DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125276/48

SUPPLEMENT APPROVAL

Genentech, Inc.
c/o Hoffman-LaRoche
340 Kingsland Street
Nutley, NJ 07110-1199

Attention: Kristine L. Ogozalek
Associate Director, Drug Regulatory Affairs

Dear Ms. Ogozalek:

Please refer to your Supplemental Biologics License Application (sBLA), dated November 11, 2011, received November 11, 2011, submitted under section 351 of the Public Health Service Act for Actemra (tocilizumab).

We acknowledge receipt of your amendments dated February 3, April 20, and June 5, 2012; and your risk evaluation and mitigation strategy (REMS) assessment dated July 7, 2011. This supplement was in response to our September 12, 2011, FDA REMS Modification Notification letter based upon our review of your July 7, 2011, REMS assessment.

This Prior Approval supplement to your biologics license application provides for modifications to the approved REMS.

We have completed our review of this supplemental application. It is approved effective on the date of this letter.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Actemra (tocilizumab) was originally approved on January 8, 2010, and a REMS modification was approved on April 15, 2011. The REMS consists of a communication plan and a timetable for submission of assessments of the REMS. Your proposed modifications consist of:

- Revision of the goals to remove informing patients about the serious risks with Actemra (tocilizumab) since the Medication Guide has been removed from REMS.
- Revision of the goals to inform healthcare providers of the serious risks associated with Actemra (tocilizumab) instead of a detailed list of safety issues.
- Removal of the Dear Pharmacist letter as prescribers are the target audience for the Communication Plan.

- Addition of the Prescriber Education Slide Deck to improve awareness of the risk of demyelination, malignancy and lipid monitoring.
- Revision of the REMS assessment plan to remove evaluation of patients' understