Reclassification of Urogynecologic Surgical Mesh Instrumentation

Food and Drug Administration

Gastroenterology-Urology Medical Devices Advisory Committee Panel

February 26, 2016

Purpose

- Obtain recommendations regarding the reclassification of urogynecologic surgical mesh instrumentation from class I to II
- Seeking Panel input on:
  - Risks to health
  - If class II is the appropriate regulatory class
  - Special controls that mitigate the risks to health

Outline

- Device Description
- Regulatory History
- Medical Device Report (MDR) Database
- Review of Published Literature
- Risks to Health and Proposed Mitigations
- Proposed Reclassification and Special Controls

Device Description

Urogynecologic Surgical Mesh Instrumentation

- Designed for use during urogynecologic surgical mesh procedures
- Does not include general instrumentation used during urogynecologic surgical mesh procedures
- General instrumentation will remain class I devices

Urogynecologic Surgical Mesh Instrumentation

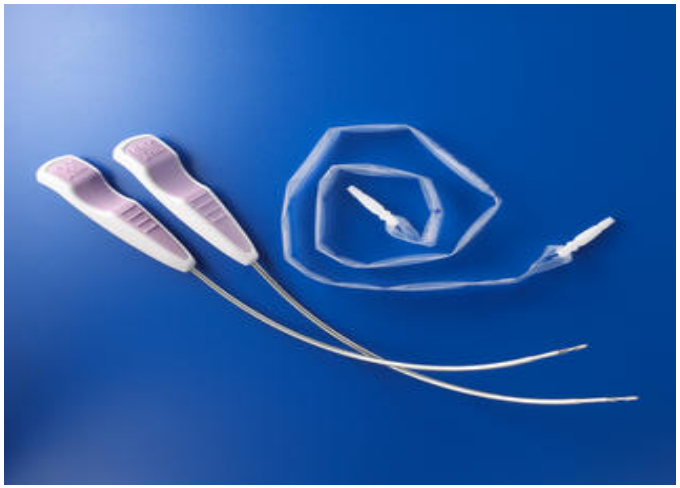
- Aids in insertion, placement, fixation, and/or anchoring
- Typically composed of a stainless-steel needle attached to a plastic handle
- Design of the instrumentation is dependent upon the urogynecologic surgical mesh procedure

Urogynecologic Surgical Mesh Procedures

- Intended to treat pelvic organ prolapse (POP) and female stress urinary incontinence (SUI)
- POP
  - Transvaginal repair
  - Abdominal repair (Sacrocolpopexy)
- SUI
  - Retropubic sling
  - Transobturator sling
  - Minisling

