THE UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF NEW YORK

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ANNIE TUMMINO, in her individual capacity, as Vice-Chair of the New York State Reproductive Rights Task Force, as Coordinator of the Morning-After Pill Conspiracy, and on behalf of women who need Emergency Contraception; ERIN T. MAHONEY, in her individual capacity, as Chair of the New York State Reproductive Rights Task Force, as Coordinator of the Morning-After Pill Conspiracy, and on behalf of women who need Emergency Contraception; CAROL GIARDINA, in her individual capacity, as Coordinator of the Morning-After Pill Conspiracy, and on behalf of women who need Emergency Contraception; KELLY MANGAN, in her individual capacity, as President of the University of Florida Campus Chapter of the National Organization for Women, as Coordinator of the Morning-After Pill Conspiracy, and on behalf of women who need Emergency Contraception; STEPHANIE SEGUIN, in her individual capacity, as Chair of the Florida National Organization for Women Young Feminist Task Force, as Coordinator of the Morning-After Pill Conspiracy, and on behalf of women who need Emergency Contraception; LORI TINNEY, in her individual capacity, as President of the Gainesville Chapter of the National Organization for Women, as Coordinator of the Morning-After Pill Conspiracy, and on behalf of women who need Emergency Contraception; JENNIFER BROWN, in her individual capacity, as Coordinator of the Morning-After Pill Conspiracy, and on behalf of women who need Emergency Contraception; CANDACE CHURCHILL, in her individual capacity, as Coordinator of the Morning-After Pill Conspiracy, and on behalf of women who need Emergency Contraception; and FRANCIE HUNT, in her individual capacity, as Coordinator of the Morning-After Pill Conspiracy, and on behalf of women who need Emergency Contraception; ASSOCIATION OF REPRODUCTIVE HEALTH PROFESSIONALS, on its own behalf and on behalf of its members and women who need Emergency Contraception; and NATIONAL LATINA INSTITUTE FOR REPRODUCTIVE HEALTH, on its own behalf and on behalf of women who need Emergency Contraception,

Plaintiffs,

CV-05-0366 (ERK/VVP)

v.

ANDREW C. VON ESCHENBACH, in his official capacity as acting commissioner of the Food and Drug Administration,

Defendant.

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SECOND AMENDED COMPLAINT

Plaintiffs, by and through their undersigned attorneys, bring this complaint against the defendant, his agents and successors in office, and in support thereof aver the following:

1. This is a challenge under the Administrative Procedures Act (APA) and the United States Constitution to the denial by the Food and Drug Administration (FDA) of a Supplemental New Drug Application (SNDA) and a citizen's petition ("citizen's petition") seeking to switch the emergency contraception ("EC") drug Plan B from prescription-only availability to over-the-counter status ("OTC switch"). Plaintiffs claim that this denial violates the rights of women who need EC to privacy and equal protection under the Fifth Amendment, and that the denial violates their rights and the rights of women who need EC because it exceeds the statutory authority of the FDA and is arbitrary and capricious. Plaintiffs seek injunctive relief requiring the defendant to approve the OTC switch, or such other equitable relief as the Court may deem appropriate, and a declaratory judgment that the FDA's denial violates the APA and violates the constitutional rights of women who need EC.

I. Jurisdiction and Venue

2. This Court has jurisdiction under 28 U.S.C. § 1331 because this case arises under the Constitution and laws of the United States.

3. Venue is proper in this district under 28 U.S.C. § 1391(d) because one of the plaintiffs resides in this district and the defendant is an officer of the United States acting in his official capacity.

II. The Parties

A. Plaintiffs

4. Plaintiff Annie Tummino is a resident of Brooklyn, New York. She sues on her own behalf, as Vice-Chair of the New York State Reproductive Rights Task Force and as Coordinator of the Morning-After Pill Conspiracy ("MAP Conspiracy"), and on behalf of women who need EC.

5. Plaintiff Erin T. Mahoney is a resident of New York, New York. She sues on her own behalf, as Chair of the New York State Reproductive Rights Task Force and as Coordinator of the MAP Conspiracy, and on behalf of women who need EC.

6. Plaintiff Carol Giardina is a resident of New York, New York. She sues on her own behalf, as Coordinator of the MAP Conspiracy, and on behalf of women who need EC.

7. Plaintiff Kelly Mangan is a resident of Gainesville, Florida. She sues on her own behalf, as President of the University of Florida Campus Chapter of the National Organization for Women, as Coordinator of the MAP Conspiracy, and on behalf of women who need EC.

8. Plaintiff Stephanie Seguin is a resident of Gainesville, Florida. She sues on her own behalf, as Chair of the Florida National Organization for Women Young Feminist Task Force and as Coordinator of the MAP Conspiracy, and on behalf of women who need EC.

