Transvaginal Surgical Mesh for Anterior POP

Obstetrics and Gynecology Devices Panel
FDA Advisory Committee

February 12, 2019

Coloplast

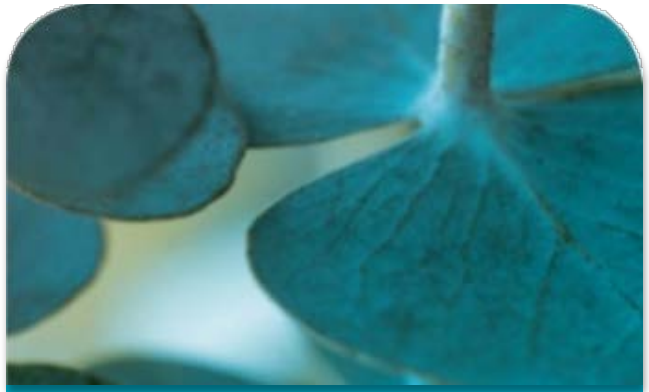
Coloplast Corp.

Mission

Making life easier for people with intimate healthcare needs

Vision

Setting the global standard for listening and responding



Values

Closeness to better understand

Passion to make a difference

Respect and responsibility to guide us

Coloplast Representatives

Dale Klous	**Coloplast** Director of Clinical Science and Office of Medical Affairs Interventional Urology
Sharon Iverson	**Coloplast** Head of Regulatory Affairs Interventional Urology
Diane Brinza	**Coloplast** Sr. Strategic Regulatory Affairs Manager Interventional Urology
Prof Jan-Paul Roovers	**Urogynecologist, Professor of Urogynecology** **Co-Lead Investigator of Restorelle 522 Study**
Janet Harris-Hicks, MD, FACOG, FPMRS	**Urogynecologist**
Karny Jacoby, MD, FPMRS, CPI	**Urologist**

Topics

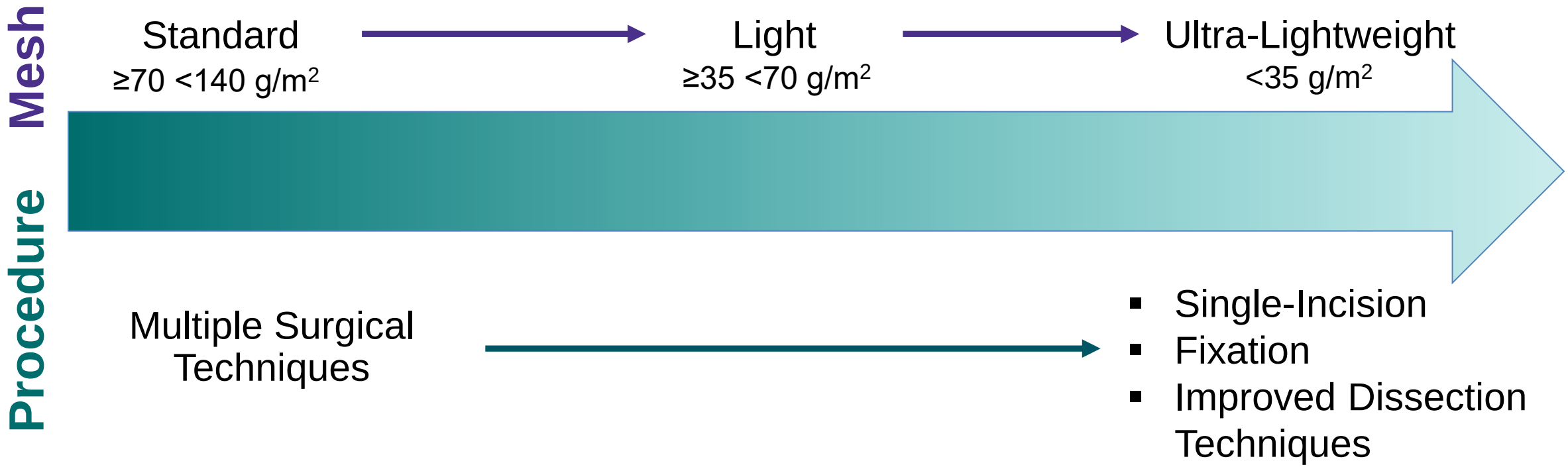
- **Safety**
- **Effectiveness**
- **Patient Population**
- **Physician Training and Education**
- **Benefit/Risk**

Context

Patients and surgeons need safe and effective options for the treatment of anterior POP

