February 2, 2015

Jeffrey Shuren, MD, JD
Director
Center for Devices and Radiological Health
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Re: Downclassification of female condoms

Dear Dr. Shuren,

The National Female Condom Coalition (NFCC) represents a diverse and wide-ranging group of advocates from the sexual health and reproductive justice, HIV/AIDS, and LGBTQ communities across the US.

We write to respectfully urge the USFDA to consider downclassification of female condoms to reflect the current state of evidence regarding the device's effectiveness and safety. We request a meeting to discuss our concerns regarding the current Class III designation of female condoms and to hear FDA's thinking about the feasibility of proceeding with a downclassification request.

As you know, female condoms are the only woman-initiated technology currently available that offers protection from both unintended pregnancy and sexually transmitted infections (STIs), including HIV.

The female condom product category has significantly evolved since the FDA first reviewed the FC1 female condom application more than 20 years ago in 1993. Multiple studies since then confirm the safety and performance of the FC2 female condom as well as the performance and safety of new female condoms. International researchers agreed on standardized definitions of female condom failure modes, and international testing standards and product guidelines for female condoms to guide the industry and validate product quality now exist.

Background
When the USFDA approved the FC1 female condom in 1993, it determined that female condoms were substantially different from male condoms and that insufficient safety and performance evidence necessitated its categorization as a Class III medical device. This Class III designation was not revisited in 2009 when the USFDA reviewed then current data and approved the FC2 female condom.

Since the FDA's 2009 review, several important changes in the female condom product category have occurred. The World Health Organization (WHO), UNAIDS, UNFPA, and Family Health International collaborated to release the *WHO/UNFPA Female Condom Generic Specifications, Prequalification and Guidelines for Procurement, 2012.* At the same time, the International Organization for Standardization (ISO) Technical Committee ISO/TC 157 published the international standard on female condoms, ISO 25841 (published 2012). This standard provides essential guidance on specifications and test methods used to verify female condom quality and was updated in 2014. Given the large number of possible female condom designs and different materials used, the standard is

not generic in the sense of specifying requirements for properties such as dimensions and strength. Instead, it requires manufacturers to verify the performance/effectiveness of any new or modified female condom design by clinical studies. Manufacturers are also required to base product specification on the properties of the condoms used in any clinical performance or effectiveness trial.

ISO is now finalizing a standard to provide guidance on the design, execution, and analysis of clinical trials on female condoms (ISO 29943-2) and male condoms (ISO29943-1). The process of getting the clinical trial guidance and standards for female condoms is supported by the WHO, USFDA, ISO, and experts in the field.

The Female Condom Technical Review Committee, first convened in 2006 by UNFPA and the WHO Department of Reproductive Health and Research (RHR), continues to evaluate female condom manufacturers' dossiers in order to make recommendations for bulk procurement of female condoms that meet a set of predetermined performance, safety, and quality requirements. In addition, UNFPA and WHO/RHR have held several workshops to assist male condom and other manufacturers interested in designing/manufacturing new female condoms. These workshops cover all manufacturer requirements from research, design, development, safety, efficacy, regulation, promotion, and procurement. Technical experts are available at these meetings in all aspects of testing, manufacture and clinical trials to support and advise manufacturers. These meetings are used to disseminate the standardized definitions of female condom failure modes which were developed by international researchers under the auspices of WHO during the first Female Condom technical Review Meeting and published in 2007.[1] These definitions are now regularly used to enable comparisons of study results.[2]

Public sector procurement of the FC2 female condom has grown. According to the Reproductive Health Interchange, international procurement agencies purchased 26.8 million units for distribution in 2014.[3] While the primary market for female condoms has been in developing countries' HIV prevention programs, purchasing by the public health sector and individual consumers has steadily increased in the US. The Female Health Company shared via personal communication in December 2013 that US consumer sales increased by more than 40% from 2012 to 2013.

The pipeline of new female condom products is growing to respond to consumer interest.[4] As new female condom products have been developed, studies in multiple countries have confirmed the safety and performance of new female condom products relative to the FC2. A summary of female condom performance and effectiveness across multiple studies shows low failure rates across all products.[5] These new products are being made available in other countries where regulatory approval is based on performance and failure mode

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[1] Beksinska, M.E., Joanis, C., Manning, J., Smit, J., Callahan, M., Deperthes, B., & Usher-Patel, M. (2007). Standardized definitions of failure modes for female condoms. *Contraception,* 75, 251– 255.

[2] Beksinska. M.E., Piaggio, G., Smit, J.A., Wu, J., Zhang, Y., Pienaar, J.; Greener, R., Zhou, Y. & Joanis, C. (2013). Performance and safety of the second-generation female condom (FC2) versus the Woman's, the VA worn-of-women, and the Cupid female condoms: a randomised controlled non-inferiority crossover trial. *Lancet Global Health*, 1 (e), 146-152.