9. Plaintiff Lori Tinney is a resident of Gainesville, Florida. She sues on her own behalf, as President of the Gainesville Chapter of the National Organization for Women, Gainesville, FL and as Coordinator of the MAP Conspiracy, and on behalf of women who need EC.

10. Plaintiff Jennifer Brown is a resident of Gainesville, Florida. She sues on her own behalf, as Coordinator of the MAP Conspiracy, and on behalf of women who need EC.

11. Plaintiff Candace Churchill is a resident of Gainesville, Florida. She sues on her own behalf, as Coordinator of the MAP Conspiracy, and on behalf of women who need EC.

12. Plaintiff Francie Hunt is a resident of Nashville, Tennessee. She sues on her own behalf, as Coordinator of the MAP Conspiracy, and on behalf of women who need EC.

13. The MAP Conspiracy is a coalition of feminist organizations leading the grassroots movement to make the Morning-After Pill an over-the-counter drug by raising public consciousness about the ways that women have to conspire to obtain it. Since February 2004, the MAP Conspiracy has organized speak-outs where women publicly testify from their own experience about their need for the Morning-After Pill and the obstacles they face obtaining it. Members of the MAP Conspiracy also testified at the December 2003 FDA public hearings on the Barr application for approval of over-the-counter status for Plan B.

14. Each of the individual plaintiffs listed in paragraphs 4-12 above has access to one or more doses of Plan B, and each of them intends, plans, and has pledged to provide Plan B to friends or other women of any age whom they learn need Plan B to prevent pregnancy. None of the individual plaintiffs listed in paragraphs 4-12 above is licensed or authorized by law in any state to prescribe or dispense drugs. Consequently, unless the OTC switch for Plan B is approved, each of the individual plaintiffs listed in paragraphs 4-12 above risks violating federal

and state criminal statutes if she carries through on her plan to provide Plan B to women who need it to prevent pregnancy. *See, e.g.*, 21 U.S.C. §§ 353(b)(1), 333(a), 333(b) (2005); § 465.015, Fla. Stat. (2004).

15. Plaintiff Association of Reproductive Health Professionals (ARHP) is a non-profit membership association composed of experts in reproductive health. These professionals include physicians, advanced practice clinicians (nurse practitioners, nurse midwives, physician assistants), researchers, educators, pharmacists, and other professionals in reproductive health, some of whom have authority to prescribe drugs and some of whom do not. ARHP and its members provide reproductive health services and education, conduct reproductive health research, and influence reproductive health policy. Specifically, ARHP works to improve the reproductive health of women by reducing the number of unintended pregnancies among women. ARHP, along with Princeton University's Office of Population Research (OPR), manages the *Emergency Contraception Hotline* (1-888-Not-2-Late) and *Website* (www.not-2-late.com), which aim to prevent unintended pregnancy by providing women and their partners information about, and rapid access to, emergency contraception. Both the *Hotline* and *Website* are highly utilized tools, currently receiving an average of 60,000 calls and 500,000 website visits per year. The *Hotline* is an automated, toll-free, 24-hour, confidential service available in both English and Spanish that gives callers general emergency contraception information and a list of the five emergency contraception providers nearest to them (including a list of pharmacists in states where pharmacists are permitted by state law to dispense EC). It is available from any phone in the United States, Puerto Rico, U.S. Virgin Islands, British Columbia, and the Yukon Territory. The *Website*, available in English, French, Spanish, and now Arabic, is the most comprehensive emergency contraception clearinghouse in the world available to anyone via the

World Wide Web. It features frequently asked questions about emergency contraception, a publications bibliography, an EC materials database, and a searchable database of EC providers across the country, Puerto Rico, Guam, U.S. Virgin Islands, and British Columbia. The full directory of providers can be searched by city, state, area code, and zip code. The NOT-2-LATE database also lists pharmacists in Alaska, California, Washington State, New Mexico, and British Columbia. ARHP and OPR work closely with local pharmaceutical associations to sign up pharmacists who dispense EC behind the counter. Hawaii has recently become the fifth state—joining Alaska, California, New Mexico and Washington—to allow direct dispensation of EC by pharmacists. ARHP is working closely with pharmacy organizations and state officials in Hawaii to list pharmacists once they are trained. ARHP has petitioned the FDA to switch EC to OTC status. The prescription requirement for Plan B interferes with ARHP's ability to educate health care providers and the public about emergency contraception, interferes with ARHP's efforts to reduce the number of unintended pregnancies and its efforts to use the *Emergency Contraception Hotline* and *Website* to achieve that goal, and interferes with its members' ability to accomplish the goal of improving the reproductive health of women. ARHP sues on its own behalf, on behalf of its members who lack prescribing authority and their patients and clients who seek emergency contraception, and on behalf of the women who utilize the Hotline and Website to obtain access to EC.

