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July 28, 2014

Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: Docket No. FDA-2014-N-0297: Proposed order to reclassify surgical mesh for transvaginal repair of pelvic organ prolapse and surgical instrumentation for urogynecologic surgical mesh procedures

and

Docket No. FDA-2014-N-0298: Proposed administrative order to require the filing of a premarket approval application if surgical mesh for transvaginal repair of pelvic organ prolapse is reclassified from class II to class III

To Whom It May Concern:

Public Citizen, a consumer advocacy group with more than 300,000 members and supporters nationwide, strongly supports (1) the Food and Drug Administration's (FDA's) proposed order to reclassify surgical mesh for transvaginal repair of pelvic organ prolapse (POP) from class II to class III and to reclassify urogynecologic surgical mesh instrumentation from class I to class II;[1] and (2) the agency's proposed order to require the filing of a premarket approval application (PMA) for surgical mesh for transvaginal POP repair.[2]

The proposed orders are consistent with the third of three actions requested in our August 25, 2011, petition to the FDA regarding non-absorbable surgical mesh products specifically designed and labeled for transvaginal POP repair (copy enclosed).[3] Such actions are clearly appropriate, because not only are general controls and special controls together insufficient to provide a reasonable assurance of safety and effectiveness for these devices but the available evidence shows that such devices (a) offer no clinically significant benefits in comparison to surgical

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[1] 79 Fed. Reg. 24634-24642.
[2] 79 Fed. Reg. 24642-24648.
[3] Carome MA, Wolfe SM, Elliott DS, Wall LL. Petition to the FDA to ban non-absorbable surgical mesh products designed and labeled for transvaginal repair of pelvic organ prolapse. August 25, 2011. Available at http://www.citizen.org/documents/Petition_to_Ban_Surgical_Mesh_for_Transvaginal_Repair_of_Pelvic_Organ_Prolapse.pdf. Accessed July 14, 2014.

repairs for POP performed without placement of surgical mesh; and (b) have high rates of serious complications, many of which require additional surgical intervention and some of which are not amenable to surgical correction and result in permanent life-altering harm, therefore presenting an unreasonable and substantial risk of illness or injury.

We believe that there is sufficient basis for the FDA to go even further, as requested in our 2011 petition, by (a) banning the marketing of all currently available non-absorbable surgical mesh products for transvaginal repair of POP; and (b) ordering all manufacturers of such devices to recall these products. Unfortunately, the agency denied our petition on May 1, 2014.[4] A review of the literature cited by the FDA in its proposed order reiterates most of the points regarding the safety and effectiveness of surgical mesh products for transvaginal POP repair that we discussed in our petition. Unfortunately, the FDA's reckless delays and inadequate action regarding surgical mesh for transvaginal POP repair have resulted, and will continue to result, in thousands of women being unnecessarily exposed to a wide array of serious risks, many of which can permanently alter their quality of life.

We offer the following additional comments regarding the proposed orders:

(1) In discussing the risks of surgical mesh for transvaginal POP repair, the FDA listed infection as one of the risks of these devices. The agency neglected to note in its discussion that infections related to these devices are inevitable given that the vaginal mucosa cannot be completely sterilized prior to transvaginal insertion of surgical mesh. Thus, the mesh, an implanted foreign body, can become contaminated with bacteria during the surgical placement, which can lead to infections and other secondary complications. Dr. Tom Margolis, a pelvic surgeon, highlighted this issue in his testimony before the Obstetrics and Gynecology Devices Panel of the Medical Devices Advisory Committee on September 8, 2011:[5]

> Transvaginal implantation of synthetic mesh, for any reason, is a surgical theory and technique that defies core surgical doctrines.
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> In 1982, the [Centers for Disease Control and Prevention] adopted the American College of Surgeons' wound classification system that classifies wounds according to the likelihood and degree of wound contamination during surgery. In this system, vaginal surgery is classified as **clean-contaminated**, carrying a risk of wound infection of 3 to 11 percent, as compared to **clean** wounds, which carry a risk of infection of 1 to 5 percent. [Emphasis added]

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[4] Food and Drug Administration. Letter regarding citizen petition-docket number FDA-2011-P-0641. May 1, 2014. http://www.citizen.org/documents/1963_FDA%20Final%20Response%20to%20Petition-Denial_May%201,%202014.pdf. Accessed July 14, 2014.

