DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 018662/S-061

SUPPLEMENT APPROVAL

Hoffmann-La Roche Inc.
Attention: Maryann Major
Director, Drug Regulatory Affairs
340 Kingsland Street
Nutley, NJ 07110

Dear Ms. Major:

Please refer to your supplemental new drug application (sNDA) dated September 17, 2008, received September 18, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Accutane® (isotretinoin) Capsules, 10, 20 and 40 mg. We note that NDA 018662 was approved under the provisions of 21 CFR 314.520 (Subpart H).

This supplemental application contains a proposed risk evaluation and mitigation strategy (REMS) for Accutane (isotretinoin) and was submitted in accordance with section 909(b)(1) of the Food and Drug Administration Amendments Act of 2007 (FDAAA). Under section 909(b)(1) of FDAAA, we identified Accutane (isotretinoin) as a product deemed to have in effect an approved REMS because there were in effect on the effective date of FDAAA, March 25, 2008, elements to assure safe use required under 21 CFR 314.520.

We also refer to your submissions dated May 30, October 3, November 17, 2008, August 25, September 1, September 30, 2009, April 2, April 7, April 21, April 27, May 4, September 15, September 23, September 29, October 5 and October 14, 2010.

In accordance with section 505-1 of the FDCA, we have determined that a REMS is necessary for Accutane (isotretinoin) to ensure the benefits of the drug outweigh the risk of teratogenicity. Your proposed REMS, as amended and appended to this letter, is approved with the minor editorial revisions listed below:

- Printing identification was redacted from all educational materials
- Completed text fields in templates and screenshots were redacted
- List of changes made to web shots were redacted
- The title of the form, “Request for Exemption for Patients with Serious Medical Reasons” was corrected in the REMS document to be consistent with the name of the appended form

The REMS consists of a Medication Guide, elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS.

As required under section 505-1(i) of the FDCA, this REMS will use a single shared system for the elements to assure safe use and implementation system in the approved REMS. This single shared system, iPLEDGE, includes the following products:

NDA 018662 Accutane® (isotretinoin) Capsules, 10, 20, and 40 mg
ANDA 075945 Amnesteem® (isotretinoin) Capsules, 10, 20, and 40 mg
ANDA 076135 Clavaris™ (isotretinoin) Capsules, 20, 30, and 40 mg
ANDA 076356 Claravis™ (isotretinoin) Capsules, 10 mg
ANDA 076041 Sotret® (isotretinoin) Capsules, 10, 20 and 40 mg
ANDA 076503 Sotret® (isotretinoin) Capsules, 30 mg

Other products may be added to the single shared system in the future if additional ANDAs are approved.

The REMS assessment plan should include, but is not limited to, the following information:

a. Reports of operational audits, including results of distribution data reconciliation
b. Results of any prescriber, pharmacist, and patient surveys
c. An evaluation of patients' understanding of the serious risks of Accutane (isotretinoin)
d. A report on periodic assessments of dispensing of the Medication Guide in accordance with 21 CFR 208.24
e. A report on failures to adhere to Medication Guide distribution and dispensing requirements, and corrective actions taken to address noncompliance
f. Non-Compliant Distribution 15-day Reports
g. Semi-annual (every 6 months) Internet Surveillance of Accutane (isotretinoin) Sales
h. Annual iPLEDGE Report with contents as described in the attachment to this letter.

You will collect and report all data required for assessments of the approved REMS until approval of your NDA is withdrawn in the Federal Register.

The requirements for assessments of an approved REMS under section 505-1(g)(3)(A) include an assessment of the extent to which the elements to assure safe use are meeting the goal or goals to mitigate a specific serious risk listed in the labeling of the drug, or whether the goal or goals or such elements should be modified.

Assessments of an approved REMS must also include, under sections 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

We remind you that in addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in Section 505-1(g)(2)(A) of the FDCA.

Prominently identify future submissions containing REMS assessments or proposed modifications with the following wording in bold capital letters at the top of the first page of the submission:

NDA 018662 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 018662
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 018662
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

As part of the approval under Subpart H, as required by 21 CFR 314.550, you must submit all promotional materials, including promotional labeling as well as advertisements, at least 30 days before the intended time of initial distribution of the labeling or initial publication of the advertisement. Send one copy to the Division of Dermatology and Dental Products and two copies of the promotional materials and the package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

CONTENT OF LABELING

The final agreed-upon product labeling is attached. As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements. 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.

We request that the revised labeling approved today be available on your website within 10 days of receipt of this letter.

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA and to CDERMedWatchSafetyAlerts@fda.hhs.gov, and a paper copy to the following address:

MedWatch Program
Office of Special Health Issues
Food and Drug Administration
10903 New Hampshire Ave
Building 32, Mail Stop 5353
Silver Spring, MD 20993

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

We also remind you of your specific reporting obligations regarding serious adverse events in patients who have received Accutane (isotretinoin). In addition to the usual postmarketing reporting of adverse drug experiences (21 CFR 314.80(c)), you will submit a 15-day report for each of the following:

- All pregnancy exposures to Accutane (isotretinoin); and
- All psychiatric events including suicides, attempted suicides, and suicidal ideation

In addition, you should continue to provide us with the following reports:

1. Annual Periodic Adverse Drug Experience Report
2. Special Pregnancy Periodic Biannual Report
3. Non-Compliant Distribution Reports
4. Psychiatric Quarterly Report

If you have any questions, call Dawn Williams, Regulatory Project Manager, at (301) 796-5376.

Sincerely,

{See appended electronic signature page}

Susan J. Walker, M.D., F.A.A.D.
Director
Division of Dermatology and Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosures:
REMS
Annual iPLEDGE Report Contents

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

/s/

SUSAN J WALKER
10/22/2010