16. Plaintiff National Latina Institute for Reproductive Health (NLIRH) is a non-profit organization formed under section 501(c)(3) of the Internal Revenue Code. NLIRH conducts an EC education and outreach project which seeks to educate providers of EC and potential users of EC about what EC is, how to use it, and how to obtain it and, for providers, how to incorporate it into their practice. NLIRH has conducted such an education and outreach project in the Bronx,

and plans additional such projects at several locations in Brooklyn and the Bronx through June of 2005. NLIRH's EC education outreach projects are impeded by the prescription requirement for EC. If EC is switched to OTC, NLIRH will be able to improve access to EC by enhancing its EC educational programs for both the health care providers and the public participants involved in those projects. NLIRH sues on its own behalf and on behalf of the women participants in its EC projects who are of childbearing age.

B. Defendant

17. Andrew C. von Eschenbach is the acting commissioner of the FDA. Von Eschenbach is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation. He is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health. He is sued in his official capacity.

III. Statutory and Regulatory Background

18. Under FDA regulations, "[a]ny drug limited to prescription use . . . shall be exempted from prescription-dispensing requirements when the Commissioner finds such requirements are not necessary for the protection of the public health by reason of the drug's toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, and he finds that the drug is safe and effective for use in self-medication as directed in proposed labeling." 21 C.F.R. § 310.200(b) (2005); *see also* 21 U.S.C. § 353(b)(3) (2005) ("The Secretary may by regulation remove drugs subject to sections 352(d) and 355 of this title from

the requirements of paragraph (1) of this subsection when such requirements are not necessary for the protection of the public health.").

19. An approved drug is suitable for OTC use when: (1) the drug is safe for self-medication, 21 C.F.R. § 310.200(b); 21 C.F.R. § 330.10(a)(4)(i); (2) the drug is effective when self-administered, 21 C.F.R. § 310.200(b); 21 C.F.R. § 330.10(a)(4)(ii); (3) the condition to be treated is self-diagnosable; and (4) the drug's labeling is tailored to self-administration, 21 C.F.R. § 310.200(b); 21 C.F.R. § 330.10(a)(4)(v).

20. By statute, the manufacturer of a prescription drug may file a supplemental new drug application with the FDA seeking to switch the drug to OTC status. 21 U.S.C. § 355(b). Such an application must be acted upon by the FDA within 180 days of its filing. 21 U.S.C. § 355(c).

21. In addition, FDA regulations explicitly authorize the use of a citizen's petition to seek a switch from prescription to OTC status: "A proposal to exempt a drug from the prescription-dispensing requirements of section 503(b)(1)(C) of the act may be initiated by . . . any interested person . . . fil[ing] a petition . . . pursuant to Part 10 of this chapter . . ." 21 C.F.R. § 310.200(b). Once a citizen's petition has been filed, the FDA is required by its regulations to either approve the petition, deny the petition, or "[p]rovide a tentative response, indicating why the agency has been unable to reach a decision on the petition, e.g., because of the existence of other agency priorities, or a need for additional information." 21 C.F.R. § 10.30(e)(2).

22. During the process of considering an application for an OTC switch, the FDA typically receives the advice of the FDA's OTC advisory committee meeting together with the FDA's advisory committee that has specific expertise in the product under consideration. In the case of Plan B, the latter committee is the Advisory Committee for Reproductive Health Drugs. These advisory committees are authorized by, *inter alia*, 21 U.S.C. § 355(n) (2005).

23. Dispensing a prescription drug other than by prescription is an act of "misbranding" under federal law. 21 U.S.C. § 353(b)(1). Introducing a misbranded drug into interstate commerce is a "prohibited act," 21 U.S.C. § 331(a), punishable by not more than one year imprisonment or a fine of up to $1000 or both. 21 U.S.C. § 333(a)(1).

IV. Factual Allegations

24. Unintended pregnancy is a significant public health problem in the United States. The United States has one of the highest rates of unintended pregnancy compared to other developed countries. The rate of teen pregnancy in the United States is also one of the highest among developed countries. Wider access to EC will reduce unintended pregnancies, including among teenagers.

25. The risks of pregnancy and childbirth, including maternal death, can be serious and exceed the risks associated with EC.

26. Plan B (Levonorgestrel) is an emergency contraceptive drug in tablet form that can be used to prevent pregnancy following an act of intercourse in which no contraceptive was used or the contraceptive method used failed.

27. When taken within 72 hours of unprotected intercourse, Plan B reduces the risk of pregnancy by approximately 89 percent after a single act of unprotected sex. As the interval between intercourse and the start of treatment increases, Plan B's effectiveness declines, and the risk of pregnancy increases. Plan B does not interfere with an established pregnancy.

