



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002

December 12, 2011

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 had 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) is approved for prescription (Rx) distribution to women under 17 years of age, and nonprescription distribution to women 17 and older. Teva Pharmaceutical Industries, Ltd. (Teva) is currently the sponsor of Plan B, but no longer markets 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. Preven, formerly marketed by Gynetics, Inc., is no longer marketed, and there are no generic equivalent products to Preven. Hereafter, we discuss your petition requests only as they relate to Plan B (although not currently marketed, but marketing could be resumed) and its marketed generics (collectively referred to below as Plan B).

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 had 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 the distribution of Plan B without a prescription to adults 18 years or older (while it remained prescription-only 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.

The June 2006 denial of the Citizen Petition was later vacated by the 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). The court ordered, among other things, that “[t]he denial of the Citizen Petition is vacated and the matter is remanded to the FDA to reconsider its decisions regarding the Plan B switch to OTC use.” *Id.* at 550. The court explained that remand on this issue “[wa]s the appropriate remedy” because “a decision whether Plan B, a systemic hormonal contraceptive drug, may be safely used without a prescription” by women younger than 17 years of age “is best left to the expertise of the FDA, to which Congress has entrusted this responsibility; it should not be made by a federal district court judge.” *Id.* at 549.

Pursuant to the court’s order, FDA has 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. The essential question at issue is whether there were sufficient data in the record to establish the safety and effectiveness of OTC use by younger women, or whether additional data in the form of the results of actual use and label comprehension studies performed using younger women as subjects would be required. FDA was aware, even at the time of the remand, that the Plan B sponsor intended to conduct actual use and label comprehension studies. FDA concluded, as a matter of science and administrative efficiency, that it would be best to review the results of these studies before resolving the essential question on remand.

The sponsor conducted its studies using Plan B One-Step instead of Plan B. Plan B One-Step 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 Plan B One-Step is a single dose tablet that contains 1.5 mg of levonorgestrel.

Whether actual use and label comprehension data were needed for approval of the nonprescription use of Plan B One-Step is directly relevant to whether those data were needed for the same approval for Plan B because of the similarities between the products and the data that the sponsor had developed to support the OTC approval of the products. Nevertheless, the two drugs are not the same product, and all of the data supporting one application cannot automatically be used for the other. In particular, because Plan B One-Step consists of a single tablet, the dosing data for Plan B One-Step could not provide support for an OTC switch of Plan B as that data would not adequately address the ability of subjects to correctly follow the directions related to the timing of a second dose that is required for proper use of Plan B.

Thus, as a scientific matter, if additional data regarding the OTC use by younger women were needed for Plan B One-Step, that type of data would also be needed for Plan B, but those Plan B One-Step studies would not be transferable to Plan B. Instead, there would need to be new studies conducted using Plan B and its labeling, because it has more complicated directions for use, raising additional questions as to label comprehension and actual use.

FDA received the results of the studies on Plan B One-Step in February 2011 when Teva submitted an SNDA requesting full nonprescription status for Plan B One-Step without an age

restriction, and concluded its review of the data on December 6, 2011. As a result of that review and further consideration by the Agency, and as discussed in greater detail below, FDA has determined that the actual use and label comprehension studies were necessary for approval of OTC use for younger women for both Plan B and Plan B One-Step. Because these data have not been presented to FDA for Plan B, the drug product that is the subject of this petition, FDA again denies your petition.

## **BACKGROUND**

### **I. Legal Framework**

FDA's authority to exempt a drug from Rx requirements is based on section 503(b) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 353(b)). Under section 503(b)(1) of the Act, we restrict a drug to Rx status when we determine that the drug is not safe for use except under the supervision of a practitioner licensed by law to administer the drug. A drug will be restricted to Rx status when FDA finds that "because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, [it] is not safe for use except under the supervision of a practitioner licensed by law to administer such drug" (21 U.S.C. 353(b)(1)). In addition, section 503(b)(3) of the Act provides that a drug subject to section 505 of the Act (21 U.S.C. 355, governing approval of new drugs) may be removed by regulation from Rx status when such requirements are deemed not necessary for the protection of the public health. For a drug to be legally marketed (whether Rx or OTC), the safety and efficacy standards set forth in section 505 of the Act must be met.