[5] Food and Drug Administration. Transcript of the September 8, 2011 meeting of the Obstetrics and Gynecology Devices Panel. http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/ObstetricsandGynecologyDevices/UCM275043.pdf. Accessed July 17, 2014.

> The vagina is classified as clean-contaminated because normal vaginal flora cannot be surgically cleansed from the operative field. These normal flora include a diverse array of bacteria, including, but not limited to, staph, strep, *Klebsiella*, *Peptococcus*, *Peptostreptococcus*, bacteroides, all of which are found in wound infections.
>
> The implantation of contaminated synthetic mesh through the vagina defies basic surgical tenets because, by definition, it is not performed in a sterile manner. In fact, so-called mesh erosion, the most common mesh complication, is in reality mesh infection with chronic wound breakdown.

(2) The FDA also noted that some of the serious complications unique to transvaginal POP repair using mesh products may require removal or excision to manage the sequelae (for example, pelvic pain; infection, including pelvic abscess; and dyspareunia [pain with sexual intercourse]). The agency noted that these complications "can be life altering for some women as mesh removal or excision may require multiple surgeries and sequelae may persist despite mesh removal."[6] The agency should also note that for some women who have suffered serious adverse events following transvaginal POP repair with surgical mesh, complete removal of the mesh is not possible. Again, Dr. Margolis highlighted this point in his testimony before the Obstetrics and Gynecology Devices Panel of the Medical Devices Advisory Committee:[7]

> What it's like to remove mesh, from the surgeon's perspective, can perhaps be appreciated by this analogy. Extirpation of vaginal mesh is akin to taking a hammer and chisel and trying to remove the rebar from a sidewalk, while leaving the cement otherwise intact and not damaging the water mains and power lines below. It is difficult, if not impossible, to remove all the mesh and do it safely.

(3) The FDA noted that the consensus the Obstetrics and Gynecology Devices Panel reached at its September 8, 2011, meeting was that "a favorable benefit-risk profile for surgical mesh used for transvaginal POP repair has not been well established."[8] However, not only has a favorable benefit-risk profile not been established for these devices, the weight of evidence currently demonstrates that the benefit-risk profile is *unfavorable*.

(4) The Obstetrics and Gynecology Devices Panel consensus was that that premarket clinical data are needed for surgical mesh for transvaginal POP repair. Moreover, a majority of the panel members "recommended that these devices be evaluated against a control arm of traditional 'native tissue' (nonmesh) repair to demonstrate a reasonable assurance of safety and effectiveness." The panel members also recommended that these studies

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[6] 79 Fed. Reg. 24634-24642.

[7] Food and Drug Administration. Transcript of the September 8, 2011 meeting of the Obstetrics and Gynecology Devices Panel. http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/ObstetricsandGynecologyDevices/UCM275043.pdf. Accessed July 17, 2014.

[8] 79 Fed. Reg. 24634-24642.

"evaluate both anatomic outcomes and patient satisfaction and that the duration of follow-up should be at least 1 year."[9] We strongly agree with the panel's consensus and its two recommendations regarding the design of PMA clinical trials of these devices.

(5) The FDA proposed requiring that PMAs for surgical mesh for transvaginal POP repair "be filed with the agency by the last day of the 30th calendar month beginning after the month in which the classification of the device in class III becomes effective, or on the 90th day after the date of the issuance of a final order under 515(b), whichever is later."[10]

This proposed timeframe, given the FDA's already prolonged delays in taking regulatory action on surgical mesh for transvaginal POP repair, is unacceptably long and will likely lead to numerous women suffering avoidable, serious harms. We therefore urge the FDA to require instead that PMAs for surgical mesh for transvaginal POP repair be filed with the agency by the last day of the sixth calendar month beginning after the month in which the classification of the device in class III becomes effective, or on the 90th day after the date of the issuance of a final order under 515(b), whichever is sooner.

Thank you for the opportunity to provide comments on these important issues.

Sincerely,

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[9] *Ibid*.
[10] 79 Fed. Reg. 24642-24648.

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Enclosure