[3] Reproductive Health Interchange (2015). RHIinterchange. Retrieved from http://www.myaccessrh.org/rhi-home.

[4] Beksinska, M.E., Smit, J., Joanis, C., & Potter, W. (2012). New female condoms in the pipeline. *Reproductive Health Matters, 20*(40):186-196.

[5] Gallo, M.F., Kilbourne-Brook, M., & Coffey, P.S (2012). A review of the effectiveness and acceptability of the female condom for dual protection. *Sexual Health,* http://dx.doi.org/10.1071/SH11037.

study data. Such data are similar to that required for approval of male condoms. While in the US, the FC2 remains the only female condom available largely due to the Class III designation.

If the Class III designation of female condom products is intended to ensure product safety, we strongly advocate no longer requiring this control since other controls already serve this purpose. The Class III designation serves as a barrier to manufacturers seeking USFDA approval and ultimately negatively impacts women and men who need more prevention options. The high costs associated with a Class III product application prohibit manufacturers from submitting their products for review, thus limiting female condom options in the US to a single product, the FC2, while women and men in other countries are able to access and choose from a number of female condom products to reduce their risk of HIV, STIs, and unintended pregnancy.

Reducing regulatory barriers to approval of new female condom products that are safe and effective would expand choice and promote individual and public health.[4] We believe the ever-growing evidence base on female condom safety and effectiveness will support a conclusion that the Class III premarket approval process is no longer needed for new female condoms. Properly designated Class I general controls and Class II special controls can reasonably be expected to ensure their safety and effectiveness. As part of the process for a petition for reclassification, we would be prepared to work with FDA to develop a new guidance document to reflect these new controls. The evidence to support our petition is as follows:

Female condoms are safe.

Twenty years of use data show that FC1/FC2 female condoms have a good safety record. New female condoms have been shown to be non-inferior to FC2.[2] A recent study of 600 women using four different female condom products indicated non-inferiority for performance for each product.[6] The *WHO Medical Eligibility Guidelines for Contraceptive Use* lists female condoms as a Category One, a product that can be used by any client.[7] The 2010 CDC *Medical Eligibility Criteria for Contraceptive Use* adapted from the WHO Guideline concurs with this recommendation. The *Family Planning: Global Handbook for Providers*, written by the US Agency for International Development (USAID), WHO, and Johns Hopkins University, states that there are no adverse side effects and no known health risks associated with using female condoms. Latex and synthetic latex female condoms are made by a dipping process that is very similar to the method used for making male latex condoms and medical gloves, products with a long history of safety. Additionally, a January 2015 search of FDA's Manufacturer and User Facility Device Experience (MAUDE) database from January 1, 1994 through December 31, 2014 resulted in only one report of an adverse event related to the FC1 and none for the FC2.

Female condoms perform well.

Millions of women and men have used female condoms (primarily the FC1/FC2 female condom) since approved by the FDA 20 years ago. Clinical data show that female condoms offer good performance and have low failure

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[6] Beksinska, M.E., Piaggio, G., Smit, J.A., Wu, J., Zhang, Y., Pienaar, J.; Greener, R., Zhou, Y. & Joanis, C. (2013). Performance and safety of the second-generation female condom (FC2) versus the Woman's, the VA worn-of-women, and the Cupid female condoms: a randomised controlled non-inferiority crossover trial. *Lancet Global Health*, 1 (e), 146-152.

[7] *WHO Medical Eligibility Guidelines for Contraceptive Use,* 4th edition, (2009) http://whqlibdoc.who.int/publications/2010/9789241563888_eng.pdf?ua=1

rates.[8] Qualitative data indicate that women are better able to negotiate safer sex practices when female condoms are available.[9] Such ability is of critical importance to women's health, particularly in contexts where male condom use is not possible. Female condoms offer women a unique and important prevention option. Studies also demonstrate the total number of protected sex acts increases when female condoms are made available to couples alongside male condoms.[10-13]

Female condoms are effective.

Three studies examining protection offered against pregnancy by the female condom indicate it is an effective contraceptive.[14-16] Together these trials indicate that perfect use of female condoms offer between .08% and 9.5% probability of pregnancy. Data from these studies indicate that typical use of female condoms results in 3.2% to 22.2% probability of pregnancy. Research also demonstrates that female condoms offer effectiveness for reducing women's risk of STIs comparable to that of male condoms. [17-19]

Standard definitions, testing procedures, and guidance exist and are accepted.