28. Switching Plan B to OTC status will promote public health because Plan B is only effective for a short time after unprotected sex, and it works most effectively if used within twenty-four hours of unprotected sex. Because contacting a physician and obtaining and filling a prescription hinder women from obtaining Plan B in a timely fashion, making Plan B available

OTC will allow more women to use the treatment, and enable more women to prevent unwanted pregnancies, to the benefit of public health.

29. Limiting Plan B to prescription use is not necessary for the protection of public health.

30. Plan B is safe for self-medication because it is not toxic to the woman (or to the embryo or fetus if a pregnancy had been previously established in the woman).

31. Plan B has a low risk of abuse or overdose, and if overdose occurs is unlikely to lead to serious consequences.

32. Plan B's side effects are well-known and minor.

33. Plan B is effective when self-administered. Its administration is simple and relies only on assessments as to time elapsed since sexual intercourse that can be independently made by the woman, and any interaction between Plan B and other drugs would be nonfatal and unlikely to seriously affect Plan B's efficacy.

34. The condition Plan B treats — contraceptive failure or failure to use contraception during intercourse — is one that is readily diagnosable by a woman.

35. Plan B has no contraindications that would pose a danger to the patient.

36 The existing patient labeling for Plan B is tailored to self-administration in that it is simple, clear, comprehensive and easy to follow.

37. Both the American Medical Association and the American College of Obstetricians and Gynecologists support switching Plan B to OTC status. *See* Dec. 5, 2000 Statement of American Medical Association; December 13, 2001 Statement of the American College of Obstetricians & Gynecologists.

38. In 1999, the FDA approved Plan B as a prescription drug. Since that date, Plan B has been prescribed many thousands of times.

39. On February 14, 2001, a group of citizen organizations, including Plaintiff ARHP, filed a petition with FDA asking the agency to switch Plan B (and another drug, Preven, that has since been removed from the market for reasons unrelated to safety and effectiveness) to OTC status. In violation of its own regulations, *see* ¶ 21 above, the FDA has failed as of the date of this Complaint to either approve, deny, or give a tentative response to the citizen's petition within 180 days of the filing of the petition, thus constructively denying the petition. After the 180 day period, the FDA gave a tentative response on September 6, 2001. Since that date the FDA has not communicated any further with the petitioners, and therefore the petition has been constructively denied.

40. On April 16, 2003, Women's Capital Corporation, the former owner of Plan B, filed a supplemental new drug application (SNDA) asking the agency to approve Plan B for OTC sale. Plan B was subsequently sold to Barr Laboratories, which maintained the SNDA.

41. On December 16, 2003, FDA's Non-prescription Drugs Advisory Committee and Advisory Committee for Reproductive Health Drugs held a joint session to discuss possible OTC status for Plan B.

42. The advisory committees, comprised of 28 members, voted as follows:

(1) **Does the Actual Use Study (AUS) demonstrate that consumers used [Plan B] as recommended in the proposed labeling?**

Yes – 27 No – 1

(2) **Are the AUS data generalizable to the overall population of potential non-Rx users of Plan B?**

Yes – 27 No – 1

(3) **Based on the AUS and literature review, is there evidence that non-Rx availability of Plan B leads to substitution of emergency contraception for the regular use of other methods of contraception?**

Yes – 0 No – 28

(4) **Do the data demonstrate that Plan B is safe for use in the non-prescription setting?**

Yes – 28 No – 0

43. Upon information and belief, all division chiefs within the Center for Drug Evaluation and Research (CDER) who reviewed the OTC switch application expressed the view to CDER based on scientific and medical data that the OTC switch should be approved.

44. By memorandum dated April 22, 2004 and signed electronically on April 28, 2004, John Jenkins, M.D., the Director of the FDA's Office of New Drugs, wrote a memorandum summarizing his "review, conclusions, and recommendations regarding" the OTC switch for Plan B (attached hereto as Ex. 1) ("the Jenkins memorandum"). This memorandum states: "[The FDA] has not heretofore distinguished the safety and efficacy of Plan B and other forms of hormonal contraception among different ages of women of childbearing potential and I am not aware of any compelling scientific reason for such a distinction in this case." (Ex. 1 at 2.) After a review of the record evidence supporting OTC use by women of all ages, the Jenkins memorandum accordingly concludes "that the available data clearly support a conclusion that Plan B meets the statutory and regulatory requirements for availability without a prescription for all age groups. Such a conclusion is consistent with how the Agency has made determinations for other OTC products, including other forms of contraception available without a prescription." (*Id.* at 3.)

