DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-045/S-011

Duramed Research, Inc.
Attention: Joseph A. Carrado, M.Sc., R.Ph.
Senior Director, 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 (the Act) for Plan B® (levonorgestrel) Tablets, 0.75 mg.

We acknowledge receipt of your submissions dated April 16, 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, and January 6, 12, 13, 14, 18, 19 and 21, 2005.

Your submission of July 21, 2004 constituted a complete response to our May 6, 2004 Not Approvable action letter.

The resubmitted supplemental new drug application provides for a switch from Rx only status to Over the Counter (OTC) status for women ages sixteen years and older. Plan B would remain Rx only for women under sixteen years of age. In addition, you have proposed that both the Rx and OTC version of Plan B be marketed in a single package.

The Center for Drug Evaluation and Research (CDER) has completed its review of this application, as amended, and has concluded that the available scientific data are sufficient to support the safe use of Plan B as an OTC product, but only for women who are 17 years of age and older. However, the Agency is unable at this time to reach a decision on the approvability of the application because of unresolved issues that relate to your NDA discussed below.

Your application has presented us with three difficult and novel issues. Specifically, you have proposed that Plan B be marketed in a single package, and sold either as Rx or OTC, depending on the age of the patient. While the Agency has allowed the same active ingredient to be marketed both Rx and OTC based on indication, strength, dosage form and route of administration, the Agency has never determined whether a drug may be both Rx and OTC based on the age of the individual using the drug. A related concern is how, as a practical matter, an age-based distinction could be enforced. In addition, we have never been confronted with whether the Rx and OTC versions of the same active ingredient may be marketed in a single package.

As you may be aware, questions have arisen over the years about whether there are any conditions under which an active ingredient may be simultaneously marketed in both a prescription drug product

and an OTC drug product. Notwithstanding our having allowed the practice in those rare instances where there is a meaningful difference in the indication, strength, dosage form or route of administration of the two products, we recognize that FDA's interpretation of section 503(b) of the Act has not been explicitly set forth in any of the regulations that discuss the process by which FDA classifies (or re-classifies) drugs as OTC or prescription. See 21 CFR 310.200 and 310.201.

In this case, we have decided that the appropriate course is to ask for public comments on whether we should initiate a rulemaking to codify our interpretation of section 503(b) regarding when an active ingredient can be simultaneously marketed in both a prescription drug product and an OTC drug product. To this end, we have decided to publish an advance notice of proposed rulemaking in the Federal Register. In addition, the notice will seek public comments on questions related to the marketing of Rx and OTC versions of the same active ingredient in a single package.

At this time, the drug product may not be legally marketed OTC. In the future, you will be notified in writing regarding changes in the status of your application.

Under 21 CFR 314.102(d), you may request an informal meeting or telephone conference to discuss what steps need to be taken before the application may be approved.

Sincerely,

Lester M. Crawford, DVM, PhD
Commissioner of Food and Drugs