



# **75<sup>th</sup> OB-GYN Advisory Panel Meeting**

## **Surgical Mesh for POP and SUI Repair**

**Herbert P. Lerner, MD**

**Division Director (acting)/ DRGUD/ODE/CDRH**

**September 8-9, 2011 – Day 1**

**Gaithersburg, Maryland**

# FDA Review Team

## ODE

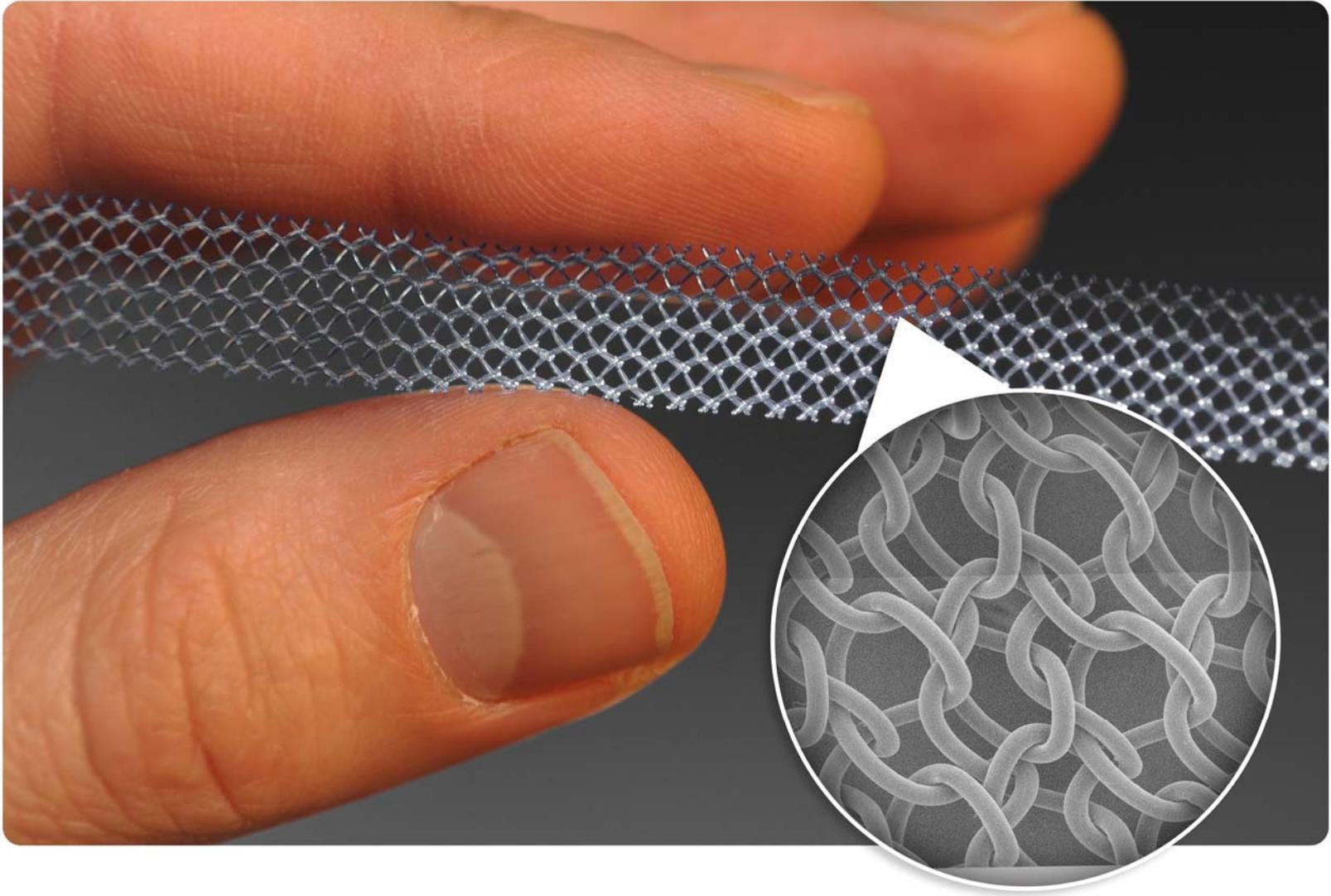
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- Sharon Andrews
- Rebecca Robinson, PhD
- Colin Pollard
- Michael Bailey, PhD
- Shanika Craig, MHA, MBA
- Joyce Whang, PhD

