers' products. The MDLs (Bard MDL 2187, American Medical Systems MDL 2325, Boston Scientific MDL 2326, Ethicon/Johnson & Johnson MDL 2327, Coloplast MDL 2387) now pending before Chief Judge Joseph R. Goodwin involve similar products intended for similar uses in the same area of the female anatomy as the products at issue herein. Cook's biologic products are similar to the biologic products already pending in the other five MDLs (MDL 2187, MDL 2325, MDL 2326, MDL 2327, and MDL 2387). Thus, these Cook women's

pelvic repair product cases will involve similar claims and defenses to those in the Bard women's pelvic repair product cases. The factual and legal issues involved in these pelvic repair product cases are inextricably intertwined no matter what manufacturer or model of the product is involved. For example, as noted above, the FDA addressed serious health concerns regarding the lack of demonstrated safety and effectiveness of *all* POP mesh products in its recent Safety Communication – irrespective of manufacturer. As stated in the FDA's warnings and its associated literature, many of the serious injuries to women associated with these products are not unique to any particular product, but rather are common throughout the industry. These injuries include multiple repair surgeries, intractable pain syndrome, shrinkage of tissue, hyperfibrotic reaction to the mesh, painful intercourse, degradation of the mesh, chronic inflammation, erosion of the mesh through tissue, infection, and alteration of the physical characteristics of the vagina and pelvic area – and occasionally physical injury to spouse. If these pelvic repair product cases are not in MDL proceedings before a single court, it would force the attorneys representing both the plaintiffs and the defendants in these cases to litigate the same issues in several different federal courts, perhaps leading to disparate and conflicting rulings. Additionally, the drain on resources resulting from litigating these cases in different courts would diminish the attorneys' abilities to fully and efficiently represent any individual client – plaintiff or defendant. It is not difficult to envision, for example, a scenario where the same plaintiffs' and defense lawyers would be required to argue the same *Daubert* motions regarding the same experts in different federal courts; which could result in potentially conflicting rulings regarding the same experts. The inefficiency and potential duplication of effort inherent in splitting these pelvic repair product cases between multiple federal district courts would only be exacerbated in the many cases that involve a single plaintiff implanted with

multiple products sold by multiple manufacturers. If MDL proceedings involving the Cook women's pelvic repair products are in a different court from the other five mesh MDL's, the same attorneys for the same victims will be forced to unnecessarily exhaust their limited time and resources traveling to and from and dealing with multiple courts' and their different schedules, potentially conflicting rulings, and generally the redundancy that the MDL process is designed to avoid.

Transfer of these Cook women's pelvic repair product cases to a single court would avoid the untenable result of dividing cases involving a single injured woman injured by multiple pelvic repair products, and sending "parts" of the same individual plaintiff's case to different federal courts. Splitting cases in this manner would destroy the very efficiency and economy that MDL's are intended to achieve. As mentioned hereinabove, the Cook women's pelvic repair products are often used in conjunction with one or more pelvic repair products by other manufacturers. In multiple-product cases (involving a single plaintiff implanted with multiple products), it is often true that different manufacturers' products are causally related to the plaintiff's injuries, and therefore more than one manufacturer is named as a defendant. If the Cook MDL were to be created and assigned to a different judge in a different court that could result in a case involving multiple defendants being divided between multiple jurisdictions in contravention of the fundamental purpose of an MDL.

The very reason for the creation of an MDL is to avoid the potential for inconsistent rulings, the unnecessary waste of time, effort and resources resulting from the duplication of effort in *multiple cases* that involve a common issue of fact. To have the Cook MDL assigned to a different judge than the other mesh MDLs in these similar cases could result in inconsistency, redundancy, and wastefulness in *the same case*. The detriments of dividing single-plaintiff cases

between different courts are many, and can only be avoided by placing these cases before a single court. Having a single Judge would avoid the nearly inevitable conflict in scheduling orders and competing deadlines between two different courts presiding over cases involving the same products – or even different aspects of a single plaintiff's case. The manufacturers in these single-plaintiff, multi-defendant actions could seek to blame the plaintiff's injuries on the other's product; all of these defendants should be in the same Court where one Judge can consider and decide such issues. Issues of confidentiality/trade secrets should be ruled on by one Judge with familiarity with the different manufacturers' products and respective positions in accordance with a single, predictable standard.[5] The same discovery taken in one plaintiff's case should not have to be rehashed in another court, with the same plaintiff, same medical witnesses, and the same experts potentially having to be deposed multiple times. Most of the same pre-trial motions – dispositive motions, *Daubert* motions, motions in limine – will apply equally to all defendants, and they should be ruled on by a single Judge. The only way to avoid these potential pitfalls would be to have the Cook MDL before a single Court along with the other five mesh MDLs. Having the Cook MDL before Chief Judge Goodwin in the Southern District of West Virginia would be the most efficient utilization of the limited resources of the Courts and would serve the convenience of the parties and their witnesses and representatives.

The overarching goal of 28 U.S.C. § 1407 for selecting a transferee forum is to find a court that will advance "the convenience of the parties and will promote the just and efficient conduct" of the transferred cases. Based on the commonality of the issues and defendants in

[5] The splitting of cases between courts due to conflicting confidentiality orders issued by the two judges could prevent a plaintiff from using discovery obtained from one defendant in one court against another defendant in the other court on such issues as the "state-of-the-art" or feasibility of safer alternative even though the manufacturer is held to the standard of an expert, and is "must keep abreast of scientific knowledge, discoveries, and advances and is presumed to know what is imparted thereby…" Borel v. Fibreboard Paper Prods. Corp., 493 F.2d 1076, 1089 (5th Cir. 1973). These issues should be dealt with by a single judge.

these cases, the commonality of counsel involved on behalf of the plaintiffs and defendants, as well as the similarity between the products and claims at issue in all of these cases, the transfer of these Cook cases to the Southern District of West Virginia for handling by Chief Judge Joseph R. Goodwin, who is already presiding over the other five (5) mesh MDLs and who is dealing with the same types of products and issues, will be convenient to all parties, their counsel and their witnesses and will provide a just and efficient forum for these cases.

Given the similarities between these Cook women's pelvic repair product cases and those biologic mesh cases[6] already before Chief Judge Joseph R. Goodwin, Chief Judge Goodwin has had an opportunity to become familiar with many of the factual and legal issues involved in this litigation and with these products in general. Based on such experience, Chief Judge Goodwin is uniquely suited to preside over MDL's involving these similar transvaginal mesh product cases. "[T]he availability of an experienced and capable judge familiar with the litigation is one of the more important factors in selecting a transferee forum...." In re Ampicillin Antitrust Litigation, 315 F. Supp. 317, 319 (J.P.M.L. 1970); See also, David H. Herr, *Multidistrict Litigation Manual* § 6.14 (2008) ("The availability of a judge experienced with the litigation may overcome otherwise significant factors in selecting a transferee district."); In re American Investors Life Ins. Co. Annuity Marketing and Sales Practices Litigation, 398 F. Supp. 2d 1361 (J.P.M.L. 2005) (appropriate forum where five constituent actions already proceeding, and judge who "has already developed familiarity with the issues present in this docket as a result of presiding over motion practice and other pretrial proceedings in the actions pending before her for the past year."). A transferee judge can gain valuable familiarity with the factual and legal issues from involvement in other litigation even if that litigation involved different facts, legal theories, and different parties. See, e.g., In re Amoxicillin Patent and Antitrust Litig., 449 F.Supp. 601, 604

[6] Including, but not limited to Bard's Pelvicol, Pelvisoft, PelviLace, derivatives of Bard's Permacol.

(J.P.M.L. 1978) (based on supervision of litigation involving another similar product, transferee judge had the opportunity "to become familiar with chemical and historical matters relating to the semisynthetic penicillin industry and that therefore assignment of the present litigation to him will promote the expeditious processing of this litigation."); In re Dollar General Corp. Fair Labor Standards Act Litig., 346 F.Supp.2d 1368, 1370 (J.P.M.L. 2004) (transferee court gained familiarity with the issues involved through his handling of an FLSA action involving a different defendant); In re Flat Glass Antritrust Litig. (No. II), 559 F.Supp.2d 1407 (J.P.M.L. 2008) (transferee judge was generally familiar with antitrust allegations based on her involvement in a prior action involving a different time period and method of price-fixing).

Judge Goodwin also has the exclusive ability to coordinate the Cook MDL in these cases with the cases involving the similar women's pelvic repair products now pending in the other five (5) MDLs. The Panel has considered favorably the transferee court's ability to coordinate with related federal court proceedings. See, e.g., In re Laughlin Products, Inc., Patent Litig., 313 F.Supp.2d 1380, 1382 (J.P.M.L. 2004) (factual and legal allegations in the actions proposed for transfer were similar to those in actions previously centralized before transferee court, and transferee judge was thus familiar with the issues and able to determine whether any distinction between the actions was warranted); In re Polychloroprene Rubber (CR) Antitrust Litig., 360 F.Supp.2d 1348 (J.P.M.L. 2005) (concluding that transfer was appropriate to a district where a related MDL was already pending involving some of the same parties, albeit a different product). The transfer of these Cook Women's Pelvic Repair product cases to the Southern District of West Virginia would facilitate the coordination of these cases with the related cases involving the similar products now pending in the other five mesh MDLs.