Urogynecologic Surgical Mesh Instrumentation

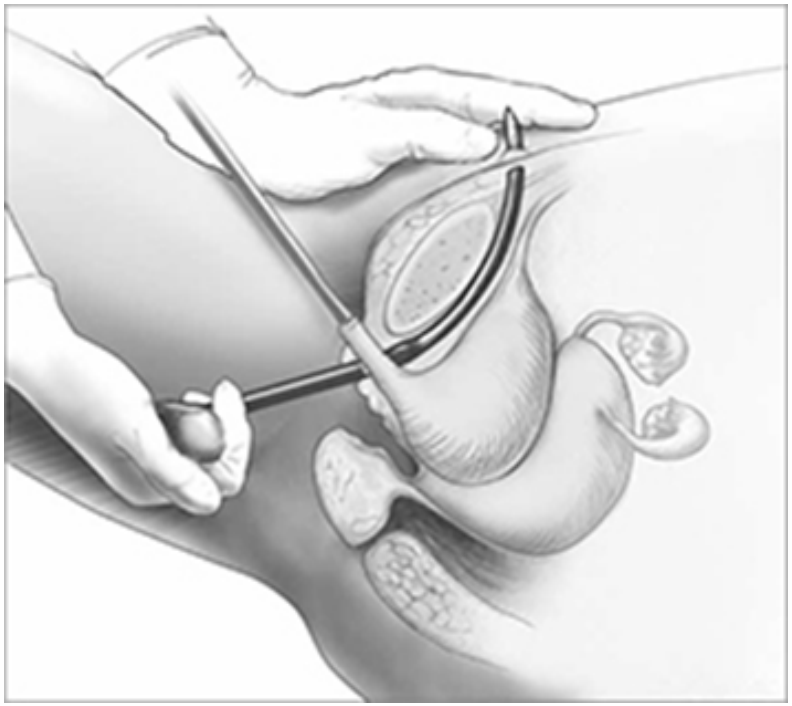
Capio Needle
Transvaginal POP Repair



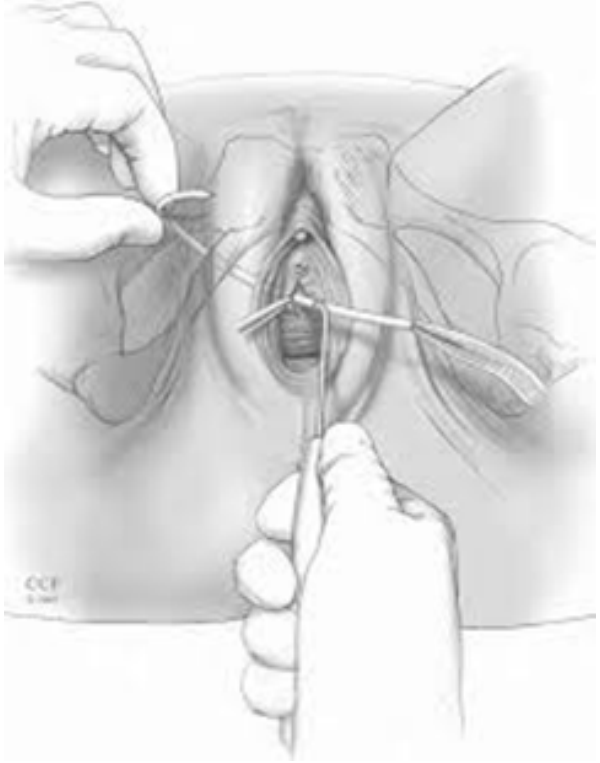
Retropubic Sling Needles

Transobturator Sling Needles

Placement of Urogynecologic Surgical Mesh



Retropubic Sling



Transobturator Sling

Implantation of Urogynecolgic Surgical Mesh

- Complex procedure
- Performed “blind”
- Relies on instrumentation, palpation of anatomic landmarks, and surgeon experience

Types of Urogynecologic Surgical Mesh Instrumentation

1. Designed, packaged, and indicated for use with one specific urogynecologic surgical mesh device (urogynecologic surgical mesh kit)
2. Designed and indicated for use with multiple urogynecologic surgical mesh devices (instrumentation and mesh packaged and marketed separately)
3. Designed and indicated for use with a urogynecologic surgical mesh device but also indicated for non-mesh urogynecologic procedures (e.g., pelvic floor repair procedures)

Regulatory History

Classification of Medical Devices

- Three classes of devices based on risks to health
  - Class I – Low risk
  - Class II – Intermediate risk
  - Class III – High risk
- Regulatory control increases with each class

Classification of Urogynecologic Surgical Mesh

- Class III
  - Transvaginal POP repair
- Class II
  - Abdominal POP repair (Sacrocolpopexy)
  - Retropubic sling for SUI
  - Transobturator sling for SUI
  - Minisling SUI

Classification of Instrumentation

- Class I devices
- Current regulations
  - 21 CFR 876.4730 (manual gastroenterology-urology surgical instrument and accessories)
  - 21 CFR 878.4800 (manual surgical instrument for general use)

Premarket Review of Urogyn Surgical Mesh Instrumentation

- Exempt from premarket notification
- Design, biocompatibility, sterilization method, etc. are not reviewed prior to marketing
- Urogynecologic surgical mesh kit – instrumentation reviewed in 510(k) submitted for surgical mesh
- Proposed reclassification – all new instrumentation to special controls and premarket notification

Reclassification Process

1. Publication of a proposed order in the Federal Register
2. Consideration of comments to a public docket
3. Meeting of a device classification panel
4. Publication of a final order

