DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 103964/5176

SUPPLEMENT APPROVAL
May 24, 2010

Hoffmann-La Roche, Inc.
Attention: Christina Kish
Associate Director Drug Regulatory Affairs
340 Kingsland Street
Nutley, NJ 07110-1199

Dear Ms. Kish:

Please refer to your supplement to your biologics license application (BLA) dated July 10, 2009, received July 13, 2009, submitted under section 351 of the Public Health Service Act for PEGASYS® (peginterferon alfa-2a) Injectable Solution.

We acknowledge receipt of your submissions dated January 22, February 8, April 6, and May 12, 2010.

This supplement to your BLA provides for changes to the **WARNINGS, Bone Marrow Toxicity and the PRECAUTIONS, Drug Interaction** subsections of the package insert to include information regarding the increased risk of pancytopenia when PEGASYS® (peginterferon alfa-2a) and ribavirin combination therapy is used with azathioprine. The supplement also provides for a proposed modification to the approved risk evaluation and mitigation strategy (REMS) and updates the Medication Guide with information regarding the revisions to the package insert described above.

We have completed our review of this application, and it is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed upon labeling text.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for PEGASYS® (peginterferon alfa-2a) was originally approved on October 31, 2008, and consists of a Medication Guide and a timetable for submission of assessments of the REMS. The proposed modified REMS contains a revised Medication Guide which adds the drug-drug interaction and adverse reaction information described above and the modification to the timetable for submission of assessments of the REMS included in your February 8, 2010 and April 6, 2010 submissions. Your February 8, 2010 submission also included a statement that the revised Medication Guide would be adequate with the proposed modifications to achieve its purpose.

Your proposed modified REMS, submitted on April 6, 2010, and appended to this letter, is approved. The REMS consists of the Medication Guide and a timetable for submission of assessments.

There are no changes to the REMS assessment plan included in your April 6, 2010 letter.

The requirements for assessments of an approved REMS under section 505-1(g)(3) include, in section 505-1(g)(3)(B) and (C), information on the status of any post-approval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

We remind you that in addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of the Federal Food, Drug, and Cosmetic Act (FDCA).

Prominently identify submissions containing REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission:

BLA 103964 REMS ASSESSMENT

NEW SUPPLEMENT for BLA 103964
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR BLA 103964
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

We request that the revised labeling approved today be available on your website within 10 days of receipt of this letter.

CONTENT OF LABELING

Within 14 days of the date of this letter, submit content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm that is identical in content to the enclosed labeling text. The content of labeling should be submitted by

updating your applications by referencing the SPL file submitted to the drug establishment registration and drug listing system. To do this, place a link in your application submissions that directs FDA to your SPL file. For administrative purposes, please designate this submission "**Product Correspondence – Final SPL for approved BLA STN 103964/5176.**" In addition, within 14 days of the date of this letter, amend any pending supplements for this BLA with content of labeling in SPL format to include the changes approved in this supplement. For additional information on submitting labeling to drug establishment registration and drug listing and to applications, see the FDA guidances at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072339.pdf and http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

PROMOTIONAL MATERIAL

All promotional materials for your drug product that include representations about your drug product must be promptly revised to make it consistent with the labeling changes approved in this supplement, including any new safety information 21 CFR 601.12(a)(4)]. The revisions to your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 601.12(a)(4) to the following address or by facsimile at 301-847-8444:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

In addition, as required under 21 CFR 601.12(f)(4), you must submit your updated final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA-2253, directly to the above address. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

If you have any questions, call Myung-Joo Patricia Hong, Regulatory Project Manager, at (301) 796-0807 or 301-796-1500.

Sincerely,

/Kendall Marcus, M.D/
For Debra Birnkrant, M.D.
Director
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure: Content of Labeling
Revised REMS