Having multiple MDL's involving similar or related products pending before a single Judge for coordination is consistent with the approach taken by the Panel in other product liability litigations. The Panel has ordered the consolidated handling of product liability actions involving different defendants – in the same MDL proceeding – including those involving broad categories of products sold by multiple manufacturers. See, e.g., In re: Denture Cream Prod. Liab. Litig., 624 F.Supp.2d 1379 (J.P.M.L. 2009) (ordering centralization of actions involving different manufacturers' brands of denture cream); In re: Gadolinium Contrast Dyes Prod. Liab. Litig., 536 F.Supp.2d 1380, 1382 (J.P.M.L. 2008) (centralizing actions against multiple defendants involving several different contrast dyes products that were chemically and pharmacologically unique and manufactured and sold by different companies); In re: FEMA Trailer Formaldehyde Prod. Liab. Litig., 528 F.Supp.2d 1350 (J.P.M.L. 2007) (centralizing actions involving trailers built and sold by several different manufacturers); In re: Human Tissue Prod. Liab. Litig., 435 F.Supp.2d 1352 (J.P.M.L. 2006) (actions against multiple defendants involving different tissue implants centralized); In re: Ephedra Prod. Liab. Litig., MDL No. 1598 (J.P.M.L. 2004) (ordering transfer of several actions against numerous defendants involving many different products containing a common ingredient); In re: Phenylpropanolamine (PPA) Prod. Liab. Litig., 173 F.Supp.2d 1377 (J.P.M.L. 2001) (transferring several actions in spite of noted "differences among the actions in terms of named defendants, specific products involved, legal theories of recovery, status as class actions, and/or types of injury alleged…."); In re: Multi-Piece Rim Prod. Liab. Litig., 464 F.Supp. 969 (J.P.M.L. 1979) (MDL treatment of actions involving different truck wheels sold by four different manufacturers and including claims against 21 other named defendants).[7] Transfer of the related cases at issue in this motion

[7] There are numerous other examples of MDL's granted in multi-product, multi-defendant cases, including those involving Darvocet, Darvon and Propoxyphene (MDL No. 2226); Chinese

involving Cook's women's pelvic repair products for coordination with similar litigation involving related products sold by other companies would likewise be in the interests of convenience for all parties, and would achieve the justice and efficiency that are the hallmarks of Section 1407. If these actions are transferred to a single judge then this Panel and that judge have the inherent authority to determine the appropriate scope and operation of the coordinated proceedings, which could best be determined if these matters are in the hands of one judge.

Another factor favoring the transfer of these cases to the Southern District of West Virginia for consolidation or coordination is that the Plaintiffs in each of the constituent cases identified in the attached Schedule of Actions (those represented by the undersigned) – represented by lawyers from different law firms from different parts of the country – support such transfer. While not controlling, the Panel has taken into consideration the parties' preferences when selecting a transferee court. See, e.g., In re Sierra Wireless, Inc., Securities Litigation, 387 F.Supp.2d 1363 (J.P.M.L. 2005) (support of responding parties weighed in favor of transferee district); In re Rubber Chemicals Antitrust Litigation, 350 F.Supp.2d 1366, 1367 (J.P.M.L. 2004) (district that was choice of all responding parties was proper transferee forum); In re PrimeVision Health, Inc. Contract Litigation, 206 F.Supp.2d 1369, 1370 (J.P.M.L. 2002) (choosing district in which all responding parties favored consolidation). Such broad-based support among the diverse Plaintiffs in this motion – and the diverse law firms that represent them – further supports the conclusion that the Southern District of West Virginia is the proper transferee district.

In sum, the Southern District of West Virginia provides a convenient and appropriate location to receive the transfer of these cases for consolidated and/or coordinated handling, in

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drywall (MDL No. 2047); latex gloves (MDL No. 1148); orthopedic bone screws (MDL No. 1014); and silicone gel breast implants (MDL No. 926).

accordance with Chief Judge Joseph R. Goodwin's handling of the other five mesh MDLs currently pending in his Court, which involve similar claims relating to similar products. Transfer of these Cook women's pelvic repair product cases to the Southern District of West Virginia, would allow a single Judge familiar with the factual and legal issues presented to coordinate this related litigation in one forum, and would avoid the numerous problems inherent in the splitting of single-plaintiff, multiple product cases.

CONCLUSION

For the foregoing reasons, Plaintiffs move for transfer pursuant to 28 U.S.C. § 1407 to the Hon. Joseph R. Goodwin, Chief Judge of the Southern District of West Virginia, and respectfully request that this motion be granted.

This 18th day of February, 2013.

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Sarah Ruth Dunnington, et. al. v. Cook, Inc., et. al., (M.D. of TN, 3:13-cv-00014);
Alice J. Johnson v. Cook, Inc., et. al., (M.D. of TN, 3:12-cv-01153);
Sheila Mansfield v. Cook, Inc., et. al., (M.D. of TN, 3:12-cv-01252);
Brenda L. Smith, et. al. v. Cook, Inc., et. al., (E.D. of KY, 5:12-cv-00229)

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Deborah Nolin v. Cook Group, Inc. (M.D. of Alabama, civil action number pending)

U.S. Food and Drug Administration

Medical Devices

FDA Safety Communication: UPDATE on Serious Complications Associated with Transvaginal Placement of Surgical Mesh for Pelvic Organ Prolapse

Date Issued: July 13, 2011

Audience:

- Health care providers who implant surgical mesh to repair pelvic organ prolapse and/or stress urinary incontinence
- Health care providers involved in the care of patients with surgical mesh implanted to repair pelvic organ prolapse and/or stress urinary incontinence
- Patients who are considering or have received a surgical mesh implant to repair pelvic organ prolapse and/or stress urinary incontinence

Medical Specialties: gynecology, urogynecology, urology, general surgery, internal medicine, family practice, emergency medicine

Device:
Surgical mesh is a medical device that is generally used to repair weakened or damaged tissue. It is made from porous absorbable or non-absorbable synthetic material or absorbable biologic material. In urogynecologic procedures, surgical mesh i permanently implanted to reinforce the weakened vaginal wall to repair pelvic organ prolapse or to support the urethra to treat urinary incontinence.

Background:
Pelvic Organ Prolapse
Pelvic organ prolapse (POP) occurs when the tissues that hold the pelvic organs in place become weak or stretched. Thirty to fifty percent of women may experience POP in their lifetime with 2 percent developing symptoms. When POP happens, the organs bulge (prolapse) into the vagina and sometimes prolapse past the vaginal opening. More than one pelvic organ can prolapse at the same time. Organs that can be involve in POP include the bladder, the uterus, the rectum, the top of the vagina (vaginal apex after a hysterectomy, and the bowel.

Stress Urinary Incontinence
Stress urinary incontinence (SUI) is a leakage of urine during moments of physical activity, such as coughing, sneezing, laughing, or exercise.

Purpose:
On Oct. 20, 2008, the FDA issued a Public Health Notification and Additional Patient Information on serious complications associated with surgical mesh placed through the vagina (transvaginal placement) to treat POP and SUI.

Based on an updated analysis of adverse events reported to the FDA and complications described in the scientific literature, the FDA identified surgical mesh for transvaginal repair of POP as an area of continuing serious concern.

The FDA is issuing this update to inform you that serious complications associated with surgical mesh for transvaginal repair of POP are **not rare**. This is a change from what the FDA previously reported on Oct. 20, 2008. Furthermore, it is not clear that transvaginal POP repair with mesh is more effective than traditional non-mesh repair ir all patients with POP and it may expose patients to greater risk. This Safety Communication provides updated recommendations for health care providers and patients and updates the FDA's activities involving surgical mesh for the transvaginal repair of POP.

exhibit 1

The FDA continues to evaluate the effects of using surgical mesh to repair SUI and will communicate these findings at a later date.

For detailed information, please see: Urogynecologic Surgical Mesh: Update on the Safety and Effectiveness of Transvaginal Placement for Pelvic Organ Prolapse.[1]

Summary of Problem and Scope:
In the Oct. 20, 2008 FDA Public Health Notification, the number of adverse events reported to the FDA for surgical mesh devices used to repair POP and SUI for the previous 3-year period (2005 – 2007) was "over 1,000." Since then, from Jan. 01, 2008 through Dec. 31, 2010, the FDA received 2,874 additional reports of complications associated with surgical mesh devices used to repair POP and SUI, with 1,503 reports associated with POP repairs and 1,371 associated with SUI repairs. Although it is common for adverse event reporting to increase following an FDA safety communication, we are concerned that the number of adverse event reports remains high.

From 2008 – 2010, the most frequent complications reported to the FDA for surgical mesh devices for POP repair include mesh erosion through the vagina (also called exposure, extrusion or protrusion), pain, infection, bleeding, pain during sexual intercourse (dyspareunia), organ perforation, and urinary problems. There were also reports of recurrent prolapse, neuro-muscular problems, vaginal scarring/shrinkage, and emotional problems. Many of these complications require additional intervention, including medical or surgical treatment and hospitalization.

In order to better understand the use of surgical mesh for POP and SUI, the FDA conducted a systematic review of the published scientific literature from 1996 – 2011 to evaluate its safety and effectiveness. The review showed that transvaginal POP repair with mesh does not improve symptomatic results or quality of life over traditional non-mesh repair. The FDA continues to evaluate the literature for SUI surgeries using surgical mesh and will report about that usage at a later date.

In particular, the literature review revealed that:

- Mesh used in transvaginal POP repair introduces risks not present in traditional nor -mesh surgery for POP repair.
- Mesh placed abdominally for POP repair appears to result in lower rates of mesh complications compared to transvaginal POP surgery with mesh.
- There is no evidence that transvaginal repair to support the top of the vagina (apical repair) or the back wall of the vagina (posterior repair) with mesh provides any added benefit compared to traditional surgery without mesh.
- While transvaginal surgical repair to correct weakened tissue between the bladder and vagina (anterior repair) with mesh augmentation may provide an anatomic benefit compared to traditional POP repair without mesh, this anatomic benefit may not result in better symptomatic results.