FDA regulations recognize three different ways to initiate FDA consideration of whether a drug approved only for prescription dispensing should be switched to OTC status. First, the Commissioner may, on her own accord, initiate a rulemaking proceeding (see 21 U.S.C. 353(b)(3); 21 CFR 310.200(b)). Second, a drug sponsor may submit a supplement to an approved drug application (21 CFR 310.200(b) ("A proposal to exempt a drug from the prescription-dispensing requirements . . . may be initiated by . . . any interested person . . . in the form of a supplement to an approved new drug application."); 21 CFR 314.71(a)). Third, an "interested person" may petition FDA under FDA's citizen petition procedures (see 21 CFR 310.200(b) ("A proposal to exempt a drug from the prescription-dispensing requirements . . . may be initiated by . . . any interested person . . . [by filing ] a petition . . . pursuant to part 10 of this chapter [21 CFR Part 10, FDA's citizen petition procedures]")).

FDA recognizes two mechanisms for FDA to make an Rx to OTC switch: (1) to issue a regulation changing the status of an Rx-only drug product to an OTC drug when the Rx requirements of section 503(b)(1) are not necessary for the protection of the public health (see 21 U.S.C. 353(b)(3)); and (2) to approve a drug application (see 21 U.S.C. 355(c), (d)), or supplemental drug application (see 21 CFR 314.71(c)), requesting a switch.

Regardless of who initiates a request for an OTC switch or which mechanism is applicable, FDA can approve the switch only where the evidence demonstrates that the Rx dispensing requirements are no longer necessary to protect the public health by reason of the drug's toxicity or other potentiality for harmful effect, or by reason of the method of the drug's use, or the

collateral measures necessary to its use, and that the drug is safe and effective for use in self-medication as directed in proposed labeling (see 21 U.S.C. 353(b)(1) & (3); 21 CFR 310.200(b)).

## II. Factual Background<sup>1</sup>

FDA's June 2006 response to the Citizen Petition explained that drug approval decisions must be based on data that demonstrate that the statutory approval requirements have been satisfied. Data to support an Rx-to-OTC switch generally may include: safety and efficacy data in an original NDA for the prescription drug; safety and efficacy data from well-controlled trials conducted to support the OTC use; other available safety data; consumer data such as actual use data, self-selection data, and label comprehension data.<sup>2</sup> Actual use and label comprehension data are usually required when relevant safety data are not otherwise available because the drug: 1) is not the subject of an OTC monograph that includes OTC labeling; or 2) has not been previously approved by FDA for OTC use.

There are no applicable OTC monographs for Plan B and, as of June 2006, no levonorgestrel emergency contraceptive had been approved for OTC use. FDA found that the Citizen Petition did not contain the type of data that FDA requires to satisfy the statutory standard before granting a switch from Rx-only to OTC status, and, therefore, you had failed to meet your burden of establishing a basis to grant your petition.

In the Citizen Petition response, FDA also described the agency's evaluation of the data submitted with the sponsor's 2003 SNDA to switch Plan B OTC for women of all ages. Unlike the petitioners, the Plan B sponsor had conducted and submitted the results of label comprehension and actual use studies. However, most of the subjects of those studies were 17 years of age or older. The response to the Citizen Petition referenced an August 26, 2005 memorandum by Dr. Steven Galson, then the Director of FDA's Center for Drug Evaluation and Research (CDER), evaluating the data. In that memo, the CDER Director explained the need for scientific data to satisfy the statutory standards for the Rx-OTC switch. He concluded that the sponsor demonstrated, through the label comprehension and actual use studies submitted with the SNDA, that women 17 and older could use Plan B safely and effectively for emergency contraception in the OTC setting. However, the sponsor had not made that showing for women 16 and younger. Dr. Galson explained that, while the actual use and labeling comprehension studies for Plan B that were submitted with the sponsor's application were well designed, there were too few women under age 17 represented in those studies. In addition, he believed that what little data there were in this age group raised questions about their ability to use the product safely and effectively. He also explained his view that extrapolation from the adult data showing safe and effective OTC use to younger women was inappropriate. The CDER Director explained

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<sup>1</sup> FDA's June 2006 response to the Citizen Petition discussed in detail the regulatory history of Plan B from the time FDA approved the new drug application for prescription use of Plan B in July 1999, through the date of the Citizen Petition response. We will not repeat that history here.