- **Each patient is unique:**
  - Anatomy
  - Preferences
- **Many factors impact surgical outcomes, including:**
  - Device characteristics
  - Patient comorbidities
  - Surgical skill and technique

Innovation in Treatment of Anterior POP



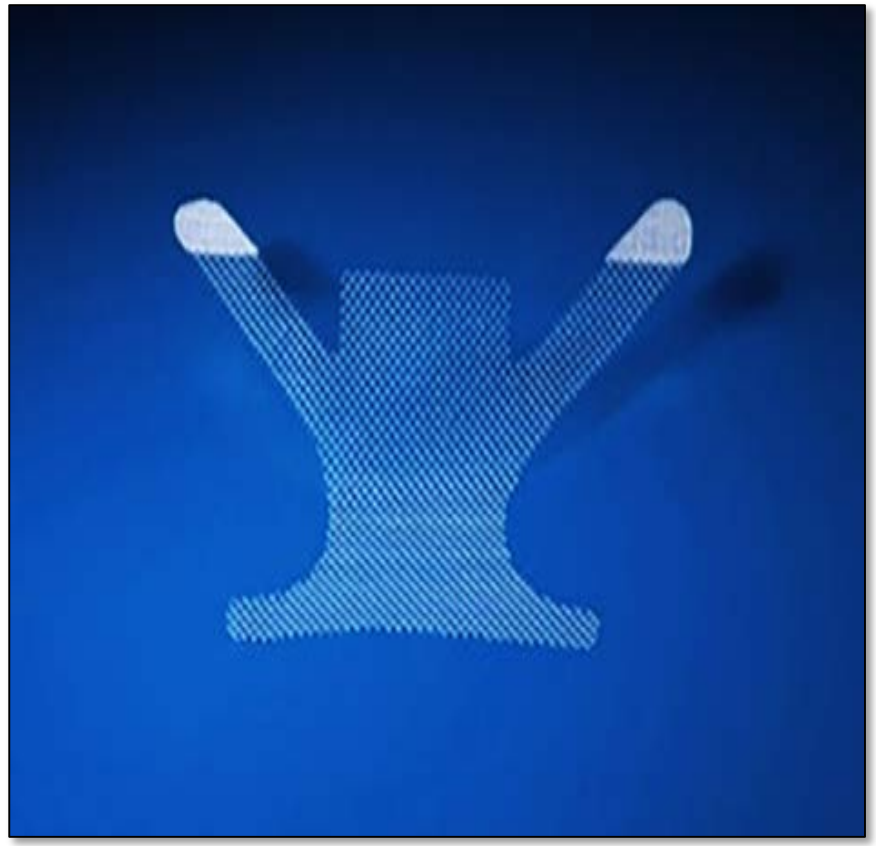
Device Characteristics

- **Lightweight, Type I macroporous (Amid classification) mesh:**
  - Reduce the inflammatory response
  - Potentially enhance mesh performance
  - Promote better integration into the host tissue

Excerpted from:
FDA Executive Summary: Surgical Mesh for Treatment of Women with Pelvic Organ Prolapse and Stress Urinary Incontinence
Obstetrics & Gynecology Devices Advisory Committee Meeting, September 8-9, 2011

Restorelle DirectFix Anterior Mesh

- **Ultra-lightweight density = 19 g/m^2**
- **Type 1 macroporous (>75 µm)**
- **Monofilament polypropylene**
- **Pre-configured shape**
- **Single-incision insertion, with fixation**



Safety

MAUDE Data (2012-2018)

- **Criteria:** Any Restorelle surgical mesh device indicated for the transvaginal treatment of anterior POP, including Restorelle DirectFix Anterior

- **Observations:**
  - Well understood safety profile with event types consistent over time
  - Many of the event types also occur in native tissue repair procedures

Safety and Effectiveness

Coloplast's Literature Search

- **Scope:** Publications relevant to the **current-generation** surgical mesh devices for anterior POP treatment (≥12-month follow-up)
- **Source:** PubMed (Jan 2011 - Nov 2018)
- **Search Criteria:** Characteristics similar to Restorelle mesh (ultra-lightweight)