The FDA's literature review found that *erosion* of mesh through the vagina is the *most common and consistently reported mesh-related complication* from transvaginal POP surgeries using mesh. Mesh erosion can require multiple surgeries to repair and can be debilitating for some women. In some cases, even multiple surgeries will not resolve the complication.

Mesh contraction (shrinkage) is a *previously unidentified risk* of transvaginal POP repair with mesh that has been reported in the published scientific literature and in adverse event reports to the FDA since the Oct. 20, 2008 *FDA Public Health Notification*. Reports in the literature associate mesh contraction with vaginal shortening, vaginal tightening and vaginal pain.

Both mesh erosion and mesh contraction may lead to severe pelvic pain, painful sexual intercourse or an inability to engage in sexual intercourse. Also, men may experience irritation and pain to the penis during sexual intercourse when the mesh is exposed in mesh erosion.

The complications associated with the use of surgical mesh for POP repair have not been linked to a single brand of mesh.

Recommendations for Health Care Providers:

As stated in the Oct. 20, 2008 Public Health Notification, the FDA continues to recommend that health care providers should:

- Obtain specialized training for each mesh placement technique, and be aware of the risks of surgical mesh.
- Be vigilant for potential adverse events from the mesh, especially erosion and infection.
- Watch for complications associated with the tools used in transvaginal placement, especially bowel, bladder and blood vessel perforations.
- Inform patients that implantation of surgical mesh is permanent, and that some complications associated with the implanted mesh may require additional surgery that may or may not correct the complication.
- Inform patients about the potential for serious complications and their effect on quality of life, including pain during sexual intercourse, scarring, and narrowing of the vaginal wall in POP repair using surgical mesh.
- Provide patients with a copy of the patient labeling from the surgical mesh manufacturer if available.

In addition, the FDA also recommends that health care providers:

- Recognize that in most cases, POP can be treated successfully without mesh thus avoiding the risk of mesh-related complications.
- Choose mesh surgery only after weighing the risks and benefits of surgery with mesh versus all surgical and non-surgical alternatives.
- Consider these factors before placing surgical mesh:
  - Surgical mesh is a permanent implant that may make future surgical repair more challenging.
  - A mesh procedure may put the patient at risk for requiring additional surgery or for the development of new complications.
  - Removal of mesh due to mesh complications may involve multiple surgeries and significantly impair the patient's quality of life. Complete removal of mesh may not be possible and may not result in complete resolution of complications, including pain.
  - Mesh placed abdominally for POP repair may result in lower rates of mesh complications compared to transvaginal POP surgery with mesh.
- Inform the patient about the benefits and risks of non-surgical options, non-mesh surgery, surgical mesh placed abdominally and the likely success of these alternatives compared to transvaginal surgery with mesh.
- Notify the patient if mesh will be used in her POP surgery and provide the patient with information about the specific product used.
- Ensure that the patient understands the postoperative risks and complications of mesh surgery as well as limited long-term outcomes data.

Recommendations for Patients:
Before Surgery

Be aware of the risks associated with surgical mesh for transvaginal repair of POP. Know that having a mesh surgery may put you at risk for needing additional surgery due to mesh-related complications. In a small number of patients, repeat surgery may not resolve complications.

Ask your surgeon about all POP treatment options, including surgical repair with or without mesh and non-surgical options, and understand why your surgeon may be recommending treatment of POP with mesh.

In addition, ask your surgeon these questions before you agree to have surgery in which surgical mesh will be used:

- Are you planning to use mesh in my surgery?

- Why do you think I am a good candidate for surgical mesh?
- Why is surgical mesh being chosen for my repair?
- What are the alternatives to transvaginal surgical mesh repair for POP, including non-surgical options?
- What are the pros and cons of using surgical mesh in my particular case? How likely is it that my repair could be successfully performed without using surgical mesh?
- Will my partner be able to feel the surgical mesh during sexual intercourse? What i the surgical mesh erodes through my vaginal wall?
- If surgical mesh is to be used, how often have you implanted this particular product? What results have your other patients had with this product?
- What can I expect to feel after surgery and for how long?
- Which specific side effects should I report to you after the surgery?
- What if the mesh surgery doesn't correct my problem?
- If I develop a complication, will you treat it or will I be referred to a specialist experienced with surgical mesh complications?
- If I have a complication related to the surgical mesh, how likely is it that the surgical mesh could be removed and what could be the consequences?
- If a surgical mesh is to be used, is there patient information that comes with the product, and can I have a copy?

After Surgery

- Continue with your annual and other routine check-ups and follow-up care. There is no need to take additional action if you are satisfied with your surgery and are not having complications or symptoms.
- Notify your health care provider if you have complications or symptoms, including persistent vaginal bleeding or discharge, pelvic or groin pain or pain with sex, that last after your follow-up appointment.
- Let your health care provider know you have surgical mesh, especially if you plan to have another surgery or other medical procedures.
- Talk to your health care provider about any questions you may have.

If you had POP surgery, but do not know whether your surgeon used mesh, ask your health care provider at your next scheduled visit.

FDA Activities:
The FDA is working in several areas to assess and improve the safety and effectiveness of urogynecologic mesh products. The FDA will:

- Convene the Obstetrics-Gynecology Devices Panel of the Medical Device Advisory Committee, on September 8-9, 2011.The panel will discuss and make recommendations regarding the safety and effectiveness of transvaginal surgical mesh for POP and SUI.
- Explore regulatory solutions to answer questions about the safety and effectiveness of urogynecologic mesh products that are now being marketed and those that will be reviewed for marketing in the future.
- Continue to monitor adverse events reported to FDA associated with surgical mesh used to repair POP and SUI, as well as assessing any and all data as it becomes available.

Reporting Problems to the FDA:
Prompt reporting of adverse events can help the FDA identify and better understand the risks associated with medical devices. If you suspect a problem with surgical mesh, we encourage you to file a voluntary report through MedWatch, the FDA Safety Information and Adverse Event Reporting program[2]. Health care personnel employed by facilities that are subject to the FDA's user facility reporting requirements[3] should follow the reporting procedures established by their facilities. Device manufacturers must comply with the Medical Device Reporting (MDR) regulations[4].

To help us learn as much as possible about the adverse events associated with surgical mesh to repair POP and SUI, please include the following information in your reports, if available:

- Manufacturer's name
- Product name (brand name)
- Catalog number
- Lot number
- Size
- Date of implant
- Date of explant (if mesh was removed)
- Details of the adverse event and medical and/or surgical interventions (if required)
- Type of procedure (e.g., anterior or posterior repair, sacral colpopexy, sling procedure for SUI)
- Surgical approach: (e.g., vaginal, abdominal, laparoscopic)
- Reason for mesh implantation: (e.g., POP of the uterus, bladder, rectum, vaginal apex or bowel, SUI)
- Specific postoperative symptoms experienced by the patient with time of onset and follow-up treatment

Contact Information:
If you have questions about this communication, please contact the Division of Small Manufacturers, International and Consumer Assistance (DSMICA) at DSMICA@FDA.HHS.GOV, 800-638-2041 or 301-796-7100.

This document reflects the FDA's current analysis of available information, in keeping with our commitment to inform the public about ongoing safety reviews of medical devices.

Additional Information

- Urogynecologic Surgical Mesh Implants[5]
- Urogynecologic Surgical Mesh: Update on the Safety and Effectiveness of Transvaginal Placement for Pelvic Organ Prolapse (July 2011) (PDF - 243KB)[6]
- Press Release: Surgical placement of mesh to repair pelvic organ prolapse poses risks[7]
- Federal Register Notice: Urogynecologic Surgical Mesh[8]

Links on this page:

1. /downloads/MedicalDevices/Safety/AlertsandNotices/UCM262760.pdf
2. http://www.fda.gov/Safety/MedWatch/HowToReport/default.htm
3. /MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/ReportingAdverseEvents/ucm2005737.htm
4. /MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/ReportingAdverseEvents/ucm2005737.htm
5. /MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/UroGynSurgicalMesh/default.htm
6. /downloads/MedicalDevices/Safety/AlertsandNotices/UCM262760.pdf
7. /NewsEvents/Newsroom/PressAnnouncements/ucm262752.htm

8. http://www.ofr.gov/OFRUpload/OFRData/2011-17695_PI.pdf

Urogynecologic Surgical Mesh:

Update on the Safety and Effectiveness of Transvaginal Placement for Pelvic Organ Prolapse

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July 2011

Exhibit "2"

I. EXECUTIVE SUMMARY

In October 2008, the FDA issued a Public Health Notification (PHN) to inform clinicians and patients of adverse events related to urogynecologic use of surgical mesh, and to provide recommendations on how to mitigate risks and how to counsel patients. Following the *PHN*, the FDA continued to monitor the outcomes of urogynecologic use of surgical mesh. A search of the FDA's Manufacturer and User Device Experience (MAUDE) database from the last 3 years (January 1, 2008 - December 31, 2010), identified 2,874 Medical Device Reports (MDRs) for urogynecologic surgical meshes, including reports of injury, death, and malfunctions. Among the 2,874 reports, 1,503 were associated with pelvic organ prolapse (POP) repairs, and 1,371 were associated with stress urinary incontinence (SUI) repairs.

The FDA also conducted a systematic review of the scientific literature to learn more about the safety and effectiveness of POP and SUI using surgical mesh. The FDA determined that (1) serious adverse events are NOT rare, contrary to what was stated in the 2008 *PHN*, and (2) transvaginally placed mesh in POP repair does NOT conclusively improve clinical outcomes over traditional non-mesh repair.