45. The Jenkins memorandum further states that "[o]ther senior officials within the Agency, including the former Commissioner (Dr. McClellan) and the Acting Center Director (Dr. Galson) have expressed concerns about the potential for unsafe, ineffective, or inappropriate use of Plan B by adolescents if it were to be made available without a prescription. These concerns appear to have been based primarily on the limited number of adolescent women included in the sponsor's label comprehension and actual use studies" (*Id* at 1)

46. Though Jenkins said that he "[is] sensitive to and respect[s] the concerns that some may have regarding non-prescription access to Plan B by adolescents," (*Id* at 2), he stated that "[p]roducts that are indicated for uses related to sexual activity in adolescents raise concerns for some people that go beyond a finding based on clinical trial data that the product is safe and effective for its intended use in adolescents. These concerns derive from individual views and attitudes about the morality of adolescent sexual behavior and also overlap with concerns about the role of parents and health care professionals in decisions about contraceptive use in adolescents." (*Id.* at 2-3.) He concluded: "While OTC access to Plan B for adolescents may be controversial from a societal perspective, I cannot think of any age group where the benefit of preventing unplanned pregnancies and abortion is more important and more compelling." (*Id.* at 3.)

47. On May 6, 2004, CDER Acting Director Steven Galson issued a "non-approvable" letter (attached hereto as Ex. 2) ("the Galson letter") to Barr rejecting the OTC switch for Plan B. That action also constructively denied the citizen's petition.

48. The Galson letter asserts that Barr's SNDA could not be approved because Barr had "not provided adequate data to support a conclusion that Plan B can be used safely by young adolescent women for emergency contraception without the professional supervision of a

practitioner licensed by law to administer the drug." (Ex. 2 at 1.) This assertion is not supported by the agency record.

49. On July 22, 2004, Barr filed an amended SNDA seeking the OTC switch only for women aged 16 and higher. By statute, the defendant was required to act on Barr's amended SNDA within 180 days after it was filed. *See* 21 U.S.C. § 355(c)(1). On January 21, 2005, the FDA announced a delay of its decision on Barr's application beyond this statutory time limit.

50. Plan B is a drug used only by women, and every woman of childbearing age is a potential user of Plan B.

51. The FDA applied a different and higher standard to Plan B's OTC switch than it has applied to OTC switches of other drugs.

52. There is no medical or scientific basis for the FDA's application of a different and higher standard to Plan B's OTC switch.

53. The FDA's application of a different and higher standard to Plan B's OTC switch was the result of factors that fall outside the FDA's statutory mandate.

54. The FDA's rejection of the OTC switch for women of all ages and the FDA's constructive rejection of the citizen's petition for the OTC switch are not supported by medical or scientific evidence and are not supported by the agency record.

55. Upon information and belief, the General Accounting Office has commenced an investigation for the United States Congress into why the FDA rejected the OTC switch on May 6, 2004.

56. Each of the plaintiffs is aggrieved on a continuing and ongoing basis by the FDA's rejection of the OTC switch for women of all ages and the FDA's constructive rejection of the citizen's petition for the OTC switch.

57. Each of the plaintiffs is injured on a continuing and ongoing basis by the FDA's rejection of the OTC switch for women of all ages and the FDA's constructive rejection of the citizen's petition for the OTC switch, and the FDA's rejection is the cause of that injury.

58. The relief sought in this complaint will redress the injury suffered by each of the plaintiffs that is caused by the FDA's constructive rejection of the citizen's petition for the OTC switch for women of all ages.

V. Causes of Action

FIRST CAUSE OF ACTION: ARBITRARY AND CAPRICIOUS

59. Plaintiffs hereby incorporate by reference ¶¶ 1-58 above.

60. FDA's denial of the OTC switch for persons of all ages is arbitrary, capricious, an abuse of discretion and otherwise not in accordance with law, in violation of 5 U.S.C. § 706(2)(a) (2005) in that the FDA required evidence of safety and efficacy beyond that required for approval of any other drugs and was improperly motivated by factors other than medicine and science.

SECOND CAUSE OF ACTION: EXCEEDS STATUTORY AUTHORITY

61. Plaintiffs hereby incorporate by reference ¶¶ 1-60 above.

62. FDA's denial of the OTC switch for persons of all ages exceeds its statutory authority in violation of 5 U.S.C. § 706(2)(c) in that it was improperly motivated by factors other than medicine and science.

THIRD CAUSE OF ACTION: RIGHT TO PRIVACY

63. Plaintiffs hereby incorporate by reference ¶¶ 1-62 above.

64. FDA's denial of the OTC switch for persons of all ages violates the Fifth Amendment to the United States Constitution and 5 U.S.C. § 706(2)(b) in that it infringes the right to privacy of women who need EC without serving any compelling, significant, or legitimate governmental interest.

