Dear [Sponsor Contact]:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) notified you by letter, dated [date of substantial equivalence determination], that the [trade name of 510(k)] was cleared under [premarket notification (510(k)) Kxxxxxx].

Section 522 of the Federal Food, Drug, and Cosmetic Act (the act), 21 U.S.C. 360l, authorizes FDA to require a manufacturer to conduct postmarket surveillance of a class II or class III device that meets any of the following criteria: (1) its failure would be reasonably likely to have serious adverse health consequences; (2) it is expected to have significant use in pediatric populations; (3) it is intended to be implanted in the body for more than one year; or (4) it is intended to be a life-sustaining or life-supporting device used outside a device user facility.

Your device is subject to postmarket surveillance under section 522 because it is a class II device that meets two of these criteria. Its failure would be reasonably likely to cause mesh erosion (i.e. organ perforation), severe pain, and fistula formation, which would meet the definition of "serious adverse health consequences" at 21 C.F.R. § 822.3(j). In addition, your device is intended to be implanted in the body for more than one year.

When FDA orders postmarket surveillance, the manufacturer must submit a plan to conduct the surveillance. FDA will then determine whether the plan will result in the collection of useful data that can reveal unforeseen adverse events or other information necessary to protect the public health. Here, FDA is concerned with potential safety risks as evidenced by adverse events reported to the FDA and in the published literature. In addition, FDA is concerned with published literature indicating lack of added clinical benefit compared to non-mesh repair. Details of the FDA concerns can be found in the “Surgical Mesh Used in Repair of Pelvic Organ Prolapse” section of the FDA Executive Summary from the September 8-9, 2011 meeting of the Obstetrics and Gynecology Devices Panel of the Medical Devices Advisory Committee (located online at: http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/ObstetricsandGynecologyDevices/UCM270402.pdf).

Accordingly, under section 522 of the act, we are ordering you to conduct a postmarket surveillance study of your device to address our questions below.
1. Among all women undergoing transvaginal pelvic organ prolapse surgery, what proportion is exposed to this device and what type of surgical procedures are performed?

2. What are the rates associated with each of the following adverse events through 36 months post-implant: mesh exposure in the vagina, mesh erosion into another organ, pelvic pain, infection (by type), de novo dyspareunia, vaginal shortening, vaginal scarring, de novo vaginal bleeding, atypical vaginal discharge, fistula formation, de novo voiding dysfunction (including de novo incontinence), neuromuscular problems (including groin and leg pain), revision/resurgery, recurrent prolapse?
   a. Are the rates of adverse events associated with use of this device non-inferior to the rates seen in patients with similar surgeries who are not exposed to mesh?
   b. Are the rates of revision/re-surgery with use of this device non-inferior to the rates seen in patients with similar surgeries who are not exposed to mesh?
   c. Among women exposed to your device for transvaginal pelvic organ prolapse surgery, what are the rates and severity of adverse events observed within 6 months, 12 months, 18 months, 24 months, and 36 months?
   d. Overall and within each vaginal compartment, what is the rate of adverse events noted with use of this device within 6 months, 12 months, 18 months, 24 months, and 36 months?
   e. For mesh exposure and erosion, what are the rates and severity of events observed within 6 months, 12 months, 18 months, 24 months, and 36 months?

3. What is the quality of life (including sexual function) for women who have received this device at 6 months, 12 months, 18 months, 24 months, and 36 months post-surgery? Does the quality of life among women who have had transvaginal pelvic organ prolapse surgery with this device differ:
   a. from those who have had similar surgeries without use of mesh?
   b. by vaginal compartment of surgery?
   c. from those who have similar conditions without surgical intervention?

4. For each vaginal compartment in which mesh is placed in your study, what proportion of women report a vaginal bulge just prior to surgery, and within 6 months, 12 months, 18 months, 24 months, and 36 months of surgery?

5. Among patients with resurgery within 36 months after initial transvaginal pelvic organ prolapse surgery with this mesh:
   a. what are the rates of adverse events and what is the quality of life during the period following resurgery?
   b. do the rates of adverse events after resurgery differ by vaginal compartment of surgery?
   c. does quality of life after resurgery differ between patients whose initial transvaginal pelvic organ prolapse surgery included this mesh compared with those whose surgery did not include mesh?

6. Is the rate of effectiveness among women in which mesh is placed non-inferior to the rate of effectiveness among women with similar surgeries who are not exposed to mesh?
a. For each vaginal compartment into which mesh is placed in your study, what proportion of women have prolapse below the hymenal ring just prior to surgery, and within 6 months, 12 months, 18 months, 24 months, and 36 months following surgery?
b. Compared to measurements of prolapse below the hymenal ring just prior to surgery, what proportion of women with mesh show improvement at 6 months, 12 months, 18 months, 24 months, and 36 months?
c. Among women in your study undergoing transvaginal pelvic organ prolapse surgery without mesh, what proportion of women have prolapse below the hymenal ring just prior to surgery, and within 6 months, 12 months, 18 months, 24 months, and 36 months following surgery?
d. Compared to measurements of prolapse below the hymenal ring just prior to surgery, what proportion of women without mesh show improvement at 6 months, 12 months, 18 months, 24 months, and 36 months?
e. For women who have had all or part their mesh removed post-operatively, what proportion of women have prolapse below the hymenal ring just prior to mesh-removal surgery, and within 6 months, 12 months, 18 months, 24 months, and 36 months of surgery?