The FDA is providing this update to advise the public and the medical community of complications related to transvaginal POP repair with mesh. The FDA plans to convene an advisory panel meeting of outside experts in September 2011 to discuss these findings and the types of clinical studies necessary to better assess the risks and benefits of using mesh to treat POP and SUI. In addition FDA is considering regulatory changes that may improve our understanding of the safety and effectiveness of this device.

The FDA continues to evaluate the effects of using surgical mesh for the treatment of SUI and will report about that usage at a later date.

II. OVERVIEW

Surgical mesh is a metallic or polymeric screen intended to be implanted to reinforce soft tissue or bone where weakness exists [1].

Surgical mesh has been used since the 1950s to repair abdominal hernias. In the 1970s, gynecologists began using surgical mesh products indicated for hernia repair for abdominal repair of pelvic organ prolapse (POP), and in the 1990s, gynecologists began using surgical mesh for surgical treatment of stress urinary incontinence (SUI) and transvaginal repair of pelvic organ prolapse (POP). To do so, surgeons cut the mesh to the desired shape and placed it through a corresponding incision. Over time, in response to a perceived demand in the surgical community, manufacturers developed mesh products specifically designed for SUI and POP. In 1996, the FDA cleared the first surgical mesh product specifically for use in SUI, and in 2002, the FDA cleared the first surgical mesh product specifically for use in POP. Over the next few years, surgical mesh products for transvaginal POP repair became incorporated into "kits" that included tools to aid in the delivery and insertion of the mesh. Surgical mesh kits continue to evolve, adding new insertion tools, tissue fixation anchors, surgical techniques, and absorbable and biologic materials.

Surgical mesh products are currently regulated as Class II devices and are reviewed under the 510(k) Premarket Notification Program. The FDA's premarket review of these devices has primarily focused on data supporting the adequacy of mechanical performance and material safety. Bench and/or animal testing have been used to confirm that engineering specifications are met and that the mesh material is biocompatible. Clinical performance data typically has not been used to support clearance for POP or SUI urogynecologic mesh products.

Surgical mesh materials can be divided into four general categories:

- non-absorbable synthetic (e.g., polypropylene or polyester)
- absorbable synthetic (e.g., poly(lactic-co-glycolic acid) or poly(caprolactone))
- biologic (e.g., acellular collagen derived from bovine or porcine sources)
- composite (i.e., a combination of any of the previous three categories)

Most surgical mesh devices cleared for urogynecologic procedures are composed of non-absorbable synthetic polypropylene.

Surgical Mesh for Urogynecologic Procedures

Surgical mesh can be used for surgical repair of SUI and POP. SUI affects an estimated 20-40 percent of women [2]. Treatment may be conservative (such as exercise to strengthen the pelvic floor muscles) or surgical. Surgical repair of SUI can be performed through an abdominal incision, using sutures (Burch urethropexy), or through a vaginal incision, by placing a biologic or synthetic "sling" (e.g., surgical mesh) under the urethra to help prevent urinary loss during physical activity.

Following promising continence outcomes using surgical mesh slings for SUI repair, surgeons began using surgical mesh to augment transvaginal POP repairs. POP occurs when the pelvic floor tissues that hold the pelvic organs in place become weakened or stretched, often from childbirth (see **Figure 1** for normal anatomy). This causes the pelvic organs to bulge (or

Figure 1.

prolapse) into the vagina. The pelvic organs sometimes prolapse past the vaginal opening, and more than one pelvic organ can prolapse at the same time. The organs involved in POP may include the bladder (cystocele) (**Figure 2**), the uterus (procidentia) (**Figure 3**), the rectum (rectocele) (**Figure 4**), the top of the vagina (apical prolapse) or the bowel (enterocele).

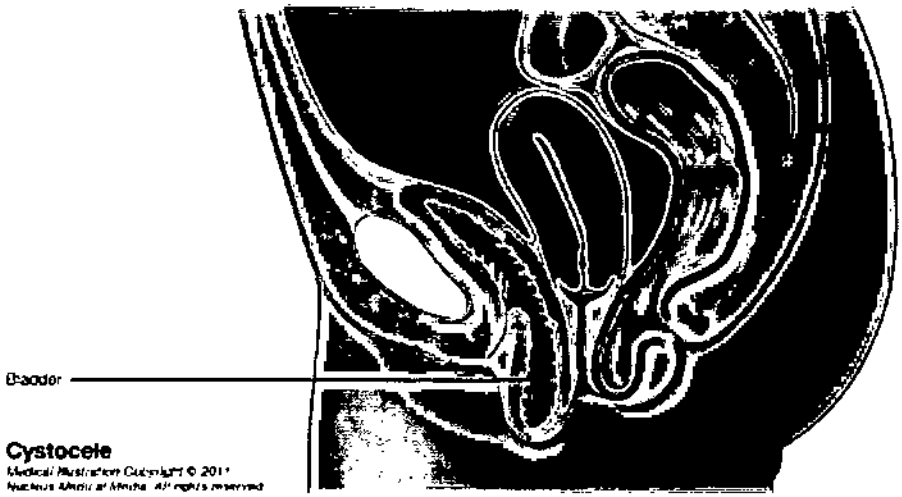

Figure 2.

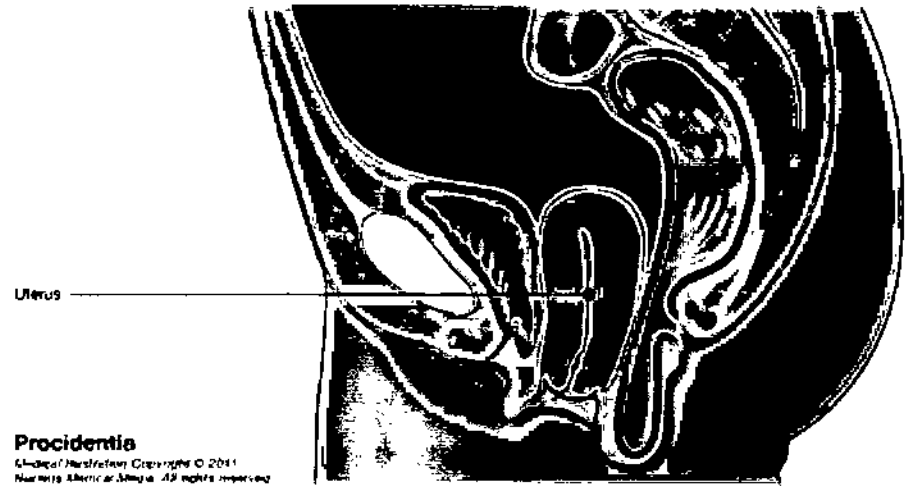

Figure 3.

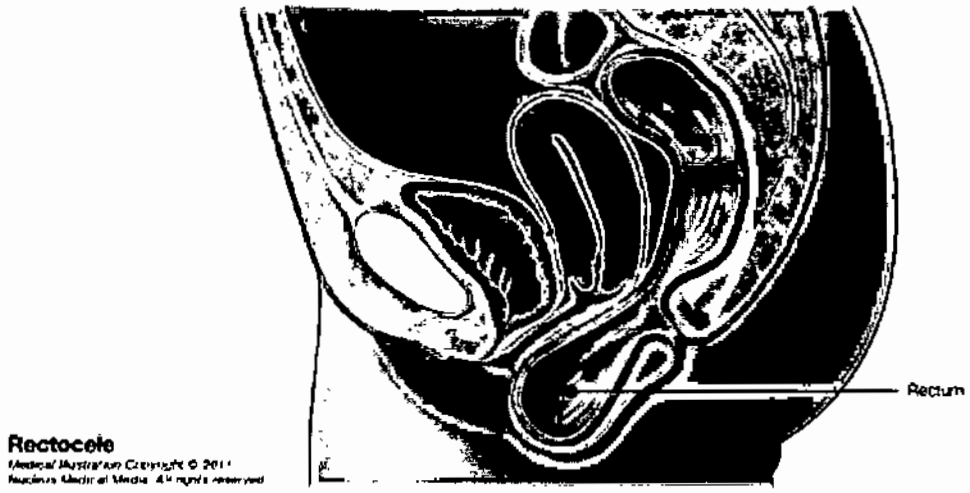

Figure 4.

Some women do not have symptoms from POP, but for others, POP may negatively impact the quality of life by causing pelvic discomfort and interfering with sexual, urinary and defecatory function, as well as other daily activities.

A woman's estimated lifetime risk of POP is 30-50 percent, with 2 percent of women becoming symptomatic [3]. Symptomatic POP can be managed conservatively with either pelvic floor muscle exercises or vaginal inserts to support the prolapsing tissue (pessaries). Surgical correction is also an option, although not all women will have long-term improvement in symptoms from traditional surgical correction without mesh [4]. In total, women have an estimated 11 percent lifetime incidence of surgery to repair POP or SUI [4].

The placement of surgical mesh is intended to increase the longevity of POP repairs. In general, mesh products for POP repair are configured to match the anatomical defect they are designed to correct. Mesh can be placed in the anterior vaginal wall to aid in the correction of cystocele (anterior repair), in the posterior vaginal wall to aid in correction of rectocele (posterior repair), or attached to the top of the vagina to correct uterine prolapse or vaginal apical prolapse (apical repair). Surgical mesh can also be placed through the abdomen (transabdominally) to correct apical prolapse. This latter procedure is known as sacral colpopexy and was described using prosthetic slings in 1974. High success rates were reported in the 1980s [30], and sacral colpopexy has become accepted in the gynecologic community as an effective surgical means to correct POP.

