NATIONAL WOMEN'S HEALTH NETWORK
A VOICE FOR WOMEN, A NETWORK FOR CHANGE

October 7, 2011

Jeffrey Shuren, M.D., J.D.
Director
Center for Devices and Radiologic Health
Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993-0002

Re: Reclassification of trasvaginally placed surgical mesh

Dear Dr. Shuren,

I am writing on behalf of the National Women's Health Network, a nonprofit advocacy organization that works to improve the health of all women. The Network brings the voices of women consumers to policy and regulatory decision-making bodies. We are supported by our members and do not take financial contributions from drug companies, medical device manufacturers, insurance companies, or any other entities with a financial stake in women's health decision-making.

We write today to urge the Food and Drug Administration (FDA) to adopt the recommendation of its Obstetrics & Gynecology Devices Panel and reclassify transvaginally placed surgical mesh for the treatment of pelvic organ prolapse (POP) to Class III. Moreover, we strongly urge the FDA to include the indication of treatment of stress urinary incontinence (SUI) in the reclassification of the product. All vaginal mesh products – no matter the indication – should be evaluated via the PMA process. Vaginal mesh is a permanent implant, failure of which can and has caused serious adverse health consequences for hundreds of thousands of women. Reclassification of both indications would be the best way to ensure consistency across the device review process for vaginal surgical mesh products.

Additionally, we commend the FDA for convening this advisory panel to assess the safety and effectiveness of vaginal surgical mesh in response to the high number of adverse events reported to the FDA. It is an essential, and too-infrequent, step in ensuring patient health for the FDA to reassess the safety and effectiveness of implanted products which are approved based on trials of

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a few years duration, or cleared via the 510(k) pathway with little to no clinical data, but which are used by patients for much longer durations. Once a product has been on the market for several years, longer-term data from a diverse group of patients using the product outside the narrow constructs of a clinical trial can reveal new safety signals that merit examination, as has been the case with vaginal mesh.

Unfortunately, however, there is a noticeable lack of rigorous, long-term data for vaginal mesh products, although they have been on the market for more than a decade. This problem was noted by the panel, which was particularly concerned that the lack of data prevented evaluators from conducting sub-analyses that would inform an understanding of how safety varies by specific product, product placement, or patient population. The Network is also concerned about this dearth of evidence and strongly agree with the panel that more data is needed. The reclassification to Class III of all vaginal mesh products would ensure that sponsors conduct preclinical studies that provide independent evidence of safety and effectiveness, and that the agency could require sponsors to conduct post-market surveillance to detect potential problems that would not have been identified in a carefully screened clinical trial population.

The Network fully supports the FDA's recommendation, put forward at the Advisory Panel meeting and echoed by panel members, to reclassify surgical mesh for POP repair to Class III. We agree that pre-market, prospective randomized controlled trials are needed to demonstrate safety and efficacy of vaginal mesh for this use. And we support the FDA's recommendation that pre-market studies compare mesh to a non-mesh control arm – without this comparison, it will be nearly impossible for health care providers to give a woman the information she needs about the risks and benefits of the different options she must choose between. To further support both the development of science-based clinical recommendations and women's informed decision making, we recommend that the FDA require sponsors to conduct post-market studies that examine whether mesh is safer in certain populations and whether the severity of the condition has an impact on the effectiveness of mesh.

We also urge the FDA to reclassify vaginal surgical mesh products used for SUI repair, known as bladder slings. The Advisory Panel did not specifically recommend that surgical mesh for SUI be reclassified to Class III, but its recommendations of additional research requirements for sponsors seeking approval of surgical mesh for this indication can be followed most effectively if mesh for SUI repair is a Class III product. The panel agreed that the agency should require preclinical studies if a mesh product is in any way different from a current product – which is a significantly higher standard than that required to demonstrate substantial equivalence, the standard for products being considered under the 510(k) process. The Panel specifically recommended that the FDA require a one-year pre-market randomized clinical trial and post-market surveillance for any new mesh product. This combination essentially describes the requirements for a product undergoing a PMA review, as a Class III product would do.

Although the FDA did not recommend reclassifying mesh for SUI repair, the agency review documents show that some FDA staff who reviewed the data were concerned about the rate and severity of adverse events reported in the literature and to the FDA. They concluded that pre and post-market studies on the safety and effectiveness of mesh for SUI repair are necessary to adequately evaluate the product – a conclusion shared by the panel. Several panel members also noted that the totality of the data on bladder slings is weak and consequently there is not enough information available for women to make informed treatment decisions. In light of these findings, we strongly agree with the call for pre and post-market studies, and believe the appropriate way to ensure that this requirement will be met is to reclassify the device for this indication.

Furthermore, reclassification for both indications will prevent sponsors from exploiting the disparity in standards that would result from reclassifying mesh for one indication without reclassifying for another, very similar indication. Several panel members raised concerns about this possibility, noting the likelihood that a disproportionate number of future applications would be for an SUI indication instead of a POP indication because it will be easier to meet the lower standard, even though surgeons will continue to use the products for both indications, regardless of the labeled indication. We urge the FDA not to let this happen – instead reclassify all vaginal surgical mesh products to Class III.

Lastly, reclassification is necessary because Class II special controls are not sufficient to provide a reasonable assurance of safety and effectiveness. The FDA noted in the Executive Summary prepared for the panel meeting, "Surgical Mesh for Treatment of Women with Pelvic Organ Prolapse and Stress Urinary Incontinence," that "it does not believe the problems associated with mesh procedures can be attributed exclusively to surgeon skill and training." Although training may reduce the number of complications, there isn't evidence showing whether, or to what extent, complications result from inadequate training or lack of surgical skill. So while it's tempting to put our trust in the skills and education of physicians, there is no evidence that training for surgeons will address complications resulting from the mesh itself. Women deserve medical care that is backed up by more than anecdotal reports and the untested hope that better trained doctors may be able to reduce their risk of being harmed by these devices. As the panel noted, there really isn't enough evidence to determine whether the problems stem from the surgeon, the patient, or the device itself.

The FDA acknowledged that it can't know how a 510(k) product performs clinically until it's on the market. That lack of clinical certainty is a reasonable trade-off for the efficient use of agency and sponsor resources with some products, but an implanted device carries inherent risks which make the need for data on product performance essential. For this reason, implanted devices should be class III so that the agency can more thoroughly evaluate clinical performance before

approving a product. Vaginal surgical mesh products, with their history of recalls due to severe, permanent side effects including crippling pain, infections, and additional surgeries, should most certainly be evaluated in this way. Women's horrifying experiences with surgical mesh – all of which has been cleared through the 510(k) process – clearly demonstrate the need for changes in FDA's treatment of implanted devices. One Panel member summed up the situation succinctly when she said, "the 510(k) process failed our patients."

In conclusion, we urge the Panel to recommend that all vaginal mesh be reclassified as Class III. We recommend that the FDA extend a 3-year grace period to manufacturers of mesh products currently on the market during which the manufacturers will be allowed to continue marketing their products while immediately beginning post-market 522 studies that will independently assess safety and effectiveness. Sponsors may then use the results of these studies in future PMA applications. In the meantime, women considering bladders slings for SUI repair must be provided with clear information about the possibility that these products may cause serious complications and must be informed that studies are underway to better determine the safety and effectiveness of these products. Women suffering with POP and SUI deserve options that are safe and effective – not the false hope offered by implants that leave them with new, and more devastating health problems.

Sincerely,

Cynthia A. Pearson
Executive Director
National Women's Health Network