DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

Our STN: 103964/5133

Hoffmann-La Roche, Inc.
Attention: Ms. Christina Kish
Sr. Program Manager
340 Kingsland Street
Nutley, NJ 07110-1199

Dear Ms. Kish:

Please refer to your Biologics License Applications (BLA) for Pegasys (peginterferon alfa-2a) submitted under section 351 of the Public Health Service Act. We also refer to the following labeling submissions:

Supplement:

BLA 103964/5133, submitted October 12, 2007, received October 15, 2007, proposed revisions to the Medication Guide that included removal of the monthly convenience package configuration of four vials (4 pack).

Amendments:

BLA 103964/5133/5001, submitted March 27, 2008, received March 28, 2008 proposed addition of stroke related information to the section of the Medication Guide entitled, "**What is the most important information I should know about PEGASYS therapy?**".

BLA 103964/5133/5002, submitted July 7, 2008, and received July 9, 2008 proposed revisions to the Medication Guide to add the following statements: "Call your doctor for medical advice about side effects" and "You may report side effects to FDA at 1-800-FDA-1088 or Roche at 1-800-526-6367". This amendment also included a change in the needle color from orange to green which has since been approved in a separate supplement (BLA 103964/5154).

We have completed our review of this supplemental biologic license application as amended. This application is approved, effective on the date of this letter, for use as recommended in the enclosed labeling. The final printed labeling (FPL) must be identical to the enclosed labeling. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

CONTENT OF LABELING

Within 14 days of the date of this letter, submit content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/oc/datacouncil/spl.html, that is identical in content to the enclosed labeling text/submitted labeling dated October 31, 2008. Upon receipt and verification, we will transmit that version to the National Library of Medicine for public dissemination.

Within 21 days of the date of this letter, amend any pending supplement for this BLA with content of labeling in SPL format to include the changes approved in these supplements

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENT

Title IX, Subtitle A, Section 901 of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amends the Federal Food, Drug, and Cosmetic Act (FDCA) to authorize FDA to require the submission of a REMS for an approved drug if the Secretary becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)). This provision took effect on March 25, 2008.

Since Pegasys (peginterferon alfa-2a) was approved in 2002, FDA has become aware of new safety information, as defined in FDAAA. This new safety information shows that there are cases of cerebrovascular complications due to stroke in patients with few or no expected risk factors for stroke.

In accordance with section 505-1 of the FDCA, as one element of a REMS, FDA may require the development of a Medication Guide as provided for under 21 CFR Part 208. FDA previously approved a Medication Guide required for distribution with Pegasys (peginterferon alfa-2a) in accordance with 21 CFR Part 208. Pursuant to 21 CFR Part 208, FDA has determined that Pegasys (peginterferon alfa-2a) poses a serious and significant public health concern requiring distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of Pegasys (peginterferon alfa-2a). FDA has determined that Pegasys (peginterferon alfa-2a) is a product that has serious risks of which patients should be made aware because information concerning the risks could affect patients' decisions to use, or continue to use Pegasys (peginterferon alfa-2a).

The Medication Guide has been revised in response to this new safety information, and is now considered to be part of a REMS.

Your proposed REMS, dated August 22, 2008, and received on August 25, 2008, is approved. The REMS consists of the final Medication Guide approved with this letter and the timetable for submission of assessments of the REMS that was included in your August 22, 2008 submission.

The timetable you submitted is as follows:

1st FDAAA assessment:	April 30, 2010	(18 months from approval)
2nd FDAAA assessment:	October 31, 2011	(3 years from approval)
3rd FDAAA assessment:	October 31, 2015	(7 years from approval)

Your assessment of the REMS should include an evaluation of:

a. Patients' understanding of the serious risks of Pegasys (peginterferon alfa-2a)
b. Because the Medication Guide is packaged with the product, issues concerning distribution and dispensing of the Medication Guide are not applicable.

Use the following designator to prominently label all submissions, including supplements, relating to this REMS:

Risk Evaluation and Mitigation Strategy (REMS)

Please note that:

- this Medication Guide must be reprinted immediately following the last section of labeling or, alternatively, accompany the prescription drug labeling [21 CFR 201.57(c)(18)] or 21 CFR 201.80(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 208.24;

- 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 [21 CFR 208.24(d)].

Please refer to http://www.fda.gov/cder/biologics/default.htm for information regarding therapeutic biological products, including the addresses for submissions.

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

If you have any questions, contact Kwadwo (Kojo) Awuah, Regulatory Project Manager, at 301-796-0608.

Sincerely,

for DB
10/31/08

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