Within 30 days of receipt of this order, you must submit your plan to conduct postmarket surveillance of your device to the address listed below. Your submission should clearly identify it as a postmarket surveillance plan and include the PS number referenced above.

You should send three (3) copies of your plan to:

Mary Beth Ritchey, PhD  
Food and Drug Administration  
10903 New Hampshire Ave  
WO66-4118  
Silver Spring, MD  20993-0002

To address the issues cited above, FDA recommends a randomized clinical trial (RCT) or prospective cohort study design that compares your device(s) to a control (e.g., transvaginal urogynecologic surgery without use of mesh) through 3 years of follow-up. Depending on the study design that you propose and justify, you may choose to work with sponsors of other transvaginal urogynecologic surgical meshes to establish a single pool of control subjects. If you believe that you have existing data to justify an alternative study design, such as a retrospective cohort study, FDA suggests you first contact us to discuss the extent of the data and its adequacy to address public health issues #2 - #6 above.

In lieu of one of the study designs recommended above, you may choose to develop a new sponsor registry or RCT/cohort study nested within a registry to address these public health questions, either as a single institution or in collaboration with other sponsors. FDA is amenable to facilitating creation of a multi-sponsor registry to address these public health questions. If you choose to address these questions through a multi-sponsor registry, please contact FDA within 15 days of receipt of this order to discuss this approach.

FDA recommends a study design including a population of women who are age 18 years or older with documented pelvic organ prolapse diagnosis for whom surgery is scheduled. FDA suggests
inclusion of and adjustment for the following risk factors: level of prolapse (above or below hymenal ring); primary versus recurrent prolapse; menopausal status; estrogen use; age; smoking; diagnosis of diabetes; body mass index; modification of mesh prior to placement (e.g., cutting); surgical technique or procedure used; hysterectomy status; concomitant procedures; surgeon training and experience with this mesh (e.g. number of years performing or volume of procedures performed in past 12 months); compartment of repair (e.g. anterior repair of prolapse). FDA recommends capture of the following infection types: perioperative infections, urinary tract infections, and vaginal infections with flora uncommon to the vaginal canal. In addition, FDA recommends use of the following quality of life measures or other validated instrument(s): Pelvic Floor Impact Questionnaire (PFIQ); Pelvic Floor Distress Inventory (PFDI); Pelvic Organ Prolapse/Urinary Incontinence Sexual Function Questionnaire (PISQ-12).

For item 2, FDA recommends classifying “severity” of mesh exposure and erosion based on need for one of the following four types of intervention: none or non-surgical medical intervention only, minor or intra-office surgical intervention, outpatient surgery, inpatient surgery. In addition, FDA recommends identifying the specific medical intervention performed. You may also choose to include questions regarding patient experience, such as asking prior to the procedure about one major physical limitation that the patient would like to improve and following up post-procedure to determine if that limitation has changed.

The clinical experience gathered from your postmarket surveillance study may lead FDA to, among other things, recommend labeling changes regarding the use of your devices.

The FDA is considering the panel’s recommendation that urogynecologic surgical mesh used for transvaginal repair of pelvic organ prolapse be reclassified from class II to class III. If meshes used for this indication are reclassified, then FDA would require clinical data to support the premarket approval application (PMA) that would be needed.

Although FDA has not come to a final decision on reclassification, you may wish to consider the data requirements for a PMA in deciding the design of your 522 study. If you are interested in utilizing data collected to fulfill this 522 order to also fulfill a possible future PMA, we suggest you indicate your interest on the cover letter of your 522 study plan and discuss with FDA possible 522 study designs that may be sufficient to support a PMA application.

Failure of a manufacturer to meet its obligations under section 522 is a prohibited act under section 301(q)(1)(C) of the act, 21 U.S.C. 331(q)(1)(C). Further, under section 502(t)(3) of the act, 21 U.S.C. 352(t)(3), a device is misbranded if there is a failure or refusal to comply with any requirement under section 522 of the act. Please note that violations of sections 301(q)(1)(C) or 502(t)(3) may lead to regulatory actions including seizure of your product, injunction, prosecution, or civil money penalties.

Sincerely yours,

Thomas Gross, MD, MPH
Acting Director
Office of Surveillance and Biometrics
Center for Devices and Radiological Health
Food and Drug Administration