FOURTH CAUSE OF ACTION: SEX DISCRIMINATION

65. Plaintiffs hereby incorporate by reference ¶¶ 1-64 above.

66. FDA's denial of the OTC switch for persons of all ages violates the Fifth Amendment to the United States Constitution and 5 U.S.C. § 706(2)(b) in that it discriminates on the basis of sex without serving any compelling, significant, or legitimate governmental interest.

FIFTH CAUSE OF ACTION: ACTION UNLAWFULLY WITHHELD OR UNREASONABLY DELAYED

67. Plaintiffs hereby incorporate by reference ¶¶ 1-66 above.

68. FDA's failure to approve the OTC switch for Plan B constitutes an action "unlawfully withheld or unreasonably delayed" in violation of 5 U.S.C. § 706(1).

VI. Prayer for Relief

WHEREFORE, Plaintiffs ask this Court:

A. To issue an injunction ordering Defendant to approve the OTC switch for persons of all ages;

B. To enter judgment declaring the denial of OTC availability to persons of all ages in violation of the United States Constitution and 5 U.S.C. § 706; and

C. In the event the Court finds that the Agency has not taken final action, to order the agency to issue a final decision on the OTC status of Plan B, and to enter a declaratory judgment that the FDA has unlawfully withheld or unreasonably delayed issuing such a decision, in violation of the Constitution of the United States and the Agency's statutory mandate.

D. To grant such other and further relief as this Court should find just and proper, including attorneys' fees and costs.

Dated: November 2, 2005.

Respectfully submitted,

/s Simon Heller
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MANGAN, SEGUIN, TINNEY, BROWN,
CHURCHILL AND HUNT

Admitted pro hac vice

Exhibit 1

MEMORANDUM

DATE: April 27, 2004

FROM: John K. Jenkins, MD
Director, Office of New Drugs

TO: NDA 21-045

SUBJECT: Review of NDA for Rx to OTC Switch for Plan B

This memorandum is intended to summarize my review, conclusions, and recommendations regarding the pending application submitted by Barr Laboratories proposing a switch to non-prescription status for Plan B (levonorgestrel) for emergency contraception. I have read and carefully considered the reviews in the action package written by Dr. Jonca Bull, Dr. Julie Beitz, Dr. Donna Griebel, and Dr. Curtis Rosebraugh. I also attended the December 16, 2003, joint meeting of the Non-Prescription Drugs Advisory Committee and the Reproductive Health Drugs Advisory Committee at which this application was presented for discussion and public input.

The drug product and indication proposed by the sponsor for non-prescription marketing (also known as over-the-counter or OTC) are identical to the approved prescription product. Plan B has previously been proven to be effective for emergency contraception, and has a well-documented safety profile. Therefore, the primary regulatory issue in considering the potential non-prescription use of this product is whether it can be used safely, effectively, and appropriately by women of child-bearing potential without need for a learned intermediary (e.g., counseling from a physician). In support of this application the sponsor submitted a label comprehension study and an actual use study, both of which have been extensively reviewed by the staff in the two divisions. In my opinion, these studies provide adequate evidence that women of childbearing potential can use Plan B safely, effectively, and appropriately for emergency contraception in the non-prescription setting. The data submitted by the sponsor in support of non-prescription use of Plan B are fully consistent with the Agency's usual standards for meeting the criteria for determining that a product is appropriate for such use. This conclusion is supported by the fact that both divisions and offices responsible for the review of this application have recommended approval and the fact that the joint Advisory Committee voted 23 to 4 in favor of recommending that Plan B be switched to non-prescription status.

Other senior officials within the Agency, including the former Commissioner (Dr. McClellan) and the Acting Center Director (Dr. Galson), have expressed concerns about the potential for unsafe, ineffective, or inappropriate use of Plan B by adolescents if it were to be made available without a prescription. These concerns appear to have been based primarily on the limited number of adolescent women included in the sponsor's label comprehension and actual use studies. While it is true that the number of

adolescents enrolled in the sponsor's studies was relatively small, these studies did not exclude adolescent women from enrollment and were conducted in settings that would be expected to capture a representative population of women who currently seek emergency contraception. Therefore, it is likely that the percentage of patients enrolled in these studies is an accurate reflection of the potential users of Plan B in an OTC setting. Furthermore, the data from these studies do not suggest that adolescent women are significantly different from older women in their comprehension of the labeling or appropriate use of the product in the OTC setting, and for some analyses the adolescent women actually performed better than older women. I, therefore, believe that the data from the studies submitted by the sponsor are sufficient and adequate on which to base a regulatory decision on whether Plan B can be used safely, effectively, and appropriately by women of childbearing potential, regardless of age, in the OTC setting. The Agency has not heretofore distinguished the safety and efficacy of Plan B and other forms of hormonal contraception among different ages of women of childbearing potential and I am not aware of any compelling scientific reason for such a distinction in this case. I would also note that the Agency has a long history of extrapolating findings from clinical trials in older patients to adolescents in both prescription and non-prescription approvals, and this practice was recently incorporated into the Pediatric Research and Equity Act (PREA).

