

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-045/S011

APPROVAL LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

21-045/S-011

Duramed Research, Inc.
Attention: Joseph A. Carrado, M.Sc., R.Ph.
Vice President, Clinical Regulatory Affairs
One Belmont Ave, 11th floor
Bala Cynwyd, PA 19004

Dear Mr. 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[®] (levonorgestrel) Tablets, 0.75 mg.

We also 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; January 9, and 30, February 6, 10, 13, 20, and 24, March 11 and 26, May 6 and 11, June 30, July 21, 2004; January 6, 12, 13, 14, 18, 19 and 21, and August 26, 2005; and August 2, 17, 18, and 23, 2006.

Your submission of July 21, 2004, constituted a complete response to our May 6, 2004, Not Approvable letter. The resubmitted supplemental new drug application provides for a switch to Over-the-Counter (OTC) status for women ages 16 years or greater and maintenance of prescription status for women under age 16. On August 26, 2005, then Commissioner Lester M. Crawford, DVM, PhD, sent you a letter indicating that the Agency was unable, at that time, to reach a decision on the approvability of the application because of unresolved issues that related to your NDA. The letter mentioned three issues: whether the same active ingredient could be marketed both Rx and OTC based solely on the age of the individual using the drug; how, as a practical matter, an age-based distinction could be enforced; and whether the Rx and OTC versions of the same active ingredient may be marketed in a single package. The letter also stated that the agency had decided to ask for public comments on whether we should initiate a rulemaking to codify our interpretation of section 503(b) of the Federal Food, Drug, and Cosmetic Act regarding when an active ingredient can be simultaneously marketed in both a prescription drug product and an OTC drug product through an advance notice of proposed rulemaking (ANPRM) that published on September 1, 2005 (70 FR 52050). The comment period closed on November 1, 2005, and the agency received about 47,000 comments. The agency hired a contractor to summarize and categorize the comments and the contractor submitted a final report on May 19, 2006.

On July 31, 2006, Dr. Andrew von Eschenbach, Acting Commissioner of Food and Drugs, sent you a letter indicating that the agency had reviewed the comments received in response to the ANPRM and determined it was not necessary to engage in rulemaking to resolve the novel regulatory issues raised by your application and that we were now proceeding with further evaluation of your application.

We met with you on August 8, 2006, and discussed how to address the issues raised in Dr. von Eschenbach's letter regarding the restriction on OTC sales of Plan B[®] to ages 18 and over, the packaging, and the Convenient Access Responsible Education (CARESM) Program.

On August 17, 18, and 23, 2006, you amended your application to propose revisions to the labeling and to the CARESM Program.

We have completed our review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that Plan B[®] is safe and effective for use under the conditions set forth in the draft labeling submitted on August 23, 2006. This application is approved, effective on the date of this letter, to allow OTC availability of Plan B[®] for consumers 18 years and older. Plan B[®] remains available by prescription only for women 17 years and younger.

The final printed labeling (FPL) must be identical to the enclosed labeling (prescription package insert, outer carton label, inner card label, and consumer information leaflet). The inner card and outer carton labels must be formatted in accordance with the requirements of 21 CFR 201.66.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-045 /S-011.**" Approval of this submission by FDA is not required before the labeling is used.

We also remind you of the activities you agreed to as specified in the CARESM Program described in your submission dated August 23, 2006. You agreed to:

- Monitor trends in the use of emergency contraception to evaluate the effectiveness of the CARESM program. Specifically, you have agreed to conduct a market research survey or surveys of a subset of healthcare professionals annually, and when practicable, in collaboration with established professional groups. Your surveys will be designed to determine whether the Rx requirement for those ages 17 and younger is being adhered to at the point of purchase and to provide signals of program effectiveness and potential problems associated with consumers' understanding of the purpose and proper use of Plan B[®].
- Using relevant survey data regularly collected by others (e.g., Centers for Disease Control's Behavioral Risk Factor Safety Surveillance (CDC BRFSS), Youth Risk Behavior Safety Surveillance (YRBSS)), to monitor for potential indicators that Plan B[®] is being used in an inappropriate manner. Potential areas of monitoring and reporting include evaluating possible correlations between increases in sexually transmitted infections (STIs) based on geographic areas and data and trends in pregnancy and/or abortion rates based on geographic areas.
- Conduct a "Point-of-Purchase Monitoring Program" to track how Plan B[®] is being sold at the time of purchase, including using anonymous shoppers who will be directed to visit locations where Plan B[®] is available and purchase the product. Using the data collected, you will document and analyze the level of comprehension of the Plan B[®] prescription age requirement and how it is handled at the point of purchase. The program will be conducted twice in the first

year and annually thereafter. The sponsor will report repeat violators to the relevant State Boards of Pharmacy.

- Report to FDA on the results of these activities on a six-month interval beginning 30 calendar days after the six-month interval commencing on the date of this approval.

Finally, we note and agree with the other elements of the CARESM Program, described in your submission of August 23, 2006, which are designed to ensure compliance with the approved labeling, and particularly the restriction of OTC use to ages 18 and older. The program includes the following elements:

- The sponsor and third party distributors, wholesalers, and chain drug companies will only distribute Plan B[®] to licensed pharmacies or other licensed healthcare clinics. As a result, Plan B[®] will not be sold at gas stations or convenience stores. Given that Plan B[®] will have both Rx and OTC labeling, the pharmacies will keep Plan B[®] behind-the-counter.
- The sponsor will conduct an education campaign that will focus initially on healthcare professionals (including prescribers and pharmacists) to raise awareness and knowledge levels about emergency contraception. The education campaign will clearly communicate the prescription age requirement and the appropriate use of emergency contraception. The campaign will include continuing education by certified professionals and educational materials (including websites and toll free numbers) that can be accessed easily and at any time.
- The sponsor will make available to State Boards of Pharmacy continuing education programs for use at annual meetings and other regional programs.
- The sponsor will provide to prescribers and healthcare professional associations materials for distribution to patients that will encourage patients to discuss any questions about emergency contraception with a healthcare professional.
- The sponsor plans to educate consumers in part by targeting consumers ages 18 to 44 to convey critical awareness and educational messages as well as information about product availability, time sensitivity of use, and the age requirements to obtain Plan B[®] as a prescription or OTC product.

Any change to the CARESM Program must be discussed with FDA prior to its implementation and is subject to FDA's review.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. The safety and effectiveness of Plan B[®] provided pursuant to a prescription in pediatric patients (those under age 18) need not be addressed under the Pediatric Research Equity Act of 2003 (PREA) because this supplemental application does not propose a new indication for women in this age group (i.e., Plan B[®] is to remain prescription for women under 18).

In addition, we request that you submit to FDA four copies of the introductory promotional materials that you propose to use for Plan B[®]. Submit all proposed materials in draft or mock-up form, not final

print. Send one copy to the Division of Reproductive and Urologic Products, one to the Division of Nonprescription Clinical Evaluation, and two copies of both the promotional materials and the package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
WO 22, Room 4447
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Please submit one market package of Plan B[®] when it is available.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call the Office of Nonprescription Products, Division of Nonprescription Clinical Evaluation at (301) 796-2080.

Sincerely,

{See appended electronic signature page}

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

Enclosure