DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

Submission Tracking Number (STN): BLA 125156/053

APPROVAL
June 22, 2010

Genentech, Inc.
Attention: Michelle H. Rohrer, Ph.D.
Vice President, Regulatory Affairs
1 DNA Way
South San Francisco, California 94080-4990

Dear Dr. Rohrer:

Please refer to your supplement to your biologics license application (BLA), dated December 18, 2009, received December 22, 2009, submitted under section 351 of the Public Health Service Act for Lucentis (ranibizumab injection). We acknowledge receipt of your amendments dated April 16, May 5, June 21 and 22, 2010. Your request to supplement your BLA for Lucentis (ranibizumab injection) to include the new indication, Macular Edema Following Retinal Vein Occlusion (RVO), has been approved.

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 in pediatric patients unless this requirement is waived, deferred, or inapplicable. We are waiving the pediatric study requirement for this application because studies would be impossible or highly impracticable as there are too few pediatric patients with macular edema following a retinal vein occlusion.

We acknowledge your written commitments as described in your letter of June 22, 2010, as outlined below:

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS OF SECTION 506B

1. Provide safety and efficacy data on at least 150 patients with macular edema following a retinal vein occlusion, followed for at least 15 months and randomized sometime within 15 months of their first treatment with Lucentis. Patients must receive 7 monthly doses of Lucentis, be evaluated monthly for the need of additional doses of Lucentis based on OCT and visual acuity criteria and if determined to not need an additional monthly dose

of Lucentis be randomized to receive an additional dose or not to receive an additional dose of Lucentis.

Final Protocol Submission: November 1, 2010

Study Start Date: March 1, 2011

Final Report Submission: October 1, 2013

We request that you submit the clinical protocol to your IND, with a cross-reference letter to this BLA, STN **[125156/053]**. Submit the final report to this BLA. Please use the following designators to label prominently all submissions, including supplements, relating to these postmarketing commitments as appropriate:

- **POSTMARKETING COMMITMENT PROTOCOL**
- **POSTMARKEING COMMITMENT – FINAL REPORT**
- **POSTMARKETING CORRESPONDENCE**
- **ANNUAL STATUS REPORTING OF POSTMARKETING COMMITMENTS**

For each postmarketing commitment subject to the reporting requirements of 21 CFR 601.70, you must describe the status in an annual report. The status report for each commitment should include:

- information to identify and describe the postmarketing commitment,
- the original schedule for the commitment,
- the status of the commitment (i.e., pending, ongoing, delayed, terminated, or submitted),
- an explanation of the status including the patient accrual rate (i.e., number enrolled to date and the total planned enrollment); and,
- a revised schedule if the scheduled milestones have changed and an explanation of the basis for the revision.

POSTMARKETING COMMITMENTS NOT SUBJECT TO REPORTING REQUIREMENTS OF SECTION 506B

2. Submit the final Clinical Study Reports from the 6 month observation periods for Study FVF4165g and FVF4166g.

   Final Report Submission: October 1, 2010

3. Submit the final Clinical Study Reports from Study FVF3426g.

   Final Report Submission: November 1, 2011

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] 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/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format that includes the changes approved in this supplemental application.

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.

If you have any questions, call Lori Marie Gorski, Regulatory Project Manager, at (301) 796-0722.

Sincerely,

Wiley A. Chambers, M.D.
Acting Director
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure: Package Insert