DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

Our STN: BL 103705/5259

AUG 22 2007

Genentech, Incorporated
Attention: Todd W. Rich, M.D.
Vice President, Clinical and Commercial Regulatory Affairs
1 DNA Way, MS# 242
South San Francisco, CA 94080-4990

Dear Dr. Rich:

Your request to supplement your biologics license application for Rituximab to update the Warnings, PML section of the package insert and to include new language in the Pregnancy Category C subsection of the Precautions section of the package insert has been approved.

As discussed in the teleconference held on July 20, 2007, between Jennifer Decad and Cindy Wilson of Genentech and Beverly Conner of this office, the Medication Guide that you submitted for review under 103705/5259 will be reviewed under STN 103705/5263 and is not subject to this approval. Please submit the proposed Medication Guide with associated carton and container labeling following the requirements as contained in 21CFR§208 as an amendment to STN 103705/5263 by August 31, 2007.

We acknowledge your written commitment in your letter of August 7, 2007, to conduct the following postmarketing study commitments as described in the August 3, 2007, e-mail communication from Beverly Conner of this office to Jennifer Decad of Genentech, as outlined below:

Postmarketing Study Commitments subject to reporting requirements of 21 CFR 601.70.

1. To submit an amendment to the Prior Approval Supplement (PAS) (STN 103705/5263) converting the current Patient Package Insert to a Medication Guide following the requirements as contained in 21CFR§208 by August 31, 2007. The amendment to the PAS will include proposed labeling in PLR format, revised container and package labeling referencing the Medication Guide and the proposed plan for distribution of the Medication Guide to patients.

2. To submit a separate subsection in the Periodic Safety Update Report (PSUR) containing the interim results of the enhanced pharmacovigilance monitoring plan for PML annually for ten years beginning in 2008. This section will contain the ongoing aspects of postmarketing surveillance described in Sections 3.3.1, 3.3.2, and 3.3.5 of the May 3, 2007, submission . This PSUR subsection should include, but not be limited to:

a. a cumulative summary of all expedited reports of PML which include the results of questionnaires and active attempts to solicit data on such events (Section 3.3.1);

b. the results of ongoing analyses to characterize observed rates of PML within all non-HIV-related specific disease categories in which PML has occurred or occurs after Rituxan administration. The results of these analyses will include a comparison of the observed rates of PML among those who have and have not received Rituxan to detect trends and estimated rates of PML with evaluation for possible risk factors, e.g., duration of Rituxan exposure, (Section 3.3.2); and,

c. the results of the proposed and ongoing pharmacoepidemiologic evaluations described under section 3.3.5.

Please use the following designators to label prominently all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- Postmarketing Study Commitment Protocol
- Postmarketing Study Commitment - Final Study Report
- Postmarketing Study Correspondence
- Annual Status Report of Postmarketing Study Commitments

For each postmarketing study subject to the reporting requirements of 21 CFR 601.70, you must describe the status in an annual report on postmarketing studies for this product. The status report for each study 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, for clinical studies, the patient accrual rate (i.e. number enrolled to date and the total planned enrollment), and
- a revised schedule if the study schedule has changed and an explanation of the basis for the revision.

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our Web site (http://www.fda.gov/cder/pmc/default.htm). Please refer to the February 2006 Guidance for Industry: Reports on the Status of Postmarketing Study Commitments - Implementation of Section 130 of the Food and Drug Administration Modernization Act of 1997 (see http://www.fda.gov/cder/guidance/5569fnl.htm) for further information.

In addition to the postmarketing commitments noted above, we request that you submit your pharmacovigilance monitoring plan to this biologics license application (BLA), STN 103705.

Pursuant to 21 CFR 201.57(c)(18) and 201.80(f)(2), patient labeling must be reprinted immediately following the last section of labeling or, alternatively, accompany the prescription drug labeling.

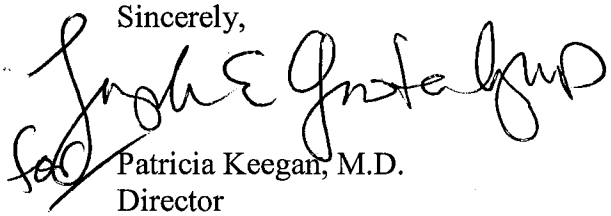
We note your July 23, 2007, submission included content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format; we will transmit that version to the National Library of Medicine for public dissemination. Within 21 days of the date of this letter, amend any pending supplements for this BLA with content of labeling in SPL format to include the changes approved in this supplement.

Marketing the product with labeling that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please refer to http://www.fda.gov/cder/biologics/default.htm for information regarding therapeutic biological products, including the addresses for submissions.

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

Sincerely,



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

Enclosure: Final Draft Labeling