International researchers developed, published, and adopted standardized definitions of performance that are now widely known and consistently used by researchers evaluating the safety and performance (functionality) of female condom products.[20-21] These standardized definitions allow comparison across products and across clinical studies. The table below illustrates outcomes found in one non-inferiority cross-over trial published by Beksinska, et al. in 2013.[8]

Female Condom Product	FC2	Cupid	Woman's Condom	VA wow
Total Condom Failure	3.43%	4.52%	3.85%	3.02%
Total Clinical Failure	2.88%	3.87%	3.05%	2.49%

[8] Beksinska, M.E., Piaggio, G., Smit, J.A., Wu, J., Zhang, Y., Pienaar, J.; Greener, R., Zhou, Y. & Joanis, C. (2013). Performance and safety of the second-generation female condom (FC2) versus the Woman's, the VA worn-of-women, and the Cupid female condoms: a randomised controlled non-inferiority crossover trial. *Lancet Global Health*, 1 (e), 146-152.

[9] Hatzell, T., & Feldblum, P. J. (2003). The female condom: Is "just as good" good enough? *Sexually Transmitted Diseases*, 440-442.

[10] Barbosa, R.M., Kalckmann, S., Berquó, E., & Stein, Z. (2007). Notes on the female condom: Experiences in Brazil. *International Journal of STD and AIDS, 18*(4): 261-266.

[11] Hoke TH., Feldblum, P.J., Van Damme, K., Nasution, M.D., Grey, T.W., Wong, E.L., Ralimamonjy, L., Raharimalala, L., & Rasamindrakotroka, A. (2007). Randomised controlled trial of alternative male and female condom promotion strategies targeting sex workers in Madagascar. *Sexually Transmitted Infections, 83*(6): 448-453.

[12] Choi, K., Hoff, C., Gregorich, S.E., Grinstead, O., Gomez, C., & Hussey, W. (2008). The efficacy of female condom skills training in HIV risk reduction among women: A randomized controlled trial. *American Journal of Public Health*, *98*(10), 1841-1848.

[13] Vijayakumar G, Mabude Z, Smit J,Beksinska M, Lurie M. A Review of the impact of the female condom on proportion of protected sex acts and STI incidence. *International Journal of STD and AIDS*. 2006; 17(10):652-659.

Standard product guidelines for testing laboratories established by the ISO also now exist to ensure female condom product quality. As previously mentioned, UNFPA/WHO developed a WHO Prequalification Scheme to ensure that female condoms considered by international procurement agencies meet international specifications for clinical performance, design, and packaging.

Leading health authorities recognize that female condoms meet a public health need.

WHO and USAID recommend counseling about and access to female and male condoms for family planning clients who are also at risk of HIV. Additionally, the US government is one of the largest donor procurers of female condoms worldwide, and the President's Emergency Plan for AIDS Relief (PEPFAR) identifies female condoms as "unique in providing a female-controlled HIV prevention option." And the Centers for Disease Control and Prevention cite condom distribution programs as effective interventions for reducing HIV and STIs.

Conclusion

For each of these reasons, we urge the FDA to reclassify female condoms from Class III to Class II.

We request the opportunity to meet with you to discuss this issue with you in more detail. Please contact Jessica Terlikowski of the National Female Condom Coalition at jterlikowski@aidschicago.org or (312) 334-0931 to schedule a meeting.

Sincerely on behalf of the National Female Condom Coalition,

Jessica Terlikowski
AIDS Foundation of Chicago, National Female Condom Coalition Secretariat

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[14] Bounds, W., Guillebaud, J., & Newman, G.B., (1992) Female condom (Femidom): a clinical study of its use-effectiveness and patient acceptability. *British Journal of Family Planning Fam Plann* 1992; 18: 36–41.

[15] Farr, G., Gabelnick, H., Sturgen, K., & Dorflinger, L. (1994). Contraceptive efficacy and acceptability of the female condom. *American Journal of Public Health* 1, 84, 1960–1964.

[16] Trussell, J (1998). Contraceptive efficacy of the Reality female condom. *Contraception,* 58: 147–148.

[17]French, P.P., Latka, M., Gollub, E.L., Rogers, C., Hoover, D.R.,& Stein, Z.A. (2003). Use-effectiveness of the female versus male condom in preventing sexually transmitted disease in women. *Sexually Transmitted Diseases*, 30(5):433–439.

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[19.] Feldblum PJ et al. (2001). Female condom introduction and sexually transmitted infection prevalence: results of a community intervention trial in Kenya. *AIDS*, 15(8):1037–1044.

[20] Beksinska, M.E., Joanis, C., Manning, J., Smit, J., Callahan, M., Deperthes, B., & Usher-Patel, M. (2007). Standardized definitions of failure modes for female condoms. *Contraception,* 75, 251– 255.

[21] Beksinska, M.E., Smit, J., Joanis, C., & Potter, W. (2012). New female condoms in the pipeline. *Reproductive Health Matters, 20*(40):186-196.