As detailed in the reviews prepared by Drs. Griebel and Rosebraugh, in addition to the studies submitted by the sponsor there exists a substantial body of data from recently completed published and unpublished studies on emergency contraception that have enrolled a substantial number of adolescent women. While none of the studies directly mimic the OTC setting for access to Plan B, I believe that these data are relevant and help to address whether adolescents can use Plan B in the OTC setting. Taken together, these additional studies do not support a concern that adolescent women are less able to understand the label directions or less likely to appropriately use the product than older women. Further, these studies found that increased access for adolescents to emergency contraception did not result in inappropriate use of Plan B as a routine form of contraception, an increase in the number of sexual partners, an increase in the frequency of unprotected intercourse, or an increase in the frequency of sexually transmitted diseases.

In summary, I concur with the recommendations from the review divisions and offices that the sponsor has provided adequate data to demonstrate that Plan B can be safely, effectively, and appropriately used by women of childbearing potential for the indication of emergency contraception without a prescription. I, therefore, recommend that this application be approved to permit availability of Plan B without a prescription and without restrictions regarding the availability of the product to adolescent women.

I am sensitive to and respect the concerns that some may have regarding non-prescription access to Plan B by adolescents. Products that are indicated for uses related to sexual activity in adolescents raise concerns for some people that go beyond a finding based on clinical trial data that the product is safe and effective for its intended use in adolescents. These concerns are derived from individual views and attitudes about the morality of

adolescent sexual behavior and also overlap with concerns about the role for parents and health care professionals in decisions about contraceptive use in adolescents. While acknowledging these concerns, I believe that the available data clearly support a conclusion that Plan B meets the statutory and regulatory requirements for availability without a prescription for all age groups. Such a conclusion is consistent with how the Agency has made determinations for other OTC products, including other forms of contraception available without a prescription. Further, I believe that greater access to this drug will have a significant positive impact on the public health by reducing the number of unplanned pregnancies and the number of abortions. While OTC access to Plan B for adolescents may be controversial from a societal perspective, I cannot think of any age group where the benefit of preventing unplanned pregnancies and abortion is more important and more compelling.

The sponsor is aware of the societal issues related to OTC access for Plan B, particularly to adolescents. They initially proposed a voluntary marketing plan called CARE (Convenient Access Responsible Education), which was designed to increase awareness of appropriate use of Plan B through education while increasing availability through OTC access. The joint Advisory Committee voted 22 to 5 (with one abstention) that this program was adequate for introduction of Plan B into the OTC setting. Subsequently, in response to concerns raised by upper management within the Agency about OTC access to plan B for adolescents, the sponsor submitted a preliminary proposal for voluntary dual Rx (for women under 16 years) and OTC marketing (for women 16 and above) of Plan B. This proposal has undergone preliminary review by the Office of Regulatory Policy in CDER and it appears that it may be feasible under the current statute and regulations, however, a formal review by the Office of Chief Counsel has not be completed. While I do not believe that restrictions on OTC availability to adolescents are warranted, and I believe that such restrictions could be counterproductive to improving access to contraceptive options for this age group, this voluntary proposal from the sponsor deserves further consideration. It may serve to responsibly address the societal concerns that have been raised by some about OTC access to Plan B for adolescents while simultaneously greatly expanding access to Plan B to the vast majority of women of childbearing potential who may greatly benefit from such access.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

John Jenkins
4/28/04 08:23:43 AM
MEDICAL OFFICER
Concurrence with division and ODE recommendations that application should be approved for non-prescription marketing without restriction based on age.

Exhibit 2

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-045/S-011

Barr Research, Inc.
Attention: Joseph A. Carrado, M.Sc., Ph.D.
Senior Director, Regulatory Affairs
One Bala Plaza, Suite 324
Bala Cynwyd, PA 19004-1401

Dear Dr. Carrado:

Please refer to your supplemental new drug application dated April 16, 2003, received April 22, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Plan B® (0.75mg levonorgestrel) tablets.

We acknowledge receipt of your submissions dated July 25 (3) and 31, August 8 (2), September 4, 8, 9, and 15, October 6, 10, 15 (2), 17, 21, 24, 29, 30 and 31, December 3 and 9, 2003; and January 9 and 30, February 6, 10, 13, 20 and 24, and March 11 and 26, 2004.