Proposed Order

- Published on May 1, 2014
  - "Reclassification of Surgical Mesh for Transvaginal Pelvic Organ Prolapse Repair and Surgical Instrumentation for Urogynecologic Surgical Mesh Procedures; Designation of Special Controls for Urogynecologic Surgical Mesh Instrumentation"
- Proposed to reclassify:
  - Surgical mesh indicated for transvaginal POP repair from class II to class III
    - Panel meeting held on September 8, 2011
    - Final order issued on January 5, 2016
  - Urogynecologic surgical mesh instrumentation from class I to class II

Public Comments

- Received 13 public comments
- 6 comments from patients supported reclassification to class II or class III
- 1 comment from a consumer group
  - Requested instrumentation have the same classification as the surgical mesh device with which it is indicated to be used
- 3 comments from consumer groups
  - Patient, Consumer & Public Health Coalition, National Center for Health Research, and the Consumers Union
  - Supported reclassification to class II

Public Comments (cont'd)

- 2 comments from clinical organizations
  - American College of Obstetricians and Gynecologists and the American Urogynecologic Society
  - Supported reclassification to class II
- 1 comment from industry (American Medical Systems)
  - Did not support reclassification
  - Stated FDA did not provide valid scientific evidence to support proposal

Medical Device Report (MDR) Database

MDR Database Overview

- MDRs used to monitor device performance, detect potential device-related safety issues, and contribute to benefit-risk assessment
- Manufacturers, importers, and device user facilities required to report known adverse events
- Provide a qualitative snapshot of adverse events for a specific device or device type when used in a “real world” environment
- Passive surveillance system
- MDRs can contain incomplete, inaccurate, untimely, unverified, or biased data

MDR Database Search

- Searched all MDRs reported from January 1, 2008, to December 2, 2015 for surgical mesh product codes
- Filtered the resulting MDRs based on terms specific to instrumentation
- Identified MDRs related to instrumentation and associated with the intra-operative placement of urogynecologic surgical mesh

Overview of MDR Search Results

- Identified 463 MDRs
  - 438 submitted by manufacturers
  - 14 submitted by a user facility
  - 11 voluntary reports
- Event types included 339 malfunctions and 124 injuries

MDRs by Product Code

Product Code	Total MDR Count
OTP - Mesh, surgical, synthetic, Urogynecologic, for Pelvic Organ Prolapse, Transvaginally Placed	186
FTL - Mesh, Surgical, Polymeric	114
OTN - Mesh, Surgical, Synthetic, Urogynecologic, For Stress Urinary Incontinence, Retropubic or Transobturator	92
PAH - Mesh, Surgical, Synthetic, Urogynecologic, for Stress Urinary Incontinence, Female, Mini-Sling	46
FTM - Mesh, Surgical	23
OTO - Mesh, Surgical, Synthetic, Urogynecologic, For Apical Vaginal and Uterine Prolapse, Transabdominally Placed	2

Patient Problem Codes

Patient Problem	Total MDR Count
No Consequence or Impact to Patient	302
No Known Impact or Consequence to Patient	54
Device Fragments in Patient	45
No Information	21
Nonresorbable Materials, Unretrieved in body	10
Foreign Body, Removal of	8
Perforation	6
Blood Loss/Hemorrhage	4

Device Problem Codes

Device Problem	Total MDR Count
Detachment of Device, or Device Component	259
Break	141
Needle	52
Suture	40
Difficult to Insert	16
Retraction Problem	13
Other	11

Manufacturer Conclusions

Manufacturer Conclusion	Total MDR Count
Device not Returned	231
Unable to Confirm Complaint	161
Conclusion not yet Available-Evaluation in Progress	92
Operational Context Caused or Contributed to Event	73
Other	32
Device Failure Occurred and was Related to Event	21
Device Discarded by User, Unable to Follow-Up	13
Human Factors Issue Use Error Caused or Contributed to Event	7 7
No Device Failure	5