## OSB-DEPI

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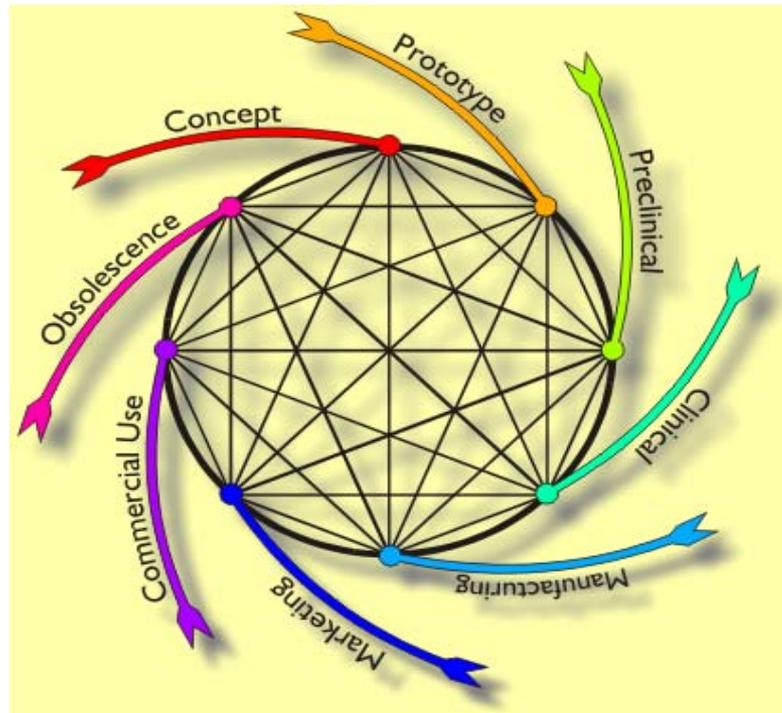




# “Total Product Life Cycle” Vision

**Efficient,  
Effective,  
and Predictable  
Product  
Development**

**Ensuring  
the Safety of  
Marketed  
Medical Devices**



**Enabling  
Technology  
and Innovation**



# Glossary - Day 1

## ***Surgical mesh***

- permanently implant
- sheet-like, with porosity for tissue in-growth
- supports weakened or damaged tissue
- may be absorbable or non-absorbable
- either synthetic or biologic material



## Glossary – Day 1

- ***Adverse events*** events which may cause harm to a patient, such as:
  - Vaginal wall erosion
  - Pain and dyspareunia (painful intercourse)
  - Bleeding, re-surgery, urinary problems
- ***MAUDE*** Manufacturer and User Device Experience – system for reporting adverse events to FDA

