DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20852

Our STN: BL 103964/5039

FEB 25 2005

Hoffmann-La Roche, Inc.
Attention: Karen Noh, Pharm.D.
Senior Program Manager
340 Kingsland Street
Nutley, NJ 07110-1199

Dear Dr. Noh:

Your request to supplement your biologics license application (BLA) for Peginterferon alfa-2a to expand the indication for Peginterferon alfa-2a (PEGASYS®) alone or in combination with ribavirin USP (COPEGUS®) to include treatment of adult chronic hepatitis C patients coinfected with HIV, who have clinically stable HIV disease has been approved.

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. We are waiving the pediatric study requirement for this application.

We acknowledge your written commitment to conduct a postmarketing study as described in your letter of February 25, 2005 as outlined below:

Postmarketing Study subject to reporting requirements of 21 CFR 601.70.

1. To conduct an international, multi-center, randomized, double-blind trial in genotype 1, chronic hepatitis C patients coinfected with HIV 1) to evaluate the safety and efficacy of Peginterferon alfa-2a in combination with higher doses of ribavirin than currently recommended for these patients, and 2) evaluate the safety of these regimens in patients of African American descent. The study will enroll 400 patients, including approximately 100 African American patients. Patients will be randomized to receive either Peginterferon alfa-2a 180 mcg per week in combination with ribavirin 800 mg daily or Peginterferon alfa-2a 180 mcg per week in combination with ribavirin 1000-1200 mg daily. The protocol will be submitted to the IND August 2005, patient accrual will begin in April 2006, and will be completed by October 2006. The study will be completed by February 2008 and the final study report, datasets and modified labeling will be submitted September 2008.

We request that you submit clinical protocols to your IND, with a cross-reference letter to this biologics license application (BLA), STN BL 103964. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to your BLA STN BL 103964.

Please use the following designators to label prominently all submissions, including supplements, relating to this postmarketing study commitment as appropriate:

- Postmarketing Study Protocol
- Postmarketing Study Final Report
- Postmarketing Study Correspondence
- Annual Report on Postmarketing Studies

For each postmarketing study subject to the reporting requirements of 21 CFR 601.70, you must describe the status in an annual report on postmarketing studies for this product. The status report for each study should include:

- information to identify and describe the postmarketing commitment,
- the original schedule for the commitment,
- the status of the commitment (i.e. pending, ongoing, delayed, terminated, or submitted),
- an explanation of the status including, for clinical studies, the patient accrual rate (i.e. number enrolled to date and the total planned enrollment), and
- a revised schedule if the study schedule has changed and an explanation of the basis for the revision.

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our Web site (http://www.fda.gov/cder/pmc/default.htm). Please refer to the April 2001 Draft Guidance for Industry: Reports on the Status of Postmarketing Studies – Implementation of Section 130 of the Food and Drug Administration Modernization Act of 1997 (see http://www.fda.gov/cber/gdlns/post040401.htm) for further information.

FDA previously approved a Medication Guide required for distribution with this product in accordance with 21 CFR Part 208. FDA hereby approves the revised draft Medication Guide you submitted on February 25, 2005.

Please note that:

- this Medication Guide must be reprinted at the end of the package insert [21 CFR 201.57(f)(2)];

- you are responsible for ensuring that this Medication Guide is available for distribution to every patient who is dispensed a prescription for this product [21 CFR 208];

- the final printed Medication Guide distributed to patients must conform to all conditions described in 21 CFR 208.20, including a minimum of 10 point text; and
- you are responsible for ensuring that the label of each container or package includes a prominent and conspicuous instruction to authorized dispensers to

provide a Medication Guide to each patient to whom the drug is dispensed, and states how the Medication Guide is provided.

Please submit all final printed labeling at the time of use and include implementation information on FDA Form 356h. Please provide a PDF-format electronic copy as well as original paper copies (ten for circulars and five for other labels). In addition, you may wish to submit draft copies of the proposed introductory advertising and promotional labeling with a cover letter requesting advisory comments to the Division of Drug Marketing, Advertising and Communication (HFD-42), Center for Drug Evaluation and Research, 5600 Fishers Lane/Room 8B45, Rockville, MD 20857. Final printed advertising and promotional labeling should be submitted at the time of initial dissemination, accompanied by an FDA Form 2253.

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence to support that claim.

Please refer to http://www.fda.gov/cder/biologics/default.htm for important information regarding therapeutic biological products, including the addresses for submissions. Effective Oct. 4, 2004, the new address for all submissions to this application is:

CDER Therapeutic Biological Products Document Room
Center for Drug Evaluation and Research
Food and Drug Administration
12229 Wilkins Avenue
Rockville, Maryland 20852

This information will be included in your biologics license application file.

Sincerely,

(b) [redacted] for MKW

Marc K. Walton, M.D., Ph.D.
Director
Division of Therapeutic Biological Internal Medicine Products
Office of Drug Evaluation VI
Center for Drug Evaluation and Research

Enclosures: Labeling