DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125387/S-015
BLA 125387/S-020

SUPPLEMENT APPROVAL

Regeneron Pharmaceuticals, Inc.
Attention: Jennifer Woo, Ph.D., PPM, RAC
Regulatory Associate IV
777 Old Saw Mill River Road
Tarrytown, NY 10591-6707

Dear Dr. Woo:

Please refer to the following Supplemental Biologics License Applications (sBLAs), submitted under section 351(a) of the Public Health Service Act for EYLEA (aflibercept) Injection:

Supplement Number	Date Submitted	Date Received
S-015	August 10, 2012	August 10, 2012
S-020	October 5, 2012	October 5, 2012

Supplement-015, submitted as a "Changes Being Effected" supplemental biologics application, proposed the addition of (b) (4)

Supplement-020, submitted as a "Prior Approval" supplemental biologics application, provides for revisions to Section 6.2 Clinical Studies Experience, the deletion of (b) (4) , and updates to Section 8.1 Pregnancy with data from a recently completed reproductive toxicity study. We acknowledge receipt of your amendment to S-020 dated April 24, 2013. This submission constituted a complete response to our April 5, 2013, action letter for S-020.

We have completed our review of these supplemental applications, as amended. The proposed changes in S-020 supersede the changes proposed in S-015. S-020 is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text and with the minor editorial revision listed below and incorporated in the enclosed labeling:

> In Section 16 How Supplied/Storage and Handling, revise the first statement of the carton contents to read, "one single-use, sterile, 3-mL, glass vial designed to deliver 0.05 mL of 40 mg/mL EYLEA."

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) 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.

The SPL will be accessible via publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes labeling changes 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.

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 regarding these supplemental applications, please contact Ms. Leanna M. Kelly, Consumer Safety Officer, at (301) 796-0471. For all other inquiries regarding this BLA, call Mr. Michael Puglisi, Regulatory Project Manager, at (301) 796-0791.

Sincerely,

{See appended electronic signature page}

Wiley A. Chambers, M.D.
Deputy Director
Division of Transplant and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

WILEY A CHAMBERS
06/07/2013