DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 18-662/S-058

Hoffman La-Roche
Attention: MaryAnn Major, Senior Program Manager
340 Kingsland Street
Nutley, New Jersey 07110-1199

Dear Ms. Major:

Please refer to your pending supplemental new drug application submitted February 16, 2007, received February 17, 2007 under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Accutane (isotretinoin) capsules, 10 mg, 20 mg, and 40 mg.

We acknowledge receipt of your submissions dated April 24, May 22, September 11 and 20, 2007.

This supplemental application, considered for approval under 21 CFR 314.520 (Subpart H), proposed changes to the iPLEDGE program, an enhanced risk minimization action plan (RiskMAP) designed to minimize drug exposure during pregnancy.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to approve the supplemental application for Accutane (isotretinoin) capsules, 10mg, 20mg, and 40mg. Accordingly, this supplemental application is approved under 21CFR 314.520 (Subpart H). Approval is effective on the date of this letter for use as recommended in the agreed upon labeling text (attached) and the components of the iPLEDGE RiskMAP.

We remind you that your Accutane RiskMAP (called iPLEDGE) is an important part of the postmarketing risk management for Accutane, and must include each of the following components:

1. Registration in the iPLEDGE program of wholesalers, prescribers, pharmacies, and patients who agree to accept specific responsibilities in order to distribute, prescribe, dispense, and use Accutane.
2. Implementation of a program and distribution of materials to educate wholesalers, prescribers, pharmacists, and patients about the risks and benefits of Accutane.
3. Implementation of a reporting and data collection system for: a) serious adverse events associated with the use of Accutane that complies with the reporting requirements for an approved NDA (21 CFR 314.80 and 314.81) and b) sales and dispensing of Accutane outside of the iPLEDGE program.
4. Implementation of a plan to monitor, evaluate, and improve minimization of drug exposure during pregnancy and compliance with restrictions for safe use under the

iPLEDGE program. A component of the evaluation program includes a pregnancy registry to elucidate the root cause of potential RiskMAP failure.

The iPLEDGE program approved on August 12, 2005, along with the changes to the iPLEDGE program, as described in the attached document, adequately addresses each of these requirements. We remind you that any change to the program must be discussed with FDA prior to its institution and is subject to FDA's determination that the required components continue to be met.

FDA will re-evaluate the adequacy of the iPLEDGE program on a continuing basis regarding its success in achieving the goal of minimizing drug exposure during pregnancy and adherence to program components.

The final printed labeling (FPL) must be identical to the agreed upon labeling text submitted September 20, 2007. Marketing the product with FPL with text that is not identical to the approved text may render the product misbranded and an unapproved new drug.

If you have any questions, please call Kalyani Bhatt, Regulatory Project Manager, at (301) 796-2110.

Sincerely,

{See appended electronic signature page}

Susan J. Walker, MD, FAAD
Director
Division of Dermatology & Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure

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

/s/

Susan Walker
10/3/2007 01:25:29 PM