DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
10903 New Hampshire Avenue
Building #51
Silver Spring, MD 20993

June 10, 2013

Bonnie Scott Jones, Esq.
Center for Reproductive Rights
120 Wall Street, 14th Floor
New York, NY 10005

Re: Docket No. 2001P-0075/CP1

Dear Ms. Jones:

This letter further responds to your citizen petition dated February 14, 2001, with supplements submitted on August 7, 2001 and February 13, 2002, which you submitted on behalf of more than 60 family planning and health organizations (Citizen Petition). You requested that the Food and Drug Administration (FDA or we) exempt from prescription dispensing requirements two emergency contraceptive drug products, Preven and Plan B, as well as any generic versions of these products. Plan B (levonorgestrel) tablets (0.75 mg) had been approved for prescription distribution to women under 17 years of age, and nonprescription distribution to women 17 and older. Teva Branded Pharmaceutical Products R&D (Teva) is currently the sponsor of Plan B, but does not currently market the drug. There are two approved generic versions of Plan B, Watson Laboratories, Inc. (Watson)'s "Next Choice" and Perrigo's "Levonorgestrel Tablets, 0.75 mg," and those products are being marketed. Plan B and its marketed generics are collectively referred to below as Plan B. Because Preven, formerly marketed by Gynetics, Inc., is no longer marketed, and there are no generic equivalent products to Preven, we do not further discuss it in this response.

Your petition contended that the prescription dispensing requirements for these products were not necessary to protect the public health and that a prescription-only (Rx) to over-the-counter (OTC) switch for consumers of all ages is authorized under 21 U.S.C. 353(b)(3) and 21 CFR 310.200. On June 9, 2006, FDA denied the Citizen Petition on the ground that it was not adequately supported by scientific evidence; neither the petitioners nor the members of the public who commented on the Citizen Petition provided FDA with sufficient data to meet the statutory and regulatory requirements for initiating rulemaking to switch Plan B to nonprescription status. Two months after the Citizen Petition response issued, in August 2006, FDA approved a supplemental new drug application (sNDA) submitted by the Plan B drug sponsor to allow distribution of Plan B without a prescription to adults 18 years or older (while it remained Rx for women younger than 18). That bifurcated approval status was the result of FDA's determination that the available data were insufficient to support approval of nonprescription use for younger women. FDA later lowered the cutoff age for nonprescription availability to 17 years of age, and that remains the current approval status for Plan B.

The June 2006 denial of the Citizen Petition was later vacated by a federal district court in a lawsuit brought by a group of individuals and reproductive health groups, including one of the petitioners, represented by your organization and seeking FDA approval of OTC availability of Plan B for all age groups. *See Tummino v. Torti*, 603 F.Supp. 2d 519 (E.D.N.Y. 2009) (hereinafter *Tummino I*). The court ordered, among other things, that "[t]he denial of the Citizen Petition is vacated and the matter is remanded to FDA to reconsider its decisions regarding the Plan B switch to OTC use." *Id.* at 550. In response to the court's order, FDA reopened the docket for the petition to accept new submissions, and reconsidered its decisions regarding the "switch to OTC use," taking into account the record before the Agency and the relevant developments since the June 2006 denial of the Citizen Petition. As a result of that review and further consideration by the Agency, FDA again determined that actual use and label comprehension studies were necessary for approval of OTC use for younger women for Plan B, and thus, FDA again denied the Citizen Petition in a letter to you dated December 12, 2011.

As you are aware, Teva markets another, similar drug product, sold under the trade name, Plan B One-Step (PBOS). PBOS was approved by the agency on July 10, 2009, as a nonprescription product for women ages 17 and over, and as a prescription product for women under age 17. PBOS is an emergency contraceptive product with a different dosing regimen but with the same active ingredient and indication as Plan B. More specifically, Plan B uses a two dose regimen with 0.75 mg of levonorgestrel in each tablet to be taken 12 hours apart, while PBOS is a single dose tablet that contains 1.5 mg of levonorgestrel.

On February 7, 2011, Teva submitted an sNDA for PBOS seeking to remove the prescription-only status for women younger than age 17 and to make PBOS nonprescription for all women of child-bearing potential. On December 7, 2011, FDA issued a complete response letter to Teva informing Teva that its application was not approved. Although FDA believed that there was adequate and reasonable, well-supported, and science-based evidence that PBOS is safe and effective and should have been approved for nonprescription use for all females of child-bearing potential, the Secretary of Health and Human Services did not agree that the application should be approved and she directed FDA to issue a complete response letter. See Statement from FDA Commissioner Margaret Hamburg, M.D. on PBOS (available at http://www.fda.gov/NewsEvents/Newsroom/ucm282805.htm) and see Statement by U.S. Department of Health and Human Services Secretary Kathleen Sebelius (available at http://www.hhs.gov/news/press/2011pres/12/20111207a.html).

