DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Silver Spring, MD 20993

STN: BL 103705/5299 October 16, 2009

SUPPLEMENTAL BLA APPROVAL

Genentech, Inc.
1 DNA Way
South San Francisco, CA 94080

Attention: Michelle H. Rohrer, PhD
Vice President, Regulatory Affairs

Dear Dr. Rohrer:

Please refer to the supplement to your biologics license application, dated September 15, 2008, received September 16, 2008, submitted under section 351 of the Public Health Service Act for Rituxan® (rituximab).

We acknowledge receipt of your amendments dated January 15 and 23, February 13, March 16, May 21 and 22, September 24, and October 9, 2009. Your May 21, 2009 submission constituted a major amendment.

This supplemental biologics license application provides for the addition of an "improvement of physical function" claim in rheumatoid arthritis.

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

FULFILLMENT OF POSTMARKETING COMMITMENTS

Your supplemental application also addressed postmarketing commitment numbers 3 and 5 identified in the February 28, 2006 approval letter for your supplemental BL 103705/5211. The commitments addressed in this application are as follows:

PMC #3 Study of the safety and efficacy or rituximab re-treatment.

PMC #5 Study of the ability of patients to mount a humoral response to vaccination following treatment with rituximab and B cell recovery.

We have completed the review of your submission and find that these commitments have been fulfilled.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at http://www.fda.gov/oc/datacouncil/spl.html, that is identical to the enclosed labeling and Medication Guide. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission "**Product Correspondence – Final SPL for approved STN BL 103705/5299**."

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 ages 0 to 17 years because evidence suggests that Rituxan® (rituximab) would be unsafe in pediatric subpopulations.

PROMOTIONAL MATERIALS

You may submit draft copies of the proposed introductory advertising and promotional labeling with a cover letter requesting advisory comments to the following address:

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

Final printed advertising and promotional labeling should be submitted at the time of initial dissemination, accompanied by a FDA Form 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 claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence to support that claim.

LETTERS TO HEALTH CARE PROFESSIONALS

If you 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 an electronic copy of the letter to both this BLA and to the following address:

MedWatch, HFD-001
Food and Drug Administration
5600 Fishers Lane, Room 12B05
Rockville, MD 20852-9787

REPORTING REQUIREMENTS

You must submit adverse experience reports under the adverse experience reporting requirements for licensed biological products (21 CFR 600.80). You should submit postmarketing adverse experience reports to the following address:

Central Document Room
Center for Drug Evaluation and Research
Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

Prominently identify all adverse experience reports as described in 21 CFR 600.80.

You must submit distribution reports under the distribution reporting requirements for licensed biological products (21 CFR 600.81).

You must submit reports of biological product deviations under 21 CFR 600.14. You should promptly identify and investigate all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA-3486 to the following address:

Division of Compliance Risk Management and Surveillance
Office of Compliance
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20903

Biological product deviations sent by courier or overnight mail should also be sent to this address.

You must submit information to your biologics license application for our review and written approval under 21 CFR 601.12 for any changes in the manufacturing, testing, packaging, or labeling of Rituxan® (rituximab) or in the manufacturing facilities.

This information will be included in your biologics license application file.

Sincerely,

/Bob. A Rappaport/

Bob A. Rappaport, MD
Director
Division of Anesthesia, Analgesia and
Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosures: Package Insert
Medication guide