Safety and Effectiveness

Literature Review – Current-generation surgical mesh devices

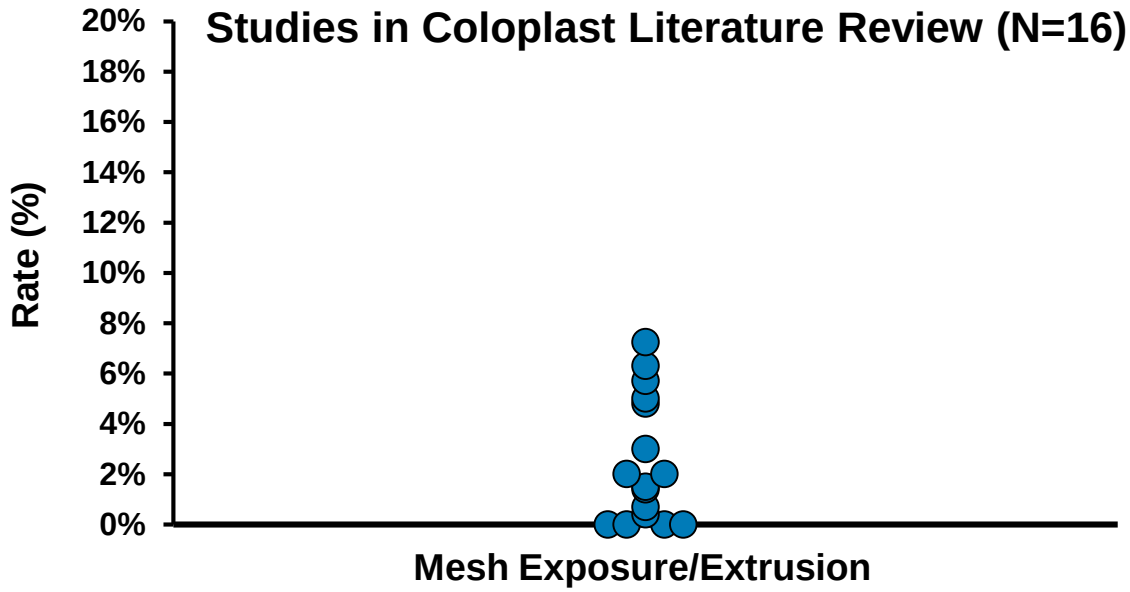
- **Two cohort studies compared mesh implants to native tissue repair (NTR) for anterior POP treatment**
  - Both showed statistically significant improvement in objective outcomes (anatomic correction) compared with NTR
    - Lo et al. (2017): 96.6 vs 73.4%, p≤0.001
    - Su et al. (2014): 98 vs. 87%, p=0.006
- **14 mesh-only cohort studies with outcomes compared to baseline**
  - All studies: improvement in objective outcomes
  - Where measured: improvements in subjective (patient-reported) outcomes
  - In 8 of 14 studies, these improvements were observed past 12 months (13-60 months)

Safety and Effectiveness

Literature Review – Current-generation surgical mesh devices

Low rates of exposure/extrusion associated with ultra-lightweight mesh

- 16 studies representing 1842 patients
- Overall incidence: **2.3%** (43/1842 patients); Range: 0.0% - 7.3%



FDA's literature review result (~11-18%) includes several mesh densities and procedures

Patient Population: Restorelle 522 Study

Dual purpose

Provide real-world post-market surveillance through 36 months

Provide 12-month effectiveness and safety outcome data to support a PMA submission

Endpoints

Primary effectiveness:

- Anatomic correction, retreatment, and patient symptoms

Primary safety:

- Device and/or procedure-related SAEs in the anterior compartment

Patient Population: Treatment Selection

Study design intentionally does not use randomization

- Public statements made from 2008 to 2011 regarding synthetic mesh devices impact the ethical and statistical assumption of equipoise to justify randomization

Patient Population: Treatment Selection

Real-world Decisions in the Restorelle 522 Study

– After a detailed and thoughtful discussion between the patient and her physician regarding the risk, benefits, alternatives and complications of surgery, the surgeon and patient select the treatment

Patient Population

In the Restorelle 522 Study, surgeon/patient treatment choice results in more patients with higher-risk of recurrence in the mesh group compared to the NTR group

Relevance:

- Coloplast believes that this observation demonstrates that surgeons and patients are actively making benefit/risk decisions

Because of differences in treatment groups, informed by real-world benefit/risk decisions, any comparison between the groups should consider the totality of the data

Physician Education and Training

Coloplast supports the professional societies in their initiatives to enhance physician education and training

Benefit/Risk

All mesh is not equal

- Published medical literature is dominated by heavyweight mesh
- Contemporary mesh is ultra-lightweight, macroporous, single incision and is associated with low incidence of exposure/extrusion

Patients and physicians need options

- Each patient is unique
- Real-world evidence suggests that patients and physicians are already making benefit/risk determinations

Thank you