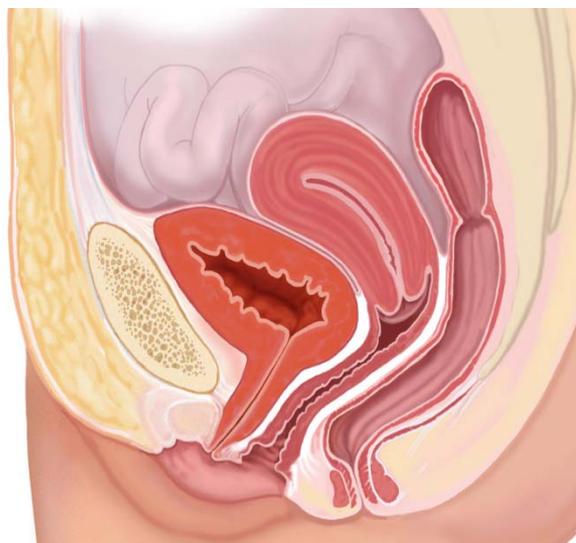


# Glossary – Day 1

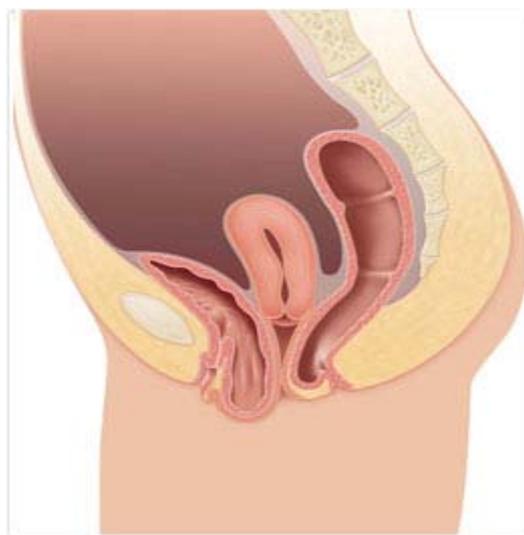
- ***Erosion*** state of being worn away, as by friction or pressure (IUGA 2011), non-specific umbrella term
- ***Exposure*** mesh that can be visualized through a disruption in the vaginal wall



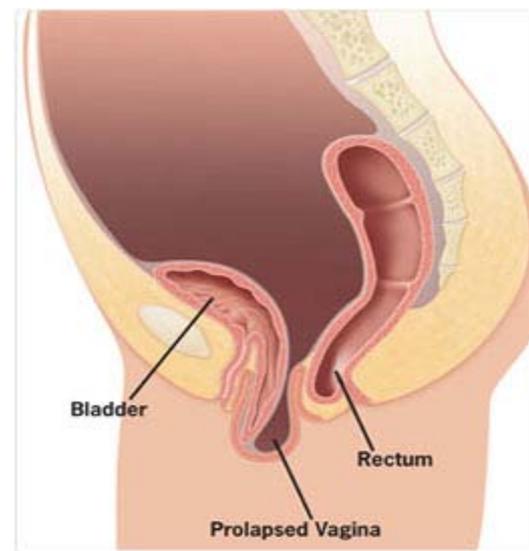
# Glossary - Pelvic Organ Prolapse (POP)



Normal Anatomy



Anterior Vaginal Wall Prolapse (Cystocele)\*



Apical Prolapse\*



# Surgical Mesh - Regulatory History

- pre-Amendments device
- Class II (Special Controls)
- 21 CFR 878.3300

*metallic or polymeric screen intended to be implanted to reinforce soft tissue or bone where weakness exists*

- Procodes FTL, FTM



## Since 1976, Brief Timeline

- 1990's new indications: SUI, then POP
- 2006 AE signals, safety problems  
FDA initial review of MAUDE, 2005-07
- 2008 FDA issues Public Health Notice regarding adverse events associated with surgical mesh when used for repair for SUI and POP



- 2010 professional societies expressed concern about adverse events associated with vaginal mesh for POP repair
- 2010 2<sup>nd</sup> FDA review of MAUDE, 2008-2010
- 2011 FDA issues new safety notice, 'white paper' analysis, points to advisory panel mtg



# Day-1 Scope of Meeting

## *Vaginal Mesh for POP Repair*

- FDA concerns re: safety and effectiveness of vaginal placement of mesh for POP repair
- FDA will present new regulatory strategy for addressing these concerns
- Presentations
  - Clinical societies
  - General public
  - Industry perspective
  - FDA presentation of S&E evidence



# Day-1 Scope of Meeting

## *Vaginal Mesh for POP Repair*

- FDA Presentations
  - summary of MAUDE data
  - review of published literature
- Panel Deliberations
  - consider evidence on mesh/POP repair
  - consider discussion questions re: need for clinical data, both premarket and postmarket
  - consider in context of possible reclassification of uro/gyn surgical mesh, need for postmarket studies



# Thank you!

- Public
- Clinical Organizations
- Industry
- Panel

...for taking the time out from your busy schedules to help FDA address this very important issue.