<sup>2</sup> Actual use studies are trials designed to assess how consumers actually use the product in an OTC setting. These trials are usually open-label and are designed specifically to assess consumer use, but they may also provide information about safety. Self-selection studies assess whether consumers can properly discern whether it would be appropriate for them to use the drug based upon their ability to self-diagnose the condition for which the drug is indicated and based upon the warnings on the product label. Label comprehension studies are designed to assess consumer understanding of proposed OTC labeling.

that he would be prepared to reevaluate his conclusions if additional data on the younger age group were provided.

As noted, in August 2006, FDA approved the SNDA submitted by the Plan B drug sponsor to allow the distribution of Plan B without a prescription to adults 18 years or older (while it remained prescription-only for women younger than 18). That approval was based in large part on Dr. Steven Galson's August 2005 evaluation. Although the CDER Director found in August 2005 that the data on label comprehension and actual use were sufficient to support approval of nonprescription use by women 17 years of age and older, the August 2006 SNDA approval permitted nonprescription distribution to women 18 years of age and older. The change from 17 to 18 was based on enforcement concerns related to underage purchases documented in a July 2006 memorandum by then Acting Commissioner Andrew von Eschenbach.

On March 23, 2009, the *Tummino* court ordered FDA to permit the drug sponsor to make Plan B available to 17-year-olds without a prescription, after finding FDA's "hypothetical" enforcement concerns "implausible" and "untenable." 603 F. Supp. 2d at 550. The court, however, declined plaintiffs' request that the court order the OTC approval for the younger age groups, recognizing that the court lacked the scientific expertise to make that decision. *Id.* at 549. Instead, the court remanded that issue to FDA to reconsider. Moreover, the court did not reject FDA's explanation that an approval of an Rx-OTC switch must be supported by adequate scientific data demonstrating that the statutory standards were satisfied for all relevant age groups, or FDA's determination that neither the Citizen Petition nor the Plan B SNDA contained such data for women under the age of 17.

After receipt of the court's March 23, 2009 order, FDA informed the drug sponsor, in an April 21, 2009 letter, that the CDER Director had already concluded in August 2005 (as discussed above) that the available scientific data were sufficient to support the safe use of Plan B as a nonprescription product for women who are 17 years or older. The only reason that Plan B was not made available to 17-year-olds at the time of FDA's August 2006 approval decision was the concern expressed by the Commissioner about the ability of pharmacies (and their professional staffs) to enforce the age restriction with respect to purchases by women under age 17 without a prescription. In the April 2009 letter to the drug sponsor, FDA explained that it had reevaluated the enforceability concerns expressed by the Commissioner and found that they were not supported by the available data. Thus, FDA concluded, based on the 2005 findings of the CDER Director, that Plan B may be made available to women 17 years and older without a prescription.

The April 2009 letter further explained that, if the sponsor wanted to make this change from 18 to 17, it needed to submit revised labeling with the age change to FDA for the agency's approval. On June 11, 2009, the sponsor submitted a supplemental application requesting a labeling change to market Plan B without a prescription to women 17 years of age and older, and to make it available by prescription only to women 16 years of age and younger. FDA approved the supplemental application on July 10, 2009.

Because of the court's remand order, on July 17, 2009, FDA also re-opened the docket for your Citizen Petition for additional comments. The docket was re-opened to provide a vehicle for the petitioners, the other plaintiffs in the *Tummino* case, and any other member of the public or scientific community, to submit any comments, evidence, and information regarding your

request that FDA approve Plan B and its generics for distribution to women of all ages without restriction. To date, no new data or information has been submitted to the docket by you or any other interested member of the public regarding the approvability of Plan B for nonprescription use by women under the age of 17.

There have been other regulatory developments regarding levonorgestrel-containing emergency contraceptives in the last several years. On June 24, 2009, FDA approved "Next Choice," a generic version of Plan B manufactured by Watson. This initial approval of Next Choice was for prescription use only, because, at that time, the Plan B drug sponsor retained marketing exclusivity for Plan B for nonprescription use until August 24, 2009. On August 28, 2009, four days after expiration of the sponsor's marketing exclusivity for Plan B for nonprescription use, FDA approved Next Choice for nonprescription use by women 17 years of age and older. In late 2010, FDA approved a second generic version of Plan B, Perrigo's "Levonorgestrel Tablets, 0.75 mg" for nonprescription use by women 17 years of age and older.