This supplemental new drug application proposes nonprescription (over-the-counter (OTC)) availability of Plan B (0.75mg levonorgestrel) tablets for emergency contraception to reduce the chance of pregnancy after unprotected sex (if a contraceptive failed or if birth control was not used).

We have completed our review of this supplement and, for the reasons described below, find that the supplemental application is not approvable at this time under section 505(d) of the Act and 21 CFR 314.125(b).

You propose OTC status for Plan B for both adults and children based primarily on an actual use study in 585 subjects. Only 29 of the 585 subjects enrolled in the study were 14-16 years of age, and none was under 14 years of age.

In a December 16, 2003 joint meeting, the Nonprescription Drugs Advisory Committee and the Reproductive Health Drugs Advisory Committee considered your proposal to switch Plan B to nonprescription status. Although the Joint Committee recommended that your proposal to switch Plan B be approved, some members of the Joint Committee, including the Chair, raised questions concerning whether the actual use data were generalizable to the overall population of nonprescription users, chiefly because of inadequate sampling of younger age groups.

Based on a review of the data, we have concluded that you have not provided adequate data to support a conclusion that Plan B can be used safely by young adolescent women for emergency contraception without the professional supervision of a practitioner licensed by law to administer the drug. In your March 11, 2004, amendment, you proposed to change the indication to allow for marketing of Plan B as a prescription-only product for women

under 16 years of age and a nonprescription product for women 16 years and older. This preliminary proposal did not include draft product labeling to demonstrate how you propose to comply with both the prescription and nonprescription labeling requirements in a single packaging configuration. Because of the preliminary and incomplete nature of the proposal, we did not conduct a complete review of this amendment during this review cycle.

Before this application can be approved, you would have to provide data demonstrating that Plan B can be used safely by women under 16 years of age without the professional supervision of a practitioner licensed by law to administer the drug. Alternatively, you could supply additional information in support of the revised indication to allow for marketing of Plan B as a prescription-only product for women under the age of 16 years and a nonprescription product for women 16 years and older, including draft product labeling. If you take the latter approach, your response to this letter would have to include details of how you propose to implement simultaneous prescription and nonprescription marketing of Plan B for women of different ages in a single packaging configuration while complying with all relevant statutory and regulatory requirements for labeling and marketing of this product. We will have to assure ourselves that your proposed approach is consistent with our statutory authority. If you pursue the alternative approach, we also would request details of your proposed program to educate consumers, pharmacists, and physicians about the dual marketing of Plan B as both a prescription and nonprescription product, as well as your proposed program to monitor implementation of this novel approach.

Wide availability of safe and effective contraceptives is important to public health. We look forward to continuing to work with you if you decide to pursue either of these options.

When you respond to the above deficiencies, include a safety update as described at 21 CFR 314.50(d)(5)(vi)(b). The safety update should include data from all non-clinical and clinical studies of the drug under consideration regardless of indication, dosage form, or dose level.

1. Describe in detail any significant changes or findings in the safety profile.

2. When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:

   - Present new safety data from the studies for the proposed indication using the same format as the original NDA submission.
   - Present tabulations of the new safety data combined with the original NDA data.
   - Include tables that compare frequencies of adverse events in the original NDA with the retabulated frequencies described in the bullet above.
   - For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.

3. Present a retabulation of the reasons for premature study discontinuation by incorporating the drop-outs from the newly completed studies. Describe any new trends or patterns identified.

4. Provide case report forms and narrative summaries for each patient who died during a clinical study or who did not complete a study because of an adverse event. In addition, provide narrative summaries for serious adverse events.

5. Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original NDA data.

6. Provide a summary of worldwide experience on the safety of this drug. Include an updated estimate of use for drug marketed in other countries.

7. Provide English translations of current approved foreign labeling not previously submitted.

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.120. If you do not follow one of these options, we will consider your lack of response a request to withdraw the application under 21 CFR 314.65. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

Under 21 CFR 314.102(d), you may request an informal meeting or telephone conference with the Divisions of Over-the-Counter Drugs and Reproductive and Urologic Drug Products to discuss what steps need to be taken before the application may be approved.

This product may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed with this change before approval of this supplemental application.

If you have any questions, call the Regulatory Project Manager at (301) 827-4260.

Sincerely,

{See appended electronic signature page}

Steven Galson, M.D., M.P.H.
Acting Director
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Steven Galson
5/6/04 04:56:02 PM

CERTIFICATE OF SERVICE

I, Simon Heller, hereby certify that on December 7, 2005, I electronically filed the foregoing with the Clerk of the Court using the CM/ECF system, which sent notification via electronic mail to F. Frank Amanat.

Dated: December 7, 2005

Respectfully submitted,

/s Simon Heller
SIMON HELLER (SH-8760)
NAN E. STRAUSS (NS-3501)
Center for Reproductive Rights
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