# Device Classification and Reclassification

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# Pre-Amendment vs. Post-Amendment Devices

The Act divided the arena of medical devices into either:

- Pre-Amendment Devices or
- Post-Amendment Devices

Depending on when the devices were introduced into interstate commerce for commercial distribution

# Classification of Pre-Amendment Devices

Pre-Amendment Devices are classified after FDA has:

- Received a recommendation from a device Classification Panel
- Published the Panel's recommendation for comment, along with a PR classifying the device; and
- Published a FR classifying the device

# Reclassification of Pre-Amendment Devices

FDA may reclassify a pre-Amendment device:

- in a proceeding that parallels the initial classification proceeding
- based upon new information respecting a device either on FDA's own initiative or upon the petition of an interested person

# Classification of Post-Amendment Devices

- Post-Amendment devices are automatically classified into Class III
- Those devices remain in Class III and require premarket approval, unless and until
  - the device is reclassified into Class I or II
  - FDA issues a SE determination
  - the device is classified into Class I or II via the Evaluation of Automatic Class III Designation (de novo review)

# Reclassification of Post-Amendment Devices

- May be initiated by either FDA or Industry
- FDA may, for good cause shown, refer the petition to a device classification panel
- the Panel shall make a recommendation to FDA respecting approval or denial of the petition

# Device Classes

A device should be placed in the lowest class whose level of control will provide reasonable assurance of safety and effectiveness.

Class I - General Controls

Class II - General and Special Controls

Class III - Premarket Approval

# Description of Classes

## Class I

Devices for which any combination of general controls are sufficient to provide reasonable assurance of the safety and effectiveness of devices

# Description of Classes (cont.)

General controls include, for example:

- prohibition against adulterated or misbranded devices
- GMPs
- registration of manufacturing facilities
- listing of device types
- record keeping
- repair, replacement, refund
- banned devices

# Description of Classes (cont.)

## Class II

1. Devices which cannot be classified into Class I because general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness of such device, and
2. For which there is sufficient information to establish special controls to provide such assurance

# Description of Classes (cont.)

Special Controls include, for example:

- Performance Standards
- Postmarket Surveillance
- patient registries
- development and dissemination of guidelines
- tracking requirements
- recommendations and other appropriate actions

# Description of Classes (cont.)

## Class III

1. Devices for which insufficient information exists to determine that general and special controls are sufficient to provide reasonable assurance of the S&E of such device, and
2. Such devices are
  - life sustaining and/or life supporting
  - substantial importance in preventing impairment of human health; or
  - present potential or unreasonable risk of illness or injury

# Restricted Devices

- Under the provision of Section 520(e) of FD&C Act, the FDA is authorized, by regulation, to restrict the sale, distribution, or use of a device if, because of its potentiality for harmful effect or the collateral measures necessary to its use, FDA determines there cannot otherwise be reasonable assurance of its safety and effectiveness.

## Restricted Devices (cont.)

- A restricted device can only be sold, distributed, or used either
  - Upon the oral or written authorization by a licensed practitioner or
  - Under such other conditions specified by regulation.
- If the device is restricted to use by persons with specific training or experience in its use or by persons for use in certain facilities, FDA must determine that such a restriction is required for the safe and effective use of the device.

## Restricted Devices (cont.)

- Devices such as cardiac pacemakers and heart valves, for example, require a practitioner's authorization.
- Hearing aids are restricted by a regulation which limits their sale to persons who have obtained a medical evaluation of their hearing loss by a physician within six months prior to the sale of the hearing aid. The labeling of hearing aids must provide information on their use and maintenance.



# Postmarket Surveillance Studies “522 Studies”

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Division of Epidemiology, OSB, CDRH

September 8, 2011

# Section 522 of FD&C Act

FDA has authority to order postmarket surveillance for Class II or Class III medical device meeting any of four criteria (details forthcoming).

Data collected via postmarket surveillance study can reveal unforeseen adverse events, the actual rate of anticipated adverse events, or other information necessary to protect the public health.

# Statutory Criterion 1

Failure of the device would be reasonably likely to have a serious adverse health consequence

- As per 822.3(j), *serious adverse health consequences* means any significant adverse experience related to a device, including device-related events that are life-threatening or that involve permanent or long-term injuries or illnesses.