MDR Review – FDA Conclusions

- Failures of urogynecologic surgical mesh instrumentation occur
- Failures have potential to adversely affect patients
- Support the need for well-designed instrumentation
- Instrumentation should be evaluated to ensure adequate performance, specifications, and labeling

Review of Published Literature

Methods

- Searched PubMed and Embase
- Used terms related to adverse events, type of urogynecologic condition, type of surgical instrumentation, study design, device name, and manufacturer name
- Limited references to those that evaluated human subjects, were written in English, and were published between 1997 and 2015
- Excluded references that evaluated male subjects, included only information on non-primary procedures, did not include a discussion of intraoperative and perioperative adverse events, included previously published data already included in the literature review, or were case reports or review articles
- Resulted in 207 references for review

Urogyn Surgical Mesh Procedures

Indication	Procedure	Number of References
SUI	Retropubic	74
	Transobturator	65
	Minisling	32
POP	Transvaginal repair	33
	Abdominal repair	3

Adverse Events

- Extracted data for three major categories of adverse events:
  - Organ perforation and injury
  - Vascular injury and bleeding
  - Nerve injury and pain

Organ Perforation and Injury

- Includes organ perforation, organ injury, urethral injury, ureteral injury, bladder injury, bladder perforation, rectal injury, cystotomy, and enterotomy

Procedure	Number of References	Rate
Retropubic	54/74	0.3-23.8%
Transobturator	25/65	0.2-5.8%
Minisling	6/32	0.2-2.6%
Transvaginal repair	16/33	0.7-13.1%
Abdominal repair	1/3	3.6%

Vascular Injury and Bleeding

- Includes hemorrhage, vascular injury, hematoma, and blood transfusion.

Procedure	Number of References	Rate
Retropubic	38/74	0.4-29.4%
Transobturator	19/65	0.2-11.9%
Minisling	6/32	1.0-20.5%
Transvaginal repair	15/33	0.7-7.7%
Abdominal repair	1/3	2.8%

Nerve Injury and Pain

- Includes nerve injury, nerve damage, leg pain, thigh pain, buttock pain, and neurological symptoms.

Procedure	Number of References	Rate
Retropubic	5/74	0.1-5.3%
Transobturator	11/65	0.8-30.8%
Minisling	5/32	1.1-4.1%
Transvaginal repair	15/33	6.0-39.1%
Abdominal repair	1/3	14.9%

Published Literature – FDA Conclusions

- Adverse events can occur as a result of urogynecologic surgical mesh instrumentation and at potentially high rates
- Data support the need for well-designed instrumentation
- Instrumentation should be evaluated to ensure adequate performance, specifications, and labeling.

Risks to Health and Proposed Mitigations

Risks to Health

- In the May 1, 2014 proposed order, the FDA identified the following risks to health:

1. *Perioperative risks*. Organ perforation or injury and bleeding (including hemorrhage/hematoma).
2. *Damage to blood vessels, nerves, connective tissue, and other structures*. This may be caused by improperly designed and/or misused surgical mesh instrumentation. Clinical sequelae include pelvic pain and neuromuscular problems.
3. *Adverse tissue reaction*. This may be caused by non-biocompatible materials.
4. *Infection*. This may be due to inadequate sterilization and/or reprocessing instructions or procedures.

Panel Question

The FDA is seeking Panel input on the identified risks to health for urogynecologic surgical mesh instrumentation.

The Panel should assess whether this list completely and accurately identifies the risks to health presented by urogynecologic surgical mesh instrumentation and whether any other risks should be included in the overall risk assessment of the device type.

Proposed Mitigations

Identified Risk	Special Controls
Perioperative injury	Non-clinical performance testing[2] Labeling Shelf life testing
Damage to blood vessels, nerves, connective tissue, and other structures[1]	Non-clinical performance testing[2] Labeling Shelf life testing
Adverse tissue reaction	Biocompatibility
Infection	Sterilization validation Reprocessing validation[3] Shelf life testing Labeling

[1] This risk was identified as “pelvic pain and neuromuscular problems” in the proposed order.
[2] This special control was described as “bench and/or cadaver testing” in the proposed order.
[3] Reprocessing validation was not identified as a special control in the proposed order.