In 2006, the Plan B sponsor also submitted an application to market another emergency contraceptive product, Plan B One-Step, which has the same active ingredient and indication as Plan B. However, Plan B and Plan B One-Step are not the same drug product; they differ in their dose and directions for use. Specifically, as noted, Plan B uses a two dose regimen with 0.75 mg of levonorgestrel in each tablet to be taken 12 hours apart, while Plan B One-Step is a single dose emergency contraceptive that contains 1.5 mg of levonorgestrel in a single tablet.

On July 10, 2009, FDA approved the application to market Plan B One-Step as a nonprescription product for women ages 17 and over, and as a prescription product for women under age 17.

On February 7, 2011, Teva submitted an SNDA for Plan B One-Step seeking to remove the prescription-only status for women younger than age 17 and to make Plan B One-Step 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. On the same date, two statements were issued regarding that decision. In one statement, FDA Commissioner Margaret Hamburg stated that "I agree with the [FDA's Center for Drug Evaluation and Research] that there is adequate and reasonable, well-supported, and science-based evidence that Plan B One-Step is safe and effective and should be approved for nonprescription use for all females of child-bearing potential." See Statement from FDA Commissioner Margaret Hamburg, M.D. on Plan B One-Step (available at <http://www.fda.gov/NewsEvents/Newsroom/ucm282805.htm>) (Hamburg Statement). However, the Secretary of Health and Human Services did not agree that the application should be approved and directed FDA to issue a complete response letter. In her statement, Secretary Kathleen Sebelius stated that "I have concluded that the data, submitted by Teva, do not conclusively establish that Plan B One-Step should be made available over the counter for all girls of reproductive age." 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>).

## ANALYSIS

As discussed above and recognized by the *Tummino* court, “[t]here are two means by which the FDA can switch a prescription-only drug to nonprescription status” – promulgating a rule through notice and comment rulemaking, or approving a drug application submitted by the drug sponsor seeking a switch. *Tummino*, 603 F. Supp. 2d at 525 (citing 21 U.S.C. 353(b)(3); 21 CFR 310.200(b)). Petitioners are not sponsors of a drug application, nor are they permitted to submit a supplement to another party’s drug application. See 21 CFR 314.71(a). Accordingly, under the regulatory framework discussed above, because petitioners have not submitted and cannot submit an application for drug approval, the only option available to them is to request that the agency initiate rulemaking pursuant to 21 U.S.C. 353(b)(3).

In the June 9, 2006 denial of your Citizen Petition, FDA determined that the petition and its supporting information did not provide sufficient data to satisfy the statutory requirements to approve an OTC switch for emergency contraceptives. Although your petition contained two expert declarations and citations to medical literature, and information about emergency contraceptive use in other countries, it did not contain labeling comprehension or actual use studies. FDA typically requires an evaluation of such data before switching an Rx product to OTC. Reviewers in CDER determined that actual use and labeling comprehension studies were lacking from your citizen petition and would be needed to support an OTC switch of Plan B (see Docket No. 2001P-0075/Reference #4 and #7). In addition, officials at FDA, including the Director of CDER at the time, found that the Plan B SNDA did not contain adequate data to satisfy the statutory requirements for a switch with respect to women under 17 years of age.

FDA made these findings regarding the inadequacy of the data for the younger age groups public, both in June 2006 when issuing its original response to the Citizen Petition, and in August 2006 when approving the Plan B SNDA. The Plan B sponsor then conferred with FDA regarding the data that FDA would require to approve nonprescription marketing to younger women. In the course of those communications, the sponsor informed FDA that it intended to conduct the required studies using Plan B One-Step, not Plan B, as the sponsor was no longer planning to market Plan B. Those communications continued as the sponsor conducted clinical trials/studies to develop data regarding whether women younger than 17 years of age can use Plan B One-Step safely and effectively, without counseling from a physician or other medical professional.

Whether actual use and label comprehension data were needed for approval of the non-prescription use of Plan B One-Step is directly relevant to whether those data were needed for the same approval for Plan B. The sponsor of the new drug applications for both products is the same and the applications originally contained similar data (with the same lack of robust actual use and label comprehension data for the younger age groups). Plan B One-Step was approved on July 10, 2009 as OTC for women 17 years of age and older, and Rx for women younger than 17 years of age. This bifurcated approval of Plan B One-Step was, like the decision on Plan B, based on the differences in the quantum of available labeling comprehension and actual use data for women 17 and older as compared to women younger than 17. As a scientific matter, if additional data were needed for OTC approval for younger women for Plan B One-Step, then

additional data would be needed for Plan B, which has more complicated directions for use, raising additional questions as to label comprehension and actual use.