Market data from manufacturers indicate that in 2010 approximately 300,000 women underwent surgical procedures in the United States to repair POP and approximately 260,000 underwent surgical procedures to repair SUI. According to industry estimates, approximately one out of three POP surgeries used mesh, and three out of four of the mesh POP procedures were done transvaginally. For SUI surgeries, over 80 percent were done transvaginally with mesh.

III. SUMMARY OF ADVERSE EVENT REPORTS

The FDA conducted a search of the Manufacturer and User Device Experience (MAUDE) database for medical device reports (MDRs) of adverse events associated with all urogynecologic surgical mesh products received from January 1, 2005 - December 31, 2010. The search identified 3,979 reports of injury, death, and malfunction. Among the 3,979 reports, 2,874 reports were received in the last 3 years (January 1, 2008 - December 31, 2010), and included 1,503 reports associated with POP repairs and 1,371 associated with SUI repairs. The number of MDRs associated with POP repairs increased by more than 5-fold compared to the number of reports received in the previous 3 years (January 1, 2005 - December 31, 2007).

Multiple factors can affect MDR reporting, including increased use of urogynecologic surgical mesh in the clinical community, increased awareness on the potential adverse events associated with mesh after the 2008 *PHN*, an increased number of new POP meshes on the market, or an increase in the number of actual adverse events associated with mesh. Determining the exact cause or causes of the increase is difficult. Regardless, the FDA believes the overall increase in the number of serious adverse event reports is cause for concern.

From 2008 to 2010, the most frequent complications reported to the FDA from the use of surgical mesh devices for POP repair included vaginal mesh erosion (also called exposure, extrusion or protrusion), pain (including painful sexual intercourse known as dyspareunia), infection, urinary problems, bleeding, and organ perforation. There were also reports of recurrent prolapse, neuro-muscular problems, vaginal scarring/shrinkage and emotional problems. Many of the MDRs cited the need for additional intervention, including medical or surgical treatment and hospitalization. Vaginal shrinkage was not reported in the previous three year period corresponding to the 2008 *PHN*.

Between 2008 and 2010, there were seven reported deaths associated with POP repairs. Follow-up investigation on the death reports revealed that three of the deaths associated with POP repair were related to the mesh placement procedure (two bowel perforations, one hemorrhage). Four deaths were due to post-operative medical complications not directly related to the mesh placement procedure.

IV. REVIEW OF THE LITERATURE

Due to ongoing concerns in the clinical community and the safety signals identified from adverse event reports, the FDA evaluated the peer-reviewed scientific literature to revisit the fundamental questions of safety and effectiveness of surgical mesh for POP and SUI. The literature presented in this document includes all relevant randomized controlled trials (RCTs), all relevant systematic reviews, and a subset of observational studies that presented data on adverse events associated with transvaginal repair of POP using mesh from January 1996 through April 2011. The FDA continues to evaluate the literature for SUI surgeries using surgical mesh and will report on that usage at a later date.

Safety

The literature review identified the following safety concerns with transvaginally placed surgical mesh for POP repair:

- Patients who undergo POP repair with mesh are subject to mesh-related complications that are not experienced by patients who undergo traditional surgery without mesh [7-9, 15, 16, 19-24].
- Adverse events associated with transvaginally placed mesh can be life-altering for some women [13, 14, 17]. Sequelae (e.g., pain) may continue despite mesh removal.
- Mesh-associated complications are not rare. The most common mesh-related complication experienced by patients undergoing transvaginal POP repair with mesh is vaginal mesh erosion [7-9, 15, 16, 19-24]. Based on data from 110 studies including 11,785 women, approximately 10 percent of women undergoing transvaginal POP repair with mesh experienced mesh erosion within 12 months of surgery [23].
- 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 [23].
- Mesh contraction, causing vaginal shortening, tightening, and/or vaginal pain in association with transvaginal POP repair with mesh, is increasingly reported in the literature [13, 17].
- New onset SUI has been reported to occur more frequently following mesh augmented anterior repair compared to traditional anterior repair without mesh [12].
- Transvaginal surgery with mesh to correct vaginal apical prolapse is associated with a higher rate of complication requiring reoperation and reoperation for any reason compared to traditional vaginal surgery or sacral colpopexy [20].
- Abdominal POP surgery using mesh (sacral colpopexy) appears to result in lower rates of mesh complications compared to transvaginal POP surgery with mesh, with the median vaginal mesh erosion rate reported at 4 percent within 23 months of surgery [22].

Effectiveness

The literature review found that while transvaginal POP repair with mesh often restores anatomy, it has not been shown to improve clinical benefit over traditional non-mesh repair, as evidenced by the following key findings:

- Transvaginal apical or posterior repair with mesh does not appear to provide any added benefit compared to traditional surgery without mesh [5-8, 18, 22, 24].
- Only two RCTs compared multi-compartment repair (including apical repair) with mesh to traditional repair, and neither found a significant improvement in effectiveness with

mesh augmentation [7, 8]. A systematic review of vaginal mesh kits for apical repair found they appear effective in restoring apical prolapse in the short-term, but long-term outcomes are unknown [21].

- Although one RCT showed anatomic benefit for posterior repair with mesh, mesh subjects in the trial had less posterior prolapse at baseline than subjects who underwent traditional repair [8]. Three other RCTs that have evaluated mesh augmentation in the posterior compartment did not show an anatomic benefit from using mesh [5, 6, 7].
- There does appear to be an anatomic benefit to anterior repair with mesh augmentation [5, 8, 9-12, 18, 19, 22, 24]. This anatomic benefit may not result in superior symptomatic outcomes or lower rates of repeat surgery for recurrent prolapse compared to traditional POP repair without mesh [26].
- Patients who undergo traditional POP repair without mesh have equivalent improvement in quality of life when compared to patients who undergo transvaginal POP repair with mesh [5, 8, 9, 11].
- Compared to traditional vaginal surgery without mesh, abdominal apical prolapse repair with mesh (sacral colpopexy) results in less recurrent prolapse, although it has not been shown to reduce the rate of repeat surgery for recurrent prolapse [22].

Limitations of Existing Literature

The existing literature has several important methodologic limitations that impact the interpretation of the available data, including:

- The majority of studies use an effectiveness outcome that pertains to ideal pelvic support, which is not necessary for most women to achieve symptomatic relief [26];
- Results reflect both primary and repeat prolapse repairs;
- In most studies subjects undergo various additional POP procedures and/or combined POP-SUI procedures;
- Adverse events are inconsistently defined and reported;
- Many studies are poorly designed and/or conducted, are underpowered, use incompletely documented inclusion/exclusion criteria, have inadequate evaluator masking, and fail to account for variable lengths of patient follow-up; and
- Very few studies extend past 2 years.

V. SUMMARY OF KEY FINDINGS

Based on evaluation of adverse event reports and assessment of the scientific literature, the FDA has NOT seen conclusive evidence that using transvaginally placed mesh in POP repair improves

clinical outcomes any more than traditional POP repair that does not use mesh, and it may expose patients to greater risk.

In particular, these products are associated with serious adverse events, including vaginal mesh erosion (also called exposure, extrusion or protrusion), a complication which can require multiple surgeries to repair and may result in continued sequelae (e.g., pain) even after mesh removal. Compounding the concerns regarding adverse events are performance data that fail to demonstrate improved clinical benefit over traditional non-mesh repair, particularly for transvaginal apical and posterior repair. While the literature suggests an anatomic benefit to anterior repair with mesh augmentation, this anatomic benefit may not result in superior clinical outcomes, and the associated risk of adverse events should be considered.

Based on these findings, the FDA is considering regulatory changes that may improve our understanding of the safety and effectiveness of these devices and has specific recommendations for patients and healthcare providers below.

VI. RECOMMENDATIONS FOR PATIENTS

The FDA recommends that women considering surgery for pelvic organ prolapse:

Before surgery:

- Be aware of the risks associated with transvaginal POP repair.
- Know that having a mesh surgery may increase the risk for needing additional surgery due to mesh-related complications. In a small number of patients, repeat surgery may not resolve complications.
- Ask their surgeons about all POP treatment options, including surgical repair with or without mesh and non-surgical options, and understand why their surgeons may be recommending treatment of POP with mesh.

After surgery:

- Continue with annual and other routine check-ups and follow-up care. Patients do not need to take action if they are satisfied with their surgery and are not having complications or symptoms.
- Notify their health care providers if they develop complications or symptoms, including persistent vaginal bleeding or discharge, pelvic or groin pain or pain with sex, that last after the last follow-up appointment.
- Let their health care providers know if they have surgical mesh, especially if planning to have another related surgery or other medical procedures.
- Talk to their health care providers about any questions or concerns.
- Ask their surgeons at their next routine check-up if they received mesh for their POP surgery if they do not know if mesh was used.

VII. RECOMMENDATIONS FOR HEALTH CARE PROVIDERS

The FDA encourages health care providers to:

- Recognize that in most cases, POP can be treated successfully without mesh thus avoiding the risk of mesh-related complications.
- Choose mesh surgery only after weighing the risks and benefits of surgery with mesh versus all surgical and non-surgical alternatives.
- Consider these factors before placing surgical mesh:
    - Surgical mesh is a permanent implant that may make future surgical repair more challenging.
    - A mesh procedure may put the patient at risk for requiring additional surgery or for the development of new complications.
    - Removal of mesh due to mesh complications may involve multiple surgeries and significantly impair the patient's quality of life. Complete removal of mesh may not be possible and may not result in complete resolution of complications, including pain.
    - Mesh placed abdominally for POP repair may result in lower rates of mesh complications compared to transvaginal POP surgery with mesh.
- Inform the patient about the benefits and risks of non-surgical options, non-mesh surgery, surgical mesh placed abdominally and the likely success of these alternatives compared to transvaginal surgery with mesh.
- Notify the patient if mesh will be used in her POP surgery and provide the patient with information about the specific product used.
- Ensure that the patient understands the postoperative risks and complications of mesh surgery as well as limited long-term outcomes data.
- Continue to follow the recommendations provided in the 2008 *PHN*.