On March 9, 2012, Teva submitted an sNDA to make PBOS available with no prescription requirements for any consumer (i.e., ending the Rx and OTC dual package configuration) and with labeling that limits OTC sales to consumers ages 15 and older. On April 30, 2013, FDA approved that sNDA. Thus, PBOS is currently approved for OTC availability to consumers ages 15 and older. In addition, FDA granted Teva three years of marketing exclusivity for the newly approved use.[1]

[1] FDA granted Teva three years of marketing exclusivity on the basis of actual use studies Teva conducted that FDA found essential to its approval. *See* 21 U.S.C. §§ 355(c)(3)(E)(iv), 355(j)(5)(E)(iv); 21 C.F.R. § 314.108(b)(5).

On April 5, 2013, the federal district court issued an opinion and order upon review of FDA's December 2011 denial of your citizen petition. *Tummino, et al. v. Hamburg, et al.*, ____ F.Supp. 2d ____, 2013 WL 1348656 (E.D.N.Y. Apr. 5, 2013) (hereinafter *Tummino II*) (judgment entered April 10, 2013). This ruling directs the defendants, Dr. Margaret Hamburg, the Commissioner of Food and Drugs and the Honorable Kathleen Sebelius, Secretary of Health and Human Services, to grant your 2001 Citizen Petition and to "make levonorgestrel-based emergency contraceptives available without a prescription and without point-of-sale or age restrictions within thirty days." The court further stated that, on remand, FDA may make appropriate labeling determinations.

On May 1, 2013, the government filed a notice of appeal and moved for a stay of the court's judgment pending appeal. On May 10, 2013, the federal district court issued another opinion and order denying the government's motion for a stay pending appeal. *Tummino, et al. v. Hamburg, et al.*, No. 12-CV-763 (ERK)(VVP) (E.D.N.Y. May 10, 2013) (hereinafter *Tummino III).* The court did, however, grant a stay pending the government's submission of a motion for stay in the Court of Appeals on the condition that the motion for a stay be filed by noon on May 13, 2013. That motion for a stay pending appeal was granted in part and denied in part by the Court of Appeals on June 5, 2013.

At this time, FDA is complying with the district court's order of April 5, 2013 to grant your petition by taking the steps described below. To comply with the *Tummino II* order, by letter dated today, FDA has invited the sponsor of PBOS to submit a supplement to its application to market the product as a nonprescription product available without point-of-sale or age restrictions.[2] FDA has indicated that the supplement can reference Teva's supplement submitted for PBOS in February 2011. *See Tummino III* at 3 (in support of FDA's December 2011 conclusion that the February 2011 sNDA was approvable). FDA has already reviewed that submission, and conducted recent reviews of PBOS related to the recent approval of that product as an OTC product for females ages 15 and up.

If Teva submits the supplement described, which can rely on the supplement submitted in February 2011, FDA, in conformance with the court's order, intends to approve in a timely manner PBOS as a nonprescription product available without point-of-sale or age restrictions. After we receive and approve Teva's supplement, we expect the sponsors of the generic versions of Plan B One-Step to submit appropriate amendments to their abbreviated new drug applications.

With respect to a supplement Teva submits to its PBOS NDA, FDA will need to determine the scope of any exclusivity after approval of the supplement. That determination could affect the labeling that could be approved for generic equivalents of Plan B One-Step.

Please be advised that FDA will not at this time take steps to change the approval status of the two-pill Plan B product or its generic equivalents. As you are aware, the district court's April

[2] In its motion for stay pending appeal, the government asserted that, because the Citizen Petition only pertained to Plan B (and not PBOS), the relief granted by the court should have been limited to Plan B. By undertaking to comply with the court order, FDA does not concede that the court had the authority to require an action related to a drug product (i.e., PBOS) that was not the subject of your Citizen Petition.

10, 2013, judgment expressly authorized FDA to comply with the judgment by making PBOS and not Plan B available if FDA believes that there is a significant difference between Plan B and PBOS. Specifically, while the Court's judgment directed the defendants to "make levonorgestrel-based emergency contraceptives available without a prescription and without point-of-sale or age restrictions within 30 days," it also provided that "FDA may determine whether any new labeling is reasonably necessary" and that, "if the FDA actually believes that there is any significant difference between the one- and two- pill products, it may limit its over-the-counter approval to the one-pill product." ECF No. 87, 04/10/13, at 1-2. FDA continues to believe, for the reasons that the government has previously explained in its briefs to the district court, there are significant differences between Plan B and PBOS under FDA's regulations and the Federal Food, Drug, and Cosmetic Act.

It is, moreover, the PBOS application that contained actual use data specifically addressing the ability of adolescents, including younger adolescents, to understand and follow the directions for safe and effective use as a nonprescription product; there are fewer data available regarding the actual use of Plan B as a nonprescription product by younger adolescents. FDA therefore believes it is appropriate and consistent with the Court's order to comply by making only PBOS (and not the two-pill product) available OTC for younger adolescents.

In conclusion, as directed by order of a federal court, your petition is granted.

Sincerely,

Janet Woodcock, M.D.
Director, Center for Drug Evaluation and Research