DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125085/225

SUPPLEMENT BLA APPROVAL
September 30, 2011

Genentech, Incorporated
Attention: Michelle Rohrer, Ph.D.
Vice President, Regulatory Affairs
1 DNA Way MS#241B
South San Francisco, CA 94080

Dear Dr. Rohrer:

Please refer to your Supplemental Biologics License Application (sBLA), dated March 31, 2011, received April 1, 2011, submitted under section 351 of the Public Health Service Act for Avastin (bevacizumab).

We acknowledge receipt of your amendments dated through September 29, 2011.

This "Prior Approval" labeling supplement to your biologics license application provides for the following additions to the package insert:

- a new subsection, titled "Ovarian Failure" (5.10), to WARNINGS AND PRECAUTIONS;
- a new subsection, titled "Females of Reproductive Potential" (8.6), to USE IN SPECIFIC POPULATIONS;
- a new subsection titled *Ovarian Failure* under ADVERSE REACTIONS (6.1);
- addition of the adverse reaction of osteonecrosis of the jaw to ADVERSE REACTIONS (6.3);
- inclusion of additional information to the subsection titled *Venous Thromboembolic Events* in ADVERSE REACTIONS (6.1); and,
- addition of information on ovarian failure to PATIENT COUNSELING INFORMATION (17).

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.

In addition, this supplement contains the final report for the following postmarketing commitment listed in the February 26, 2004, letter for STN 125085/0:

PMC #10 To assess the relative impact on fertility and gonadal function of bevacizumab in combination with chemotherapy, as compared to patients receiving chemotherapy alone. This will be evaluated in 2700 subjects, enrolled in the planned NSABP study, C-08, of whom 50 percent will be randomized to receive bevacizumab. The final protocol will be submitted by June 30, 2004, patient accrual will be completed by December 29, 2006, the portion of the study will be completed by December 31, 2007, and the final report for this portion of the study submitted by June 30, 2008.

The above commitment is fulfilled. You no longer have to report on this commitment.

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 125085/225**."

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.

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
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.

All promotional materials for your drug product that include representations about your drug product must be promptly revised to make it consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 601.12(a)(4)]. The revisions to your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 601.12(a)(4) to the address above or by fax to 301-847-8444.

LETTERS TO HEALTH CARE PROFESSIONALS

We acknowledge that you will issue a letter communicating important safety-related information about this drug product (i.e., a "Dear Health Care Professional" letter); we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this BLA to the following address:

MedWatch Program
Office of Special Health Issues
Food and Drug Administration
10903 New Hampshire Ave
Building 32, Mail Stop 5353
Silver Spring, MD 20993

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 Ms. Sharon Sickafuse, Senior Regulatory Health Project Manager, at (301) 796-2320.

Sincerely,

/Patricia Keegan/
Patricia Keegan, M.D.
Director
Division of Oncology Products 2
Office of Hematology and Oncology Drug Products
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling