DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 103964/5204

SUPPLEMENT BLA APPROVAL
September 29, 2011

Hoffmann-La Roche, Inc.
Attention: Steven Toma, Pharm.D.
Associate Director, Pharma Development Regulatory
340 Kingsland Street
Nutley, NJ 07110

Dear Dr. Toma:

Please refer to your Supplemental Biologics License Application (sBLA), dated November 30, 2010, received November 30, 2010, submitted under section 351 of the Public Health Service Act for PEGASYS® (peginterferon alfa-2a).

We acknowledge receipt of your amendments dated February 14, 2011, March 7, 2011, March 11, 2011, April 8, 2011, April 25, 2011, April 28, 2011, May 5, 2011, May 10, 2011, May 11, 2011, May 19, 2011, June 30, 2011 (2), July 21, 2011, July 27, 2011, August 11, 2011, August 19, 2011, August 25, 2011, August 26, 2011, August 29, 2011, September 8, 2011 (2), September 14, 2011 and September 26, 2011.

This supplemental application provides for the use of a135 mcg/0.5ml and 180 mcg/0.5 ml PEGASYS disposable autoinjector (DAI), revisions to the package insert, and a proposed modification to the approved risk evaluation and mitigation strategy (REMS).

The REMS for PEGASYS® (peginterferon alfa-2a) was originally approved on October 31, 2008. The REMS consisted of a Medication Guide and a timetable for submission of assessments of the REMS. You submitted a request for FDA to release the REMS requirement on April 1, 2011. Because we approved your request to release the REMS requirement on May 9, 2011, the proposed REMS modification included in this supplement is no longer applicable. Therefore, we consider this supplement to provide only for the use of the disposable autoinjector and labeling changes described above.

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

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the 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 to the enclosed labeling (text for the package insert, Medication Guide) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements. Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf. For administrative purposes, please designate this submission "**Product Correspondence – Final SPL for approved BLA STN 103964/5204**."

Also within 14 days, amend all pending supplemental applications for this BLA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] in MS Word format that includes the changes approved in this supplemental application.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Please submit these labels electronically according to the guidance for industry titled "Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)." Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Product Correspondence – Final Printed Carton and Container Labels for approved BLA STN 103964/5204**." Approval of this submission by FDA is not required before the labeling is used.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

PMC-1 Monitor Pegasys pre-filled syringes (SIN-PFS) subvisible particles (b) (4) as extended characterization testing at release for commercial product and develop a sufficient number of lots for testing at 2-8ºC and under stressed and/or accelerated conditions. When sufficient data have been collected based on manufacturing schedules, submit the data and overall conclusions to FDA.

The control strategy for subvisible particles in the (b) (4) size range will be re-assessed based on the following:

- Available data from the (b) (4) from the commercial batches
- Available data on aggregate level from SE-HPLC from the commercial batches

The timetable you submitted on September 14, 2011, states that you will conduct this study according to the following schedule:

Final Report Submission: 09/2012

PMC-2 Perform a feasibility study to assess available analytical techniques to analyze subvisible particles in the (b) (4) size range for Pegasys SIN PFS.

The control strategy for subvisible particles in the (b) (4) size range will be re-assessed based on the following:

- Outcome of the feasibility study and the availability of a suitable technique for the monitoring of subvisible particles in the (b) (4) size range for Pegasys SIN-PFS

The timetable you submitted on September 14, 2011, states that you will conduct this study according to the following schedule:

Final Report Submission: 09/2012

PMC- 3 Measure (b) (4) leachables including identification and semiquantification in syringes from both suppliers.

The timetable you submitted on September 8, 2011, states that you will conduct this study according to the following schedule:

Final Report Submission: 09/2012

PMC-4 Measure (b) (4) levels on syringes for three commercial batches from both suppliers. Perform a (b) (4) sensitivity/spiking study for Pegasys. This study will employ (b) (4) derivatives at different concentration levels, being added to Pegasys product solution and assessed for protein quality. Based on the results of this testing, a control strategy assessment for (b) (4) in the syringe will be performed.

The timetable you submitted on September 8, 2011, states that you will conduct this study according to the following schedule:

Final Report Submission: 09/2012

Submit clinical protocols to IND 5102, 7823, 8694, or 10144 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all final reports to this BLA. In addition, under 21 CFR 601.70 you should include a status summary of each commitment in your annual progress report of postmarketing studies to this BLA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) to:

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

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form

FDA 2253. 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.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

If you have any questions, call Abiola Olagundoye, Pharm.D., Regulatory Project Manager, at (301) 796-3982 or (301) 796-1500.

Sincerely,

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

ENCLOSURE(S):
Content of Labeling
Carton and Container Labeling