DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 18-662/S043

Hoffman La-Roche Inc.
Attention: Joanna Waugh, BSc., Hons.
Group Director, Drug Regulatory Affairs
340 Kingsland Street
Nutley, NJ 07110

Dear Ms.Waugh:

Please refer to your supplemental new drug application dated May 1, 2001, received May 2, 2001, submitted 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 May 17, November 21 and December 12, 2001; January 15, February 28, March 4, April 29, (electronic mail) May 1, (electronic mail) and May 2, 2002 (electronic mail) (3).

This supplemental new drug application provides for additional safety and efficacy information for Accutane (isotretinoin) Capsules, l0 mg, 20 mg, and 40 mg, in pediatric labeling for the treatment of severe recalcitrant nodular acne. This supplemental new drug application does not significantly affect the size of the patient population to be given the drug, since Accutane was already approved for the treatment of severe recalcitrant nodular acne without reference to age restrictions.

We have completed the review of this supplemental 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 supplemental application is approved effective on the date of this letter.

In addition, the approved labeling for supplemental new drug application, S047 (Blister Pak), approved on April 12, 2002, has revisions in the Important Information for All Patients section to be consistent with the agreed to labeling in supplemental new drug application, S043.

The final printed labeling (FPL) must be identical to the enclosed labeling text (package insert, patient package insert, blister pak).

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 18-662/S043 and NDA 18-662/S047." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your postmarketing commitment specified in your electronic mail submission dated May 2, 2002.

This commitment is listed below.

The analysis presented in the original study report (MO 1513), as described in the MO 1513 report, was found subsequent to the submission, to be possibly an unvalidated representation of adjusted Bone Mineral Density (BMD). Within 6 months, a recalculation of the existing unadjusted data (including study NR 15919) using a published volumetric methodology (Bone Mineral Apparent Density-BMAD) will be submitted. These recalculated data may then be used to support a subsequent labeling revision.

Final Study Report Submission: Within 6 months of the date of this letter

If needed, submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "**Postmarketing Study Protocol", "Postmarketing Study Final Report", or "Postmarketing Study Correspondence."**

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 further pediatric study requirements 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 submit one copy to this Division 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

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

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, please call Kalyani Bhatt, Project Manger, at 301-827-2020.

Sincerely,

{See appended electronic signature page}

Jonathan K. Wilkin, M.D.
Director
Division of Dermatologic & Dental Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

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

/s/

Jonathan Wilkin
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Labeling discussions, both internally and with the sponsor, led to several differences in final agreed to labeling from labeling proposed in earlier reviews.