

## **Plan B Advisory Committee Meeting Agenda December 16, 2003**

### **Introduction**

Plan B was approved for prescription use on July 28, 1999 for the following indication:

Plan B<sup>®</sup> is an emergency contraceptive that can be used to prevent pregnancy following unprotected intercourse or a known or suspected contraceptive failure. To obtain optimal efficacy, the first tablet should be taken as soon as possible within 72 hours of intercourse. The second tablet should be taken 12 hours later.

Two major studies were the basis for the FDA's approval. Both were double-blind randomized trials comparing the Plan B levonorgestrel regimen of emergency contraception to the "Yuzpe regimen", a combined levonorgestrel and ethinyl estradiol regimen. Plan B demonstrated efficacy compared to the Yuzpe regimen, which led to its approval for marketing as a prescription drug. The efficacy of Plan B when dosed appropriately is not an issue for discussion at this meeting.

Women's Capital Corporation, the applicant for the original prescription NDA, submitted an application for Plan B's switch from prescription to non-prescription status in April 2003. The purpose of this advisory committee meeting is to discuss whether Plan B meets regulatory requirements for non-prescription marketing.

### **Regulatory Requirements for non-prescription marketing**

The Durham-Humphrey Amendment to the Federal Food, Drug, and Cosmetic Act was enacted in 1951 and formally differentiates between prescription and non-prescription drugs. This is articulated in the Code of Federal Regulations 21 CFR 310.200(b) which states:

"Any drug limited to prescription use under section 503(b)(1)(C) of the act 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".

This provides that a drug be sold without a prescription if it is safe and if adequate directions for use can be written which are readily discernible by a layperson. There are several questions that must be answered in order to determine whether a product is suitable for a prescription to non-prescription switch. These questions include:

Does the product have:

- An acceptable safety profile based on prior prescription marketing experience

- Low misuse and abuse potential
- Reasonable therapeutic index of safety

And

- Can the condition be adequately self-recognized and successfully self-treated with minimal health care provider intervention
- Do the benefits from the switch clearly outweigh the risks
- Is the self-treatment product safe and effective during consumer use

If the answers to the above questions are yes, then the proposed product meets regulatory requirements for safety and effectiveness and is a candidate for non-prescription marketing.

The switch of a prescription drug to non-prescription status requires a review of the post marketing safety data and a determination that consumers can adequately use the product in a non-prescription setting. Other types of data that may be necessary for a prescription to non-prescription switch can include clinical studies (depending on the indication and whether the proposed switch dose has been studied), further safety studies, label comprehension studies and actual use studies. Label comprehension studies and actual use studies may be necessary to demonstrate that consumers understand when and how to use a product. During the development of Plan B for possible non-prescription marketing, the sponsor identified several issues that would need to be addressed:

- Proper self-selection for use
- Correct use at proper intervals
- Correct use by people with low literacy
- Use by women who are already pregnant
- Impact on use of more effective methods of birth control

The sponsor conducted and submitted the following studies to address these issues: a labeling comprehension study, an actual use study. In addition, the sponsor compiled information on postmarketing safety, submitted a search of the literature and a draft proposed non-prescription label.

This briefing package summarizes the review of submitted materials performed by the Division of OTC Drug Products and the Division of Reproductive and Urologic Drug Products.

As Advisory Committee members consider the information provided in this briefing document and in the meeting presentations they should prepare to address the Discussion Points listed below.

## Draft Discussion Points

*The actual use study (AUS) was conducted in five family planning clinic settings across five states and five pharmacy stores in the state of Washington. A total of 585 subjects ages 14-44 years were enrolled from family planning clinics (94%) and pharmacy stores (6%) in the United States. Subjects were only allowed to purchase one package of Plan B, but were allowed additional purchases after undergoing a re-enrollment process. The duration of the study was 4 weeks.*

1. Does the AUS demonstrate that consumers used the product as recommended in the proposed labeling?
2. Are the data from the AUS generalizable to the overall population of potential non-prescription users of Plan B?
3. Based on the data from the AUS and the review of the literature, is there evidence that non-prescription availability of Plan B leads to substitution of emergency contraception for the regular use of other contraceptive methods?
4. Do the data presented in the NDA demonstrate that Plan B is safe for use in the non-prescription setting?
5. Are the sponsor's plans for introduction of Plan B into the non-prescription marketplace adequate with respect to consumer access and safe use? In answering this question, you may consider other distribution mechanisms such as non-prescription restricted distribution.
6. Based on the data presented in the NDA, do you recommend that Plan B be switched from prescription to non-prescription status?
  - a) If yes, are there any additions or modifications you would recommend with regard to the proposed labeling and distribution plan?
  - b) If no, what additional information would be required?