DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20852

Our STN: BL 103964/5037

MAY 13 2005

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

Dear Dr. Carey:

Your request to supplement your biologics license application (BLA) for Peginterferon alfa-2a to include treatment of adult patients with HBe Antigen positive and HBe Antigen negative chronic hepatitis B who have compensated liver disease and evidence of viral replication and liver inflammation 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 neonates and infants for this application. We are deferring the postmarketing study requirement for subjects 2 to 17 years of age.

We acknowledge your written commitments to conduct postmarketing studies as described in your letter of May 12, 2005, and as outlined below:

Postmarketing Study subject to reporting requirements of 21 CFR 601.70.

1. To assess the safety and efficacy of Peginterferon alfa-2a versus a no-treatment control in 110 pediatric HBeAg positive patients chronically infected with the hepatitis B virus, who have compensated liver disease. The protocol will be submitted to BB-IND (b)(4) by November, 2009. Patient accrual will begin May, 2010 and will be completed by November, 2011. The study will be completed by May, 2013 and the final study report, data sets and modified labeling will be submitted by November, 2013.

2. To conduct an international, multi-center, randomized, study to evaluate the safety and efficacy of 24 weeks versus 48 weeks of Peginterferon alfa-2a treatment and 90 mcg versus 180 mcg doses of Peginterferon alfa-2a in 530 adult chronic hepatitis B patients with compensated liver disease who are HBeAg positive. The protocol will be submitted November, 2005. Patient accrual will begin May, 2006 and end November, 2007. The study will end May, 2009 and the final study report, data sets and modified labeling will be submitted November, 2009.

3. Submit immunogenicity data from an analysis of the presence of neutralizing and non-neutralizing antibodies from all available patient samples for baseline, week 4, week 24 and week 60 from the pivotal studies WV16240 and WV16241. The final study report will be submitted November 2005

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 May 12, 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.

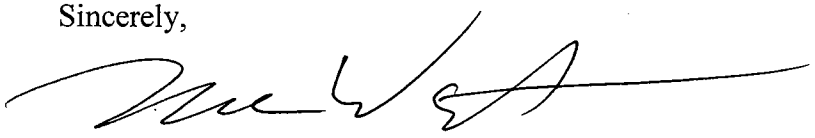
All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence to support that claim.

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,



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