# Statutory Criterion 2

*Expected* to have significant use in pediatric populations

- New provision as of FDAAA 2007
- “Significant” pediatric use is defined on a case-by-case basis
- Leeway written into the statute to allow for studying devices not specifically labeled for pediatrics

# Statutory Criteria 3 and 4

Intended to be implanted in the body for more than one year

Intended to be a life-supporting device used outside of a user facility

- As per 822.3(f), *life-supporting or life-sustaining device used outside a device user facility* means that a device is essential to, or yields information essential to, the restoration or continuation of a bodily function important to the continuation of human life and is used outside a hospital, nursing home, ambulatory surgical facility, or diagnostic or outpatient treatment facility. A physician's office is not a device user facility.

## Section 522 of FD&C Act (cont.)

- 522 order can be issued any time after approval/clearance
  - Exception is FDAAA allows for 522 to be issued as a condition of approval for pediatric devices
- Study duration is 36 months for non-pediatric studies
- Longer surveillance for pediatric devices
- Noncompliance may lead to regulatory actions

# 522 - Failure to Comply

- 21 CFR 822.20
  - Warning Letter
  - Device misbranded (under section 502(t)(3) of FD&C Act)
  - Seizure of device
  - Civil Money Penalties
  - Prosecution



# Pre-522 Process

- Examples of situations that may raise postmarket questions, during both the premarket and postmarket periods, are listed below:
  - to confirm the nature, severity, or frequency of suspected problems reported in adverse event reports or in the published literature
  - to obtain more experience with a change from hospital use to use in the home or other environment or with new patient populations
  - to address long term or infrequent safety and effectiveness issues of implantable and other devices for which the premarket testing provided only limited information
  - to better define the association between problems and devices when unexpected or unexplained serious adverse events occur after a device is marketed, if there is a change in the nature of serious adverse events, or if there is an increase in the frequency of serious adverse events

# Pre-522 Process

- Some of the elements discussed by the pre-522 team include:
  - Are the statutory criteria met?
  - What is the public health question?
  - What is the public health question based on?
  - Is the public health issue sponsor-specific, device-specific, or device type-specific?
  - For a device for which a condition of clearance is being considered, can and should the public health question be addressed premarket rather than as part a 522 study?
  - Is there any other source of data or action, or a combination thereof, that may be used to address the public health question?
  - Does another ongoing study address the public health question?
  - What type(s) of 522 study design(s) should be recommended?
  - What combination of efforts should be considered to address the public health question?

# Issuing 522 Order

- Order issued by OSB Director
- Identifies
  - premarket submission(s) involved (i.e., 510(k), PMA, PDP, or HDE)
  - public health question(s)
  - rationale for the 522 order
  - study design recommendations to assist in preparing the postmarket surveillance plan
- Sponsor must submit postmarket surveillance plan within 30 days of receipt of the 522 order

# Elements of 522 Study Plan

- Background (e.g., regulatory history, brief description of device, indications for use)
- Purpose of study (i.e., public health question(s) from 522 order)
- Study objectives and hypotheses
- Study design
- Study population
- Sample size calculation
- Primary and secondary endpoints
- Length of follow-up, follow-up schedule, description of baseline and follow-up assessments
- Description of data collection procedures
- Statistical analysis
- Data collection forms, informed consent forms, and IRB approval forms
- Reporting requirements for interim and final reports
- Study milestones/timeline elements

# Study Plan Agreement

FDA evaluates proposed study plans for administrative completeness and whether the plan will result in collection of useful data that will answer the surveillance question(s).

Failure to have an approved postmarket surveillance plan or failure to conduct postmarket surveillance in accordance with the approved plan constitutes failure to comply with section 522 of FD&C Act.

# 522 Study Monitoring

- Interim and Final reporting schedule is part of study plan
  - Typical schedule for Interim reporting is every 6 months for first 2 years and annually thereafter
- After approval of the study plan, the contents of the original submission and any amendments, supplements or reports may be disclosed in accordance with the Freedom of Information (FOI) Act.
- FDA posts information about postmarket surveillance studies on the 522 webpage:

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pss.cfm>