

/S/

NDA 20-687

FEB 18 2000

Population Council  
Attention: Sandra P.-Arnold  
1230 York Avenue  
New York, NY 10021

Dear Ms. Arnold:

Please refer to your new drug application (NDA) dated March 14, 1996, received March 18, 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for mifepristone 200 mg tablets.

We acknowledge receipt of your submissions dated September 18 and 26, 1996; January 30, March 6 and 31, July 28, August 5, September 3 and 24, November 26, 1997; January 30, February 19, April 27, June 25, October 26, December 7 and 8, 1998; February 8, 22, March 31, April 28, May 10, 20, June 3 (2), 15, 25, 30, July 14, 22, August 3, 13, 18, 30, September 3, 8, 13, 30, October 5, 26, 28, November 16, 29 (2), December 6, 7, 23, 1999; January 21, 28 (2), and February 16, 2000. Your submission of August 18, 1999 constituted a complete response to our September 18, 1996 action letter.

We have completed the review of this application, as amended, and it is approvable. Before this application may be approved, however, it will be necessary for you to address the following:

**Chemistry**

Drug Substance

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Drug Product

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Redacted 1

pages of trade

secret and/or

confidential

commercial

information

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**Labeling**

Address the recommendations in the enclosed draft labeling for the Physician Insert and Patient Package Insert.  
It will be necessary for you to submit revised draft labeling for the drug. We recommend that the

labeling be identical in content to the enclosed draft labeling (text for the Physician Package Insert and Patient Package ~~Insert~~).

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

#### **Phase 4 Commitments**

We remind you of your commitments dated September 16, 1996, to perform the following Phase 4 studies:

1. To monitor the adequacy of the distribution and credentialing system,
2. To follow-up on the outcome of a representative sample of mifepristone-treated women who have surgical abortion because of the method failure,
3. To assess the long-term effects of multiple use of the regimen,
4. To ascertain the frequency with which women follow the complete treatment regimen and the outcome of those who do not,
5. To study the safety and efficacy of the regimen in women (1) under 18 years of age, (2) over age 35, and (3) who smoke,
6. To ascertain the effect of the regimen on children born after treatment failure.

#### **Distribution Plan**

We have completed our review of this application, including the restrictions on the distribution and use of this product proposed in your January 21, 2000 submission, entitled "Distribution Plan". We have concluded that adequate information has not been presented to demonstrate that the drug, when marketed in accordance with the terms of distribution proposed, is safe and effective for use as recommended. The restrictions on distribution will need to be amended.

We have thus considered this application under the restricted distribution regulations contained in 21 CFR 314.500 (Subpart H) and have concluded that restrictions as per CFR 314.520 on the distribution and use of mifepristone are needed to assure safe use of this product.

### Promotional Activities

Please note that promotional activities for this NDA are subject to 21 CFR 314.550. As such, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please send one copy to the [redacted] and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20857

Under 21 CFR 314.50(d)(5)(vi)(b), we request that you update your NDA by submitting all safety information you have regarding your new drug. Please provide updated information as listed below. The update should cover all studies and uses of the drug including: (1) those involving indications not being sought in the present submission, (2) other dosage forms, and (3) other dose levels, etc.

1. Retabulation of all safety data including results of trials that were still ongoing at the time of NDA submission. The tabulation can take the same form as in your initial submission. Tables comparing adverse reactions at the time the NDA was submitted versus now will certainly facilitate review.
2. Retabulation of drop-outs with new drop-outs identified. Discuss, if appropriate.
3. Details of any significant changes or findings.
4. Summary of worldwide experience on the safety of this drug.
5. Case report forms for each patient who died during a clinical study or who did not complete a study because of an adverse event.
6. English translations of any approved foreign labeling not previously submitted.
7. Information suggesting a substantial difference in the rate of occurrence of common, but less serious, adverse events.

Within 10 days after the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the application. 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.

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The drug product may not be legally marketed until you have been notified in writing that the application is approved.

If you have any questions, call

[Redacted]

Sincerely,

[Redacted]

/S/

Center for Drug Evaluation and Research

Enclosure

APPEARS THIS WAY  
ON ORIGINAL