NDA 20-874

Pharmacia & Upjohn
Attention: P.K. Narang, Ph.D., F.C.P.
Liason Director, Regulatory Affairs
7000 Portage Road
Kalamazoo, MI 49001

Dear Dr. Narang:

Please refer to your new drug application (NDA) dated September 25, 1997, received September 26, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lunelle™ Monthly Contraceptive Injection (medroxyprogesterone acetate/estradiol cypionate).

We acknowledge receipt of your submissions dated November 24 and December 12, 1997; and May 21, June 5, 29 (2), and 30, July 15, 16 and 28, August 7, 11, 12 and 13, October 1 and 26, November 4, 1998; February 24, April 12, 15 and 27, August 6, 18, 20, 25, 26, and 31, September 1, 3, 7 and 27, October 8, 12, 13 and 25, April 6, May 2, 15, 22, and 31, June 6 and 7, July 11 and 27, August 9, September 12, October 4 and 5, 2000. Your submission of April 6, 2000 constituted a complete response to our October 15, 1999 action letter.

This new drug application provides for the use of Lunelle™ Monthly Contraceptive Injection (medroxyprogesterone acetate/estradiol cypionate) Injection for the prevention of pregnancy.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted October 5, 2000, patient package insert submitted October 4, 2000, immediate container and carton labels submitted October 13, 1999). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative purposes, this submission should be designated "FPL for approved NDA 20-874." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your post marketing commitment specified in your submission dated October 4, 2000. This commitment, along with any completion dates agreed upon, is listed below.

To conduct a study post-approval to evaluate the theoretical effects of Lunelle™ Monthly Contraceptive Injection on bone mineral density and to compare those results to that of depot

medroxyprogesterone acetate (DMPA) over a two year period. The final protocol for this study will be submitted for review within six months of approval.

Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. If an IND is not required to meet your post marketing commitments, please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21 CFR 314.81(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these post marketing commitments must be clearly designated "Post Marketing Commitments."

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Be advised that, as of April 1, 1999, 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 (63 *FR* 66632). We are waiving the pediatric study requirement for this action on this application.

In addition, 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 Division of Reproductive and Urologic Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Jennifer Mercier, Regulatory Project Manager, at 301-827-4260.

Sincerely,

Florence Houn, M.D., M.P.H., F.A.C.P.
Director
Office of Drug Evaluation III
Center for Drug Evaluation and Research