DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

sBLA 125156/S-069
sBLA 125156/S-076

SUPPLEMENT APPROVAL

Genentech, Inc.
Attention: Tania Gonzalez, PhD
Regulatory Project Management
1 DNA Way
South San Francisco, CA 94080-4990

Dear Dr. Gonzalez:

Please refer to your Supplemental Biologics License Application (sBLA 125156/S-069), dated June 7, 2011, received June 8, 2011, submitted under section 351 of the Public Health Service Act for Lucentis (ranibizumab injection).

Your submission dated June 15, 2012, constituted a complete response to our complete response letter dated December 6, 2011.

This "Prior Approval" supplement to your biologics license application provides for revisions to the Lucentis package insert to describe observations of pre-injection intraocular pressure increase, observations of tear of retinal pigment epithelium among patients with neovascular age-related macular degeneration (AMD), and additional information regarding placental and embryo-fetal development.

We also refer to your Supplemental Biologics License Application (sBLA 125156/S-076), dated October 10, 2011, received October 11, 2011, submitted under section 351 of the Public Health Service Act for Lucentis (ranibizumab injection).

We acknowledge receipt of your amendments dated:

December 23, 2011	January 12, 2012	January 27, 2012
February 8, 2012	February 9, 2012	February 13, 2012
February 27, 2012	March 15, 2012	March 16, 2012
April 27, 2012	May 4, 2012	May 17, 2012
June 29, 2012	July 20, 2012	August 6, 2012
August 7, 2012	August 8, 2012	August 9, 2012

This "Prior Approval" efficacy supplement to your biologics license application provides for a new indication: treatment of patients with diabetic macular edema.

We have completed our review of these supplemental applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text, which reflects the changes provided in both sBLA 125156/S-069 and sBLA 125156/S-076.

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. For administrative purposes, please designate this submission "**Product Correspondence – Final SPL for approved BLA STN 125156/S-069 and BLA STN 125156/S-076**"

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

We acknowledge your October 10, 2011, submission containing final printed carton and 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 125156/S076**." Approval of this submission by FDA is not required before the labeling is used.

We also make note of the labeling communications on August 2, and August 7, 2012, and to your submission dated August 8, 2012, where you describe the timetable for proposed revisions of the carton and vial labels.

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. We are waiving the pediatric study requirement for this application because the necessary studies are impossible or highly impracticable considering that there too few children to study with diabetic macular edema.

POSTMARKETING COMMITMENTS SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

1. Evaluate the efficacy of Lucentis in bilateral dosing for the treatment of patients with diabetic macular edema.

   The timetable you submitted on August 9, 2012, states that you will conduct this trial according to the following schedule:

Final Protocol Submission:	01/2014
Trial Completion:	11/2018
Final Report Submission:	07/2019

2. Evaluate the efficacy of Lucentis for the treatment of diabetic macular edema if treatment is discontinued after at least 1 year of therapy.

   The timetable you submitted on August 9, 2012, states that you will conduct this trial according to the following schedule:

Final Protocol Submission:	01/2014
Trial Completion:	11/2018
Final Report Submission:	07/2019

Submit clinical protocols to your IND 8633 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:

U.S. Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
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 Office of Prescription Drug Promotion (OPDP), 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, please call Constantine J. Markos, B.S., Pharm.D., R.Ph., Regulatory Health Project Manager, at (301) 796-3871.

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(S): Package Insert
Carton and vial labels

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
08/10/2012