Proposed Reclassification and Special Controls

Proposed Reclassification

- Valid scientific evidence demonstrates that special controls are necessary to provide a reasonable assurance of safety and effectiveness
- Urogynecologic surgical mesh instrumentation should be reclassified from class I to class II (special controls).

Panel Question

The FDA is seeking Panel input on whether urogynecologic surgical mesh instrumentation should be reclassified from class I.

The Panel should assess whether general controls alone or the combination of general and special controls provide reasonable assurance of safety and effectiveness of urogynecologic surgical mesh instrumentation.

Special Controls

- The device must be demonstrated to be biocompatible;
- The device must be demonstrated to be sterile, including adequate reprocessing for reusable devices;
- Performance data must support the shelf life of the device by demonstrating package integrity and device functionality over the requested shelf life;
- Non-clinical performance testing must demonstrate that the device meets all design specifications and performance requirements, and that the device performs as intended under anticipated conditions of use; and

Special Controls (cont'd)

- Labeling must include:
  - Information regarding the mesh design that may be used with the device;
  - Detailed summary of the clinical evaluations pertinent to use of the device;
  - Expiration date; and
  - Where components are intended to be sterilized by the user prior to initial use and/or are reusable, validated methods and instructions for sterilization and/or reprocessing of any reusable components.

Panel Question

If the Panel finds that class II regulatory controls are needed to provide reasonable assurance of safety and effectiveness for urogynecologic surgical mesh instrumentation, the FDA seeks Panel input on the proposed special controls for these devices.

The Panel should assess whether the identified special controls appropriately mitigate the identified risks to health and whether additional or different special controls are needed.

Proposed Regulation

§ 884.4910 Specialized surgical instrumentation for use with urogynecologic surgical mesh.

(a) *Identification*. Surgical instrumentation for use with surgical mesh for urogynecological procedures is a prescription device used to aid in insertion, placement, fixation, or anchoring of surgical mesh for procedures including transvaginal pelvic organ prolapse repair, sacrocolpopexy (transabdominal pelvic organ prolapse repair), and treatment of female stress urinary incontinence. Examples of such surgical instrumentation include needle passers and trocars, needle guides, fixation tools, and tissue anchors. This device does not include manual gastroenterology-urology surgical instrument and accessories (§ 876.4730) nor manual surgical instrument for general use (§ 878.4800).

Proposed Regulation (cont'd)

- *Classification*. Class II (special controls). The special controls for this device are:
  - The device must be demonstrated to be biocompatible;
  - The device must be demonstrated to be sterile, including adequate reprocessing for reusable devices;
  - Performance data must support the shelf life of the device by demonstrating package integrity and device functionality over the requested shelf life;
  - Non-clinical performance testing must demonstrate that the device meets all design specifications and performance requirements, and that the device performs as intended under anticipated conditions of use; and
  - Labeling must include:
    - Information regarding the mesh design that may be used with the device;
    - Detailed summary of the clinical evaluations pertinent to use of the device;
    - Expiration date; and
    - Where components are intended to be sterilized by the user prior to initial use and/or are reusable, validated methods and instructions for sterilization and/or reprocessing of any reusable components.

Conclusion

- Reclassify urogynecologic surgical mesh instrumentation from class I to class II with special controls
- Subject these devices to premarket notification requirements.
- Develop new regulation under Part 884, Obstetrical and Gynecological Devices.

Acknowledgements

Office of Device Evaluation

Jacqueline Cunkelman, M.D.

John Doucet, Ph.D.

Benjamin Fisher, Ph.D.

Angela Krueger

Christine Lee

Herbert Lerner, M.D.

Joyce Whang, Ph.D.

Office of Surveillance and Biometrics

Perpetual Azubuike

Hind Baydoun

Cynthia Bushee

Dongyi (Tony) Du, M.D., Ph.D.