After the original Citizen Petition denial in 2006, multiple CDER memoranda, meeting minutes, and communications to the sponsor on the design and execution of the requisite actual use and labeling comprehension studies reflect FDA's continuing consideration regarding the data that would be necessary to establish the safety and effectiveness of nonprescription use by a younger population of women. For example, FDA met with the sponsor on May 22, 2007 to discuss the design and conduct of the actual use and labeling comprehension studies necessary to support approval of Plan B One-Step as an OTC product without an age restriction. During that meeting, FDA scientists provided guidance on matters related to study design, including the types of questions young girls should be asked to assess comprehension, the labeling of the product, and the number of study subjects needed in the younger age groups.

The sponsor notified the agency about its difficulty in recruiting younger women for its actual use study. An internal CDER memorandum from a medical officer in the Division of Reproductive and Urologic Drugs, dated September 20, 2007, discussed the ages and numbers of patients he believed would be adequate to support approval of OTC use in the younger population of women. In that memo, the medical officer concluded that "[a]ccess to OTC emergency contraception to adolescents of all ages would provide a significant public health benefit, and data are needed to determine if this adolescent subpopulation can appropriately self-select and use this product as labeled in a safe and effective manner."

CDER and Teva met again on June 1, 2009 and April 28, 2010 to further assess the type and amount of data necessary to support OTC approval without age restrictions. At the 2009 meeting, FDA again reiterated what information would need to be provided to support a full OTC switch of either Plan B or Plan B One-Step. The meeting minutes state "if you intend to pursue an OTC switch for adolescents 17 years and younger, you would need to submit an efficacy supplement containing the information and/or data to address the concerns regarding nonprescription use of Plan B by women 16 years of age and younger..." At the 2010 meeting, the agency discussed its view of the data needed in terms of adequate enrollment in the various younger age groups for OTC approval of Plan B One-Step.

On February 7, 2011, Teva submitted an SNDA for Plan B One-Step seeking approval of the product OTC for all women of child bearing potential. The supplement included the results of Teva's studies regarding the safe and efficacious use of Plan B One-Step by women under 17. Teva included the results of its labeling comprehension study that was designed to assess several important aspects of younger women's understanding of the product itself and how it is intended to be used.<sup>3</sup> For example, it evaluated women's comprehension of the following key elements of the Plan B One-Step label:

1. Plan B One-Step is indicated for prevention of pregnancy after unprotected sex;
2. Plan B One-Step should be taken as soon as possible after sex;

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<sup>3</sup> The result of the labeling comprehension study were published in 2009. See Raymond EG, L'Engle KL, Tolley EE, Rocciotti N, Arnold MV et al, "Comprehension of a Prototype Emergency Contraception Package Label by Female Adolescents. *Contraception* 2009; 79: 199-205.

3. Plan B One-Step does not prevent sexually transmitted diseases or HIV/AIDS;
4. Plan B One-Step should not be used in place of regular contraception;
5. Plan B One-Step should be taken within 72 hours after sex; and
6. Plan B One-Step should not be used by women who are already pregnant.

Teva also included the results of its actual use study. That study was an open-label, single-arm, naturalistic study to determine the percentage of subjects who correctly self-select and use Plan B One-Step under simulated OTC conditions. The two primary objectives of the study were:

1. to determine the percentage of subjects who appropriately self-selected; and
2. to determine the proportion of subjects who correctly used Plan B One-Step under simulated OTC conditions.

Correct self-selection was defined as wanting to use the product for its indication and not having an allergy to levonorgestrel, a positive pregnancy test, or a known pregnancy. Correct use was defined as taking Plan B One-Step within 72 hours following unprotected sex. The secondary objectives were to estimate the incidence of adverse events and repeat use of emergency contraception during the 8-week follow-up period.

