DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 012541/S-083

**SUPPLEMENT APPROVAL**

Pharmacia & Upjohn Company
Attention: Michele Burtness
235 East 42nd St.
New York, NY 10017

Dear Ms. Burtness:

Please refer to your Supplemental New Drug Application (sNDA) dated December 12, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Depo-Provera® (medroxyprojesterone acetate), Injectable Suspension.

This Prior Approval supplemental new drug application provides for the following changes:

1. Removed CONTRAINDICATIONS: Known or suspected pregnancy or as a diagnostic test for pregnancy, Undiagnosed vaginal bleeding, Known or suspected malignancy of breast, and (b) (4)
2. Removed WARNING subsections: (b) (4)
3. Added subsections to PRECAUTIONS: Breast Cancer, Hepatic Dysfunction, Decrease in Bone Mineral Density, Cushingoid Symptoms, Effects on Hypothalmic-Pituitary-Adrenal Axis, Pediatric Use, and Interference with Laboratory Tests
4. Modified the wording of Carcinogenesis, Mutagenesis, Impairment of Fertility section.
5. Removed Carcinogenesis, Mutagenesis, Impairment of Fertility as a stand-alone section and added it to PRECAUTIONS as a subsection.
6. Added language to the DRUG INTERACTIONS section to address in-vitro experience with drug interactions during the concomitant administration of CYP3A4 inhibitors.
7. Added adverse reactions to the ADVERSE REACTIONS section: These included euphoria, corticoid-like effects (e.g., Cushingoid syndrome), malaise, erectile dysfunction and hypercalcemia.
8. Re-organized the ADVERSE REACTION section to align with current labeling practices.
9. Added the following section to DOSAGE AND ADMINISTRATION: Geriatric Use, Hepatic Impairment, and Renal Impairment. Further subdivided Geriatric with subsections Renal Carcinoma and Endometrial Carcinoma.
10. Removed The PATIENT INFORMATION and (b) (4) sections.

## APPROVAL & LABELING

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

## CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling text for the package insert and Medication Guide, with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As at: http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

## PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at: http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at: http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For

more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

**REPORTING REQUIREMENTS**

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 Jeannette O'Donnell, Regulatory Project Manager, at (240) 402-4978 or email: Jeannette.Odonnell@fda.hhs.gov.

Sincerely,

*{See appended electronic signature page}*

Geoffrey Kim, MD
Director
Division of Oncology Products 1
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**

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/s/

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GEOFFREY S KIM
06/11/2015