VIII. FDA ACTIVITIES

Safety Communication

The FDA is issuing a new FDA *Safety Communication* that provides an update to the 2008 FDA *PHN*. The *Safety Communication* focuses on transvaginal POP repair with mesh. The objective of the *Safety Communication* is to inform health care providers and patients that the risks of serious complications associated with transvaginal POP repair with mesh are NOT rare, contrary to what was stated in the 2008 *PHN*. This updated communication identifies vaginal shortening, tightening, and/or pain due to mesh contraction as a previously unidentified risk of transvaginal POP repair with mesh, and it provides recommendations for patients and health care providers.

Consideration of Regulatory Changes

The FDA is considering regulatory changes that may improve our understanding of the safety and effectiveness of this device. Considerations include:

- A change in risk classification of mesh used for transvaginal POP repair from Class II to Class III, which would require manufacturers to submit premarket approval applications, including relevant clinical data for these devices.

- Clinical studies to address the risks and benefits of mesh used to treat POP and SUI.
- Expanded post-market monitoring of device performance.

Advisory Meeting

On September 8-9, 2011, the FDA will convene a meeting of the Obstetrics-Gynecology Devices Panel of the Medical Devices Advisory Committee to discuss the safety and effectiveness of transvaginal placement of mesh for POP and SUI procedures. A notice of this meeting was published in the Federal Register.

IX. HOW TO REPORT INFORMATION TO THE FDA

Prompt reporting of adverse events can help the FDA identify and better understand the risks associated with medical devices. The FDA encourages health care professionals and consumers to report suspected problems with surgical mesh to the FDA by filing a voluntary report through MedWatch, the FDA Safety Information and Adverse Event Reporting program. Health care personnel employed by facilities that are subject to the FDA's user facility reporting requirements should follow the reporting procedures established by their facilities. Device manufacturers must comply with the Medical Device Reporting (MDR) regulations.

X. CONCLUSION

The FDA has identified serious safety and effectiveness concerns over the use of surgical mesh for the transvaginal repair of pelvic organ prolapse (POP) based on a review of adverse events reported to the FDA and an assessment of the scientific literature.

In addition to providing an updated FDA *Safety Communication* to promote understanding of the risks associated with transvaginal POP repair using surgical mesh and to encourage informed decision-making by patients and health care providers about the use of mesh, the FDA will convene an Advisory Panel of outside experts to consider clinical studies that may improve our understanding of the safety and effectiveness of urogynecologic mesh.

XI. SOURCES

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XII. GLOSSARY OF TERMS USED IN THIS DOCUMENT

Anterior repair	surgical repair to correct weakened tissue between the bladder and vagina
Apical repair	surgical repair to correct prolapse of the top of the vagina
Colostomy	surgical procedure in which the healthy end of the large intestine or colon is brought through the anterior abdominal wall to provide an opening for feces to leave the body instead of the rectum
Colporrhaphy	surgical correction of the vagina
Cystocele	prolapse of the bladder into the vagina
Dyspareunia	painful sexual intercourse
Federal Register	the official daily publication for rules, proposed rules, and notices of federal agencies and organizations, as well as executive orders and other presidential documents.
Mesh erosion	mesh that wears through ("erodes") tissue and becomes exposed, also called exposure, extrusion or protrusion
Morbidity	diseased state, disability, or poor health
Pelvic organ prolapse (POP)	bulge of organs/structures surrounding the vagina into the vagina or extending beyond the vaginal opening, caused by laxity of supporting tissue of the vagina
Posterior repair	surgical repair to correct prolapse of the tissue between the vagina and rectum
Procidentia	prolapse of the uterus
Rectocele	prolapse of the rectum
Sacral Colpopexy	surgical correction of vaginal apical prolapse (via abdominal or laparoscopic route) in which mesh is attached to the vaginal apex on one end and the sacrum on the other
Stress Urinary Incontinence (SUI)	leakage of urine during moments of physical activity
Vaginal apex	top of the vagina

UNITED STATES OF AMERICA

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

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CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

MEDICAL DEVICES ADVISORY COMMITTEE

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OBSTETRICS AND GYNECOLOGY MEDICAL DEVICES PANEL

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September 8, 2011
8:00 a.m.

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presentation electronically, whether it's your slides or testimonials or anything, you can do so outside or to Shanika Craig, our Federal Officer, so that we can have access to those presentations.

So now we're going to move on. And the next part will be our industry presentations. And let us see. The first will be AdvaMed. So we have an on-time start and that means an on-time finish.

MR. SECUNDA: Good morning, distinguished members of the FDA Advisory Committee and FDA. I'm Jeff Secunda, Vice President of Regulatory Affairs at AdvaMed. AdvaMed is the world's largest medical technology association representing medical device manufacturers.

The majority of surgical mesh device manufacturers have joined together under AdvaMed to create the Transvaginal Mesh Working Group. This working group represents approximately 90 percent of the mesh sold to treat pelvic organ prolapse. Today, this working group will present their perspective on surgical mesh for pelvic organ prolapse.

The manufacturers of transvaginal mesh strongly believe that these devices are safe and effective for treating pelvic organ prolapse, and we are confident that they can continue to be appropriately regulated within Class II and the S10(k) clearance paradigm.

The current regulatory pathway has fostered the development and continued improvement of devices to treat this critical women's health issue. And in the hands of experienced surgeons, these devices are safe and

effective, with clearly established benefit/risk profiles based on clinical data.

We are aligned with most of FDA's recommendations to further clarify the benefit/risk profile for new mesh devices through clinical trials, longer-term postmarketing trials, a continued emphasis on training, and improved patient and physician labeling.

To ensure these are integrated into the regulation, we are further recommending that FDA define these requirements in a special controls document, as allowed by the 510(k) regulation.

I'd like now to outline our presentation. Dr. Suzette Sutherland, a urologist in private practice, who specializes in female urology and pelvic floor reconstruction; Dr. Piet Hinoul, Medical Director for Women's Health and Urology at Ethicon, will discuss the effectiveness and safety data and why we believe it shows a favorable benefit/risk profile for pelvic organ prolapse. Ginger Glaser, Senior Director of Global Quality and Regulatory Affairs at American Medical Systems, will outline device manufacturers' proposals and describe how fully utilizing the existing FDA pathway will allow FDA to enforce these proposals.

Given the limited time we have to speak today, we are not able to go into great detail on some issues. We look forward to answering any questions you may have to further clarify our perspective and proposals on transvaginal mesh.

I would now like to turn over the lectern to

Dr. Suzette Sutherland.

DR. SUTHERLAND: Good morning. I'm Suzette Sutherland. Thank you for the opportunity to speak today. My disclosure is that AdvaMed is sponsoring me to be here today. But let me be clear about the reason I'm really here. For the last seven years I've been performing pelvic organ prolapse procedures with mesh. For many women, a mesh procedure is their only chance for a durable repair.

I come here today because I'm concerned that we are mischaracterizing the real risks and benefits of these procedures, and so doing may be inadvertently scaring women away from a procedure that may provide them a real and lasting benefit.

Now, I have no doubt that there are women who have suffered from complications from these procedures, as many that we've heard here today. Just as women, however, have suffered from complications from the other surgical options that we have available today.

Correction of pelvic prolapse is a complex problem. But in the case of mesh repairs, serious complications are very rare and most cases easily manageable in the hands of an experienced surgeon. What's equally as important is that, what I see clinically and based on the data that's available to date, I believe transvaginal mesh procedures will provide a lasting benefit and impact on a woman's life.

As you can imagine from these pictures, pelvic organ prolapse

is a very distressing condition, and we've heard that from others here today as well. The woman's uterus, bladder, bowel can literally be protruding out of the vagina, causing a wide range of urinary, bowel, and sexual problems, not to mention the sensation of a large bulge or even pain.

From a surgical perspective, adequately treating symptomatic prolapse can be very complicated because not all bulges are alike. Prolapse can occur in a multitude of compartments, the anterior, posterior, apex, or any combination thereof.

In addition to the transvaginal mesh surgeries we have available, we currently have several different types of surgeries to treat prolapse, including simple transvaginal colporrhaphy with a concomitant apical repair, and what's been considered by some to be the gold standard, abdominal sacrocolpopexy, which, I'd like to make very clear, also uses synthetic mesh.

But all women are not appropriate candidates for all procedures. The reasons surgeons began reinforcing prolapse repairs with mesh in the first place is because some women simply don't have enough native tissue strong enough to stitch together to provide a lasting and durable repair. For these women, the additional support provided by the mesh may be their only hope for a durable repair.

One of the most important steps, however, in this surgical process is counseling the patient about her condition and her options, taking

into consideration what type of prolapse she has, the degree, the severity thereof, prior surgeries, especially when it comes to prolapse, concomitant pelvic symptoms such as pressure, bulge, any medical comorbidities, age, sexual activity, and so on. There are a lot of variables that go into making the decision of what type of procedure is appropriate for a given woman.