Pursuant to the procedures set forth in 21 CFR 314.101-314.170, FDA proceeded to determine whether the SNDA met the standards for approval set forth in the Act, 21 U.S.C. 353(b)(3), 355, and in FDA regulation 21 CFR 310.200. In a memorandum reviewing that application, dated October 4, 2011, an Associate Director in CDER's Office of New Drugs from the Pediatric and Maternal Health Staff states, "This product is already approved as a prescription product, and thus the safety and efficacy in the pediatric population have been established. Additional data were needed to support that the benefits and risks would be the same if the product was available OTC without a learned intermediary." The author further discusses the importance of having such data when she states, "The studies provide data to demonstrate that women of child bearing potential of all ages can appropriately self-diagnose and administer Plan B One-Step in an OTC setting...The safety and efficacy of OTC Plan B One-Step in this application is supported by the totality of the data submitted to support the application."

As noted, FDA ultimately concluded that the application, including the data from the new studies, provided "adequate and reasonable, well-supported, and science-based evidence that Plan B One-Step is safe and effective and should be approved for nonprescription use for all females of child-bearing potential." *See* Hamburg Statement. As part of the anticipated approval, FDA was prepared to determine that the clinical study that Teva submitted for Plan B One-Step was essential to any approval of non-prescription marketing of the product and thus grant 3-years of exclusivity.<sup>4</sup> As explained above, this SNDA included data in the form of both a clinical actual use study and a labeling comprehension study that FDA concluded in its scientific review memoranda supported the safe and effective OTC use of Plan B One-Step in women

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<sup>4</sup> The statutory requirements for granting this exclusivity (see 505(c)(3)(E)(iv) and 505(j)(5)(F)(iv) of the Act, and 21 CFR 108(b)(5)) are that the clinical studies be, among other things, essential to the approval of the supplement. FDA's final determination on exclusivity was not made because FDA determines whether to grant exclusivity after product approval.

under age 17. FDA believed that the clinical study submitted met the requirements to support exclusivity, that is, that these data were essential to approval.

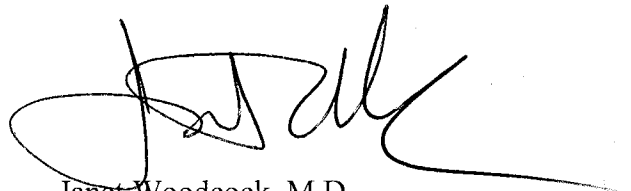
In contrast to the new data presented in the 2011 SNDA for Plan B One-Step, no new data have been presented to the agency on Plan B. After the remand by the *Tummino* court, FDA reopened the docket for your Citizen Petition to accept new data and information. Despite FDA's statements regarding the insufficiency of the data and the opportunity to supplement the record, neither you nor any other interested party has submitted any new data or information regarding the approvability of Plan B for nonprescription use by women under the age of 17.

At the *Tummino* court's direction, we have reevaluated whether actual use and labeling comprehension data would be needed to support a switch with respect to Plan B. Our review of the data submitted in support of the application for Plan B One-Step provides the final confirmation, and we now reaffirm our earlier conclusion that additional data would be needed to support safe and effective OTC use of the product by women under age 17. Actual use and labeling comprehension data would be needed to determine, among other things, whether women under 17 can understand that they would need to take two pills twelve hours apart, and whether they actually would do so correctly. The data submitted by Teva in its SNDA for Plan B One-Step included a labeling comprehension study and an actual use study that CDER scientists concluded were necessary and addressed the deficiencies in the original data that led to the earlier bifurcated approval status. This type of data, i.e., actual use and labeling comprehension studies conducted with adequate numbers of younger subjects, has not been presented to the agency with respect to Plan B. Thus, FDA reconfirms its conclusion that neither the information contained in the administrative record for the citizen petition, nor the data and information in the Plan B SNDAs, were adequate to support OTC use in women under age 17.

Therefore, upon reconsideration and following a re-analysis, we conclude that FDA needs additional data to support a switch of Plan B for women younger than 17 years of age. Neither your petition nor any of the public comments to the docket contain sufficient data to satisfy the statutory requirements for FDA to remove the Rx requirements for Plan B for women under the age of 17. In addition, FDA does not have any data from other sources that would be sufficient to support such a switch. In the absence of such data, FDA declines to initiate a rulemaking to switch Plan B from Rx to OTC for women under the age of 17.

In conclusion, for the reasons discussed above, after a careful reconsideration, your petition is denied.

Sincerely,

A handwritten signature in black ink, appearing to read 'Janet Woodcock', with a long horizontal flourish extending to the right.

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