Fariha Farooq

Nilsa Loyo-Berríos, Ph.D., MSc

Francisco Martinez-Murillo

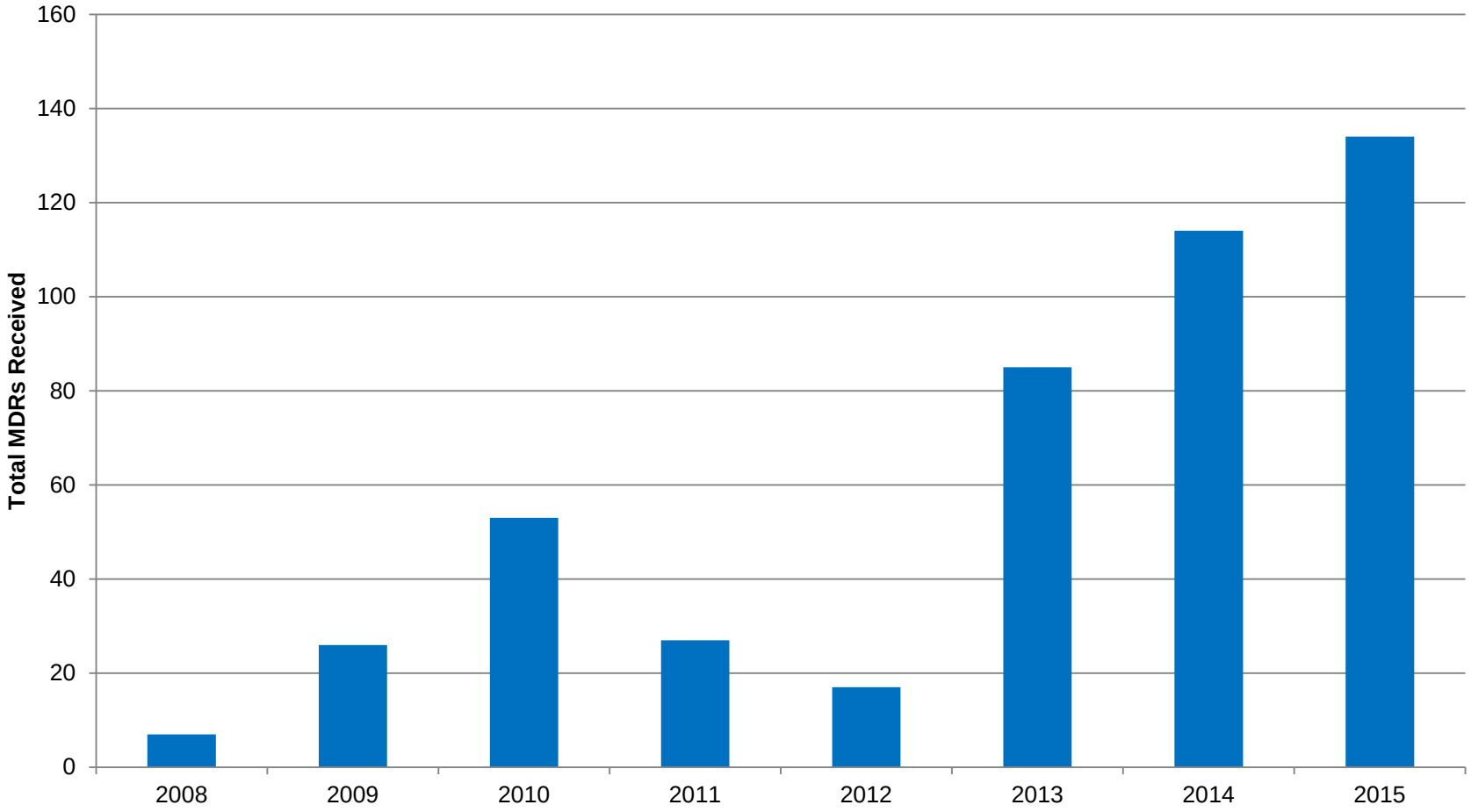
Nishant Mishra

Nancy Pressly

Bobak Shirmohammadi

Backup Slides

MDRs Per Year



Recalls

- Capio Needle (2005)
  - Class II recall
  - Sterility compromised due to package integrity failure
- Monarc Sling Needle Passers (2014)
  - Class II recall
  - Sterility compromised due to package integrity failure