I unfortunately don't have the opportunity and the time allotted to go through how I weigh all of these considerations, but I'd be happy to answer any specific questions you may have later.

Like many surgeons, I've been turning increasingly to mesh surgeries over the years because of unacceptable rates of recurrence that have been seen with traditional surgeries and the high efficacy and durability appreciated thus far with mesh repairs. While this does not seem to be discussed much, the rates of reoperation for recurrence following traditional procedures are unacceptable.

Before transvaginal mesh kits became available, I, like many other surgeons, was cutting my own mesh in order to try to address this problem of recurrence.

The advance of transvaginal mesh kits made these procedures more consistent and allowed surgeons to be more effective in reaching parts of the deeper vagina that were previously a significant challenge. Adequate and safe access through the vagina, rather than abdominally, is less invasive and translates to advantages to the patient with respect to less postoperative

pain and shorter recovery times. The use of standardized tools has been a big advance.

But the issue of improved efficacy with mesh still seems to be in question, as it translates to a decrease in recurrence rates. Recent randomized controlled trials and case series on transvaginal mesh noted anatomical superiority with the use of mesh.

While mesh also demonstrated improvements in quality of life measures, these improvements were, however, equivocal to the non-mesh groups. This may be because most of these studies go out to only one year. Since prolapse is a progressive problem, this is not a sufficient amount of time for evaluation following prolapse procedures.

As a surgeon, I feel strongly that anatomical superiority clearly predicts better future outcomes with better sensitivity. This is not only through continued anatomical success, but through quality of life differences that may be appreciated as the number and degree of the anatomical failures in the non-mesh group increases over time.

Now, there's been a lot of focus on the potential complications of transvaginal mesh. As with any surgical procedure, there is a learning curve. And during my own learning curve, I noted some complications such as vaginal mesh exposures and obstructing symptoms from overly tensioned mesh. But I quickly learned to appreciate the differences in the surgical dissection technique necessary for successful vaginal mesh repair as opposed

to a non-mesh repair.

As with all surgery, there is a skill or an art to performing these vaginal mesh procedures, with the goal of providing support for the vagina while maintaining a functional vaginal space. Appreciating the surgical nuances between mesh and non-mesh repairs helps keeps these complications to a minimum.

In my own experience, mesh erosions into the bladder, urethra, or bowel are very rare, and mesh exposures that can't be easily managed are also very rare.

With respect to vaginal mesh exposures through the vaginal wall, most occur within the first year and are associated with poor initial wound healing along the incision lines. Treating this can often be done with simple transvaginal estrogen therapy to promote re-epithelialization over the graft or minor surgical excision of the exposed graft repair.

In the case of mesh erosion into neighboring organs, again, very rare. In experienced hands, these have been able to managed by minimally invasive means either through transvaginal or endoscopic excision, with resolution of associated symptoms.

In the case of dyspareunia or pelvic pain, severe cases are usually associated with the over-tensioning of the mesh in an attempt to provide maximal support. This can often be addressed through manual vaginal physical therapy or releasing incisions into the mesh to eliminate the

tension.

Again, it's vital for us as surgeons to discuss with women all of the risks of the surgical options. Traditional colporrhaphy, as you see on the left, is associated with a high recurrence and reoperation rate. And compared to the transvaginal techniques, abdominal sacrocolpopexy, displayed on the right, is associated with a higher risk of intraoperative bleeding, bowel, bladder, or ureteral injuries, postoperative small bowel obstruction, postoperative pain, and vaginal mesh exposures deep at the apex that is often much more difficult to excise and repair.

Now, I'm not trying to say that anterior colporrhaphy or sacrocolpopexy are not good procedures, but I'm just trying to put their risks into perspective with the transvaginal mesh risks. These complications of the abdominal sacrocolpopexy, as well as recurrences from the colporrhaphy procedures, have just as much impact on the patient, if not more, than those associated with transvaginal mesh.

In summary, transvaginal mesh kits have brought important new choices to women. For many women, it's the best option for a durable and lasting repair. Of course, each woman's situation is unique and it's up to her and her doctor to decide which type of treatment is really best for her.

While transvaginal mesh kits have helped the surgical community to standardize these procedures, the complexities of pelvic organ prolapse surgery still needs to be respected and should only be done by

experienced surgeons who understand the pelvic anatomy and surgical techniques necessary to successfully work with mesh in the vagina.

There has been great progress made in this area of women's health in a short amount of time. And while I'm not a regulatory expert, I do hope that we don't slow down the medical advances we have seen thus far by putting undue restrictions on these devices that have helped so many women.

We need to give women accurate information about the risks and benefits of every procedure so we ensure that they take advantage of the surgical option that may be in their best interests overall.

Thank you for your time.

DR. HINOUL: Thank you. Good morning. I'm Dr. Piet Hinoul, the Worldwide Medical Affairs Director for Women's Health and Urology of Ethicon. I came to Ethicon two years ago, and up until that time I was a practicing urogynecologic surgeon. I've performed of hundreds of transvaginal mesh procedures and traditional procedures to treat pelvic organ prolapse, and as a result, I have seen firsthand the clinical benefit this treatment option can provide women.

Today, I'm speaking on behalf of the Transvaginal Mesh Working Group through AdvaMed. In the next few minutes I would like to address the question that the FDA asked you to consider. I will highlight the data that demonstrate a favorable benefit/risk profile of transvaginal mesh

repair for prolapse, and I will also outline the clinical proposals that the working group is suggesting to continue to ensure the safety and effectiveness on both existing products and new products coming to the market.

Device manufacturers have been consistently improving these products and conducting studies on these devices since they first became available. The first five-year studies on transvaginal mesh kits are being reported upon and additional studies are underway. This is, of course, in addition to the rigorous bench and animal testing that occurred before surgeons ever used these meshes.

Today, to help you in your deliberations, we would like to provide context of how these devices are being used, our analysis of the data, as well as our proposals to further the progress that has already been made in this important field in female health.

As Dr. Sutherland has just explained, pelvic organ prolapse is a complex disease involving several anatomic compartments and different levels of disease, which can be addressed through different surgical options, each with their own potential merits and their own potential complications.

Patients and doctors need to consider all the factors we just mentioned, as well as the patient's medical history, the surgeon's training and experience, and available data on intervention, to make an informed decision on which surgical approach is best for that patient.

Transvaginal mesh, like all medical treatments, is not the optimal solution for everyone, but it will be for some.

Starting with the FDA's question on whether there is adequate assurance of effectiveness, current data demonstrate that transvaginal mesh is effective; first, because it demonstrates a statistically significant high anatomic cure rate than traditional surgeries; secondly, there is also significant improvement in quality of life measures that is comparable to traditional surgery.

The first measure of efficacy is anatomic cure, which is measured by the POP-Q score, and that is a measure that the National Institute of Health and multiple medical societies have determined is the most objective outcome measure. And we are aware of the ongoing scientific discussions regarding whether the current staging of pelvic organ prolapse actually correlates with the patient symptoms. Regardless of the outcome of the scientific discussions, anatomic assessment will remain a cornerstone in assessing prolapse.

Now, let's look at the literature addressing anatomic cure rates. Among the randomized controlled trials for pelvic organ prolapse, seven compared transvaginal polypropylene mesh to traditional vaginal surgery. These data clearly show that transvaginal mesh is efficacious in restoring pelvic floor anatomy. In fact, in five of the seven, the difference between the two were statistically significant. Even the two studies, by Dr. Iglesia and

Dr. Carey, that did not reach significance, trended in the same direction, showing higher efficacy for the mesh arm in their studies.

The second measure considered in the studies was quality of life, or often referred to as QoL. The quality of life improvements reported in these studies for mesh were both clinically and statistically significant. And in the studies, where improvement in both groups were compared, the improvements were similar.

Now, I would like to briefly focus on the largest randomized controlled trial conducted to date on transvaginal mesh. This landmark article, recently published in *The New England Journal of Medicine*, specifically addressed women with isolated anterior vault prolapse.

This was a multicenter study that followed 389 women, comparing mesh to traditional colporrhaphy. They used a compound outcome measure for defining success, looking at both anatomic cure as well as the most specific prolapse symptom, the feeling of bulge. This article reports on these endpoints at one-year follow-up.

Women using mesh had an 82 percent anatomic cure rate as opposed to 48 percent cure rate in the traditional native repair arm. Mesh kits were superior for symptomatic outcome as well: 75 percent in favor of mesh versus 62 percent for colporrhaphy. The compound measure thus yielded a significant difference in favor of mesh, with a combined anatomic and functional success of 61 versus 35 percent.

Therefore, this study provides Level I evidence and is a clear indication that transvaginal mesh kits are a valuable treatment option, from both an anatomic as well as a functional viewpoint, for women suffering from anterior vaginal wall prolapse.

So we looked at effectiveness. Now, let's turn our attention to safety.

The FDA poses the question of whether there's adequate assurance of safety of transvaginal mesh for prolapse. The data demonstrates that there is adequate assurance of safety when we consider the two incidents of serious adverse events. Serious adverse events that are mesh-specific are very low.

Looking at the FDA's MAUDE database, which is designed to identify new events and signals, there have been new adverse events related to vaginal mesh identified since the initial introduction of these products. Although rates vary, the types of events remain the same.

We know from the literature that exposures are the most commonly reported adverse events for transvaginal mesh kits. We believe it's important to understand an essential distinction between mesh exposure, where a piece of mesh is exposed into the vagina, and mesh erosion, where we are actually referring to a perforation into a hollow organ by the mesh. Not differentiating between the two may lead one to over-interpret its clinical importance.

