DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 18-662/S048/S-052

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

Dear Ms. Waugh:

Please refer to your supplemental new drug application S-048 dated March 22, 2002, received March 25, 2002, and S-052 dated May 15, 2003, received May 16, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Accutane (isotretinoin) Capsules, 10 mg, 20 mg, and 40 mg.

Your submission for S-048 dated March 14, 2003, constituted a complete response to our December 15, 2002 action letter.

Supplemental new drug application S-048 provides for the printed text and video storyboard presentation of the submitted video on birth defects entitled: "Be Aware: The Risk of Pregnancy While on Accutane".

Supplemental new drug application S-052 provides for revisions to the following: boxed CONTRAINDICATIONS and WARNINGS section, Warnings (Lipids and Skeletal subsection), PRECAUTIONS, Information for Patients and Prescribers, Drug Interactions; Pediatric Use, boxed Information for Pharmacists section; Patient Information/Consent Form; System to Manage Accutane Related Teratogenicity S.M.A.R.T. Guide to Best Practices; Be Smart Be Safe Be Sure Accutane Pregnancy Prevention and Risk Management Program for Women; Be Smart Be Safe Be Sure Accutane (isotretinoin) Risk Management Program for Men; and the Accutane Qualification Sticker.

We completed our review of these applications, as amended. These applications are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert; text for the Patient Information/Consent (for female patients concerning birth defects); Informed Consent/Patient Agreement (for all patients); Medication Guide; Accutane Qualification Sticker; booklet for prescribers entitled System to Manage Accutane Related Teratogenicity (S.M.A.R.T.) Guide to Best Practices; Be Smart Be Safe Be Sure: Accutane Pregnancy Prevention and Risk Management Program for Women; Be Smart Be Safe Be Sure: Accutane (isotretinoin) Risk Management Program for Men; and printed text and video storyboard presentation for the video entitled "Be Aware: The Risk of Pregnancy While on Accutane".

Please submit the FPL electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – NDA. Alternatively, you may 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 15 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 S-048 and S-052." Approval of this submission by FDA is not required before the labeling is used.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this Division, Division of Dermatologic and Dental 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, MD 20857

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

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 Kalyani Bhatt, Regulatory Project Manager, at (301) 827-2020.

Sincerely,

{See appended electronic signature page}

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

Enclosures

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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