Mesh erosion complications are so rare that we learn about them in the literature through case reports. The long-term data we have for sacrocolpopexy, which uses exactly the same material as these mesh kits, has long established this.

For transvaginal meshes, when exposures occur, nearly half can be treated nonsurgically, as shown in a large meta-analysis by the Society of Gynecologic Surgeons, of 10,000 women treated by mesh.

One of the most important questions we need to ask ourselves is also why these adverse events are occurring. And the risk factors for mesh exposures are becoming more and more apparent. Several studies published this year show that hysterectomy, patient age, smoking, diabetes, and surgeon experience predispose patients to mesh exposure. Patient selection and risk factors, appropriately stated in the device's labeling, as well as the surgeon's training, are therefore part of our proposal.

Another adverse event that has attracted the attention is the occurrence of dyspareunia, or painful intercourse. It's important to note that dyspareunia is inherent to the condition of prolapse. And as you can see in the study quoted by Lowman, dyspareunia at baseline and new onset of dyspareunia post-intervention is prevalent for all treatment options.

While there has been a lot of focus on the complications of transvaginal mesh, it is important to note that the total complication rate for traditional repair, sacrocolpopexy, and mesh kits are all very similar, at 15, 17

and 15 percent, respectively, as shown in this meta-analysis on procedures addressing apical support.

Note that the total reoperation rate is indeed higher for the mesh kits, but most of these constitute ambulatory procedures for mesh exposure, while those for traditional repair and sacrocolpopexy are often major in patient operative procedures to treat wound problems, fistula injury, and bleeding.

Let us know turn to the question of whether the benefits of transvaginal mesh outweigh the risks. The data says yes. The benefits are clear in the areas of anatomic restoration and quality of life measures.

Risk is well defined. There have been no new events identified since the introduction of the products, and their rates remain low.

This is a complicated disease with a variety of presentations and available interventions. As I noted earlier, these treatment options are not one size fits all, nor are they each the most appropriate for all patients. It comes down to the surgeon individualizing the patient's care to her specific condition, but also to the patient-specific goals and expectations.

So turning to the FDA's questions regarding whether clinical studies should be performed premarket for transvaginal mesh, our position is yes, because, for transvaginal products, clinical data should continue to be generated for all new products, to assure new products remain as safe and effective as the current interventions.

We also want to make sure, however, that we are clear on what a clinical trial is meant to achieve. The appropriate trial design must be developed in conjunction with surgeons, manufacturers, and FDA because we firmly believe that one trial design will not apply to all new pelvic floor devices. The type of study will depend on the specific question of safety and efficacy asked, depending on the product differences from current products.

The study will also have to address the indication for use and the target population. Equally important can be to confirm whether key claims are met or when specific research questions need to be answered.

For these reasons, we have reservations about the FDA study design proposal because we don't believe that one clinical design can fit all. We agree that multiple efficacy endpoints assessing both functional and anatomical outcomes are needed. However, because of the low rate of adverse events, a trial powered for non-inferiority would require an unacceptably large number of patients in order to meet that endpoint, with little gain in patient protection.

There are also some practical limitations regarding a surgical randomized controlled trial design that we must consider. First, surgeon and patient preference to one type of surgery over another will influence recruitment. Also, ensuring that the control arm, the traditional repair, is performed in a standard fashion is not always easy. And lastly, blinding the assessor has proven to be difficult, as incision size and adverse events reveal

what type of surgery was actually performed.

Therefore, we believe that for the introduction of the majority of new devices, a single-arm, prospective trial with multiple efficacy endpoints assessing functional anatomy will appropriately address the questions regarding continued safety and efficacy.

As I mentioned, we feel the study should be powered to address these multiple efficacy endpoints that assess both anatomy and symptoms.

In conclusion, we believe the benefit/risk profile of transvaginal mesh is comparable to traditional surgeries. In fact, the data demonstrate that transvaginal mesh is superior or equivalent to traditional surgery with respect to anatomy and is comparable in quality of life measures.

Serious adverse events, including mesh erosion, not to be confused with exposures, are rare. And mesh exposure, the most common adverse event, is usually minor and well manageable.

Nevertheless, device manufacturers are committed to collecting long-term data to further elucidate the benefit/risk ratio and to perform premarket clinical trials for new devices for this indication.

As a gynecologic surgeon who has seen firsthand the positive difference these procedures can make in a woman's life, and now as a medical director committed to ensuring safety and efficacy of these products, I want to make sure that this is an option that remains available for the

patients that need it.

I would now like to introduce Ginger Glaser, the Senior Director of Global Quality and Regulatory Affairs at American Medical Systems, to discuss our regulatory proposals in greater detail. Thank you.

MS. GLASER: Thank you, Dr. Hinoul. And good afternoon, everyone. I would like to focus my presentation on the question FDA is posing to you regarding the appropriate regulatory pathway for transvaginal mesh.

As the members of the Advisory Committee have seen from the briefing booklets, due to their evaluation of the literature and MAUDE data, FDA believes additional regulatory controls are needed for this product category.

As Dr. Hinoul described, these devices have been shown to be a safe and effective treatment option for women with prolapse.

We do agree that the early experience with these devices, as is common with all new devices, has identified areas for further study that may facilitate the continued achievement of possible optimal patient outcomes. Thus, we agree that FDA should utilize additional regulatory tools that are available within the Class II 510(k) process to ensure such information is collected and that patients and physicians receive the information that they need to continue to use the product safely and effectively.

In fact, of the types of controls that FDA has referenced, we

agree with nearly all of them. Specifically, as you just heard, we agree that new products should have premarket clinical trials prior to the product gaining marketing clearance.

We also suggest that the following actions should be required: collecting additional postmarket clinical data on current products; revising the physician labeling for transvaginal mesh to have standardized content that clearly presents the safety and effectiveness information based on clinical evidence, and creating standardized patient labeling that clearly describes the risks and benefits of the devices for patients who are considering mesh repairs; requiring conduct of rigorous and specific preclinical or bench studies that are specific to the intended device use. In addition, device-specific physician training programs should be required.

We are committed to implementing, and in many cases have already implemented, these actions. And although not a topic for FDA controls, we have also committed to working with the certified boards and specialty societies in developing practice guidelines and training programs to assist surgeons using transvaginal mesh.

Our position on regulatory controls differs from that of FDA in only two points, one of which is simply a matter of degree. First, as you heard from Dr. Hinoul, we would like to discuss a more appropriate design for the premarket clinical trials than what's proposed by the FDA in their briefing materials. Second, unlike FDA, we believe that there is no need to reclassify

transvaginal mesh for prolapse repair into Class III because all the necessary controls are available within the Class II 510(k) paradigm.

Based on the data Dr. Hinoul just presented, we have demonstrated that there is sufficient information available to establish these special controls.

Historically, the 510(k) guidance on surgical mesh was applied to transvaginal mesh for prolapse repair as it was the only relevant guidance document available from FDA. This guidance is not specific to the nuances of transvaginal mesh placement for prolapse. Thus, in addition to following this guidance, manufacturers have conducted postmarket clinical trials and offered extensive physician training programs supporting the use of our devices.

We believe there is no need to reclassify transvaginal mesh prior to fully utilizing the many other regulatory mechanisms available within the existing Class II 510(k) regulatory framework.

Fully utilizing the existing framework would have the benefit of providing the information that physicians and FDA are seeking, while at the same time allowing manufacturers an efficient system in which we can provide surgeons and patients with continually improved devices.

As FDA clearly points out in their briefing booklet, the special controls provisions of the regulations give FDA the authority to create very specific regulatory requirements for Class II 510(k) devices. These special

controls may cover a wide range of activities, such as preclinical testing, premarket clinical studies, physician training, labeling requirements, and postmarket activities such as clinical studies, registries, or enhanced surveillance.

Additionally, as FDA also references in their briefing materials, 522 orders that specify postmarket clinical study requirements are also applicable to Class II 510(k) products. The proposed special controls provide sufficient evidence to address the concerns being discussed today.

Although, as we stated earlier, we do not believe a randomized controlled trial versus traditional repair is needed for premarket approval in most cases, such a trial could be required in a special controls document, as described in the regulations for Class II 510(k) devices.

The regulation describes special controls as those steps needed to provide reasonable assurance of the safety and effectiveness of the device. It does not define nor preclude any type of study design or duration either for premarket or postmarket clinical requirements. Neither does it require comparison only to other devices.

Based on the breadth of regulatory controls available for Class II 510(k) products, we believe that transvaginal mesh for the treatment of prolapse should remain in Class II and that special controls and 522 studies should define the requirements that address all of the questions raised by FDA and then ensure the continued safety and effectiveness of both current

and future devices.

From our perspective, the issue isn't that the regulatory framework governing transvaginal mesh is broken and needs to be replaced, but rather that it has not been fully utilized. We have demonstrated our intent to meet and exceed FDA requirements for our devices, and we are committed to continuing to improve our devices, our training, and the information provided in our labeling so that patients and physicians have the best information on which to base a decision on if and when they should use transvaginal mesh.

Finally, on behalf of the members of the Surgical Mesh Working Group, I would like to conclude by thanking you for giving us the opportunity to present the data showing that transvaginal mesh is a safe and effective treatment option that can continue to be regulated under the Class II 510(k) pathway.

We have the data available to create special controls, and we look forward to the opportunity to continue to discuss the proposed controls and clinical trial designs with FDA. Thank you.

DR. FALCONE: Okay, we're going to have the other presentation. Does that conclude your presentation?

MR. SECUNDA: Yes, it does.

DR. FALCONE: Okay. So we're going to go on to hear from Cook Medical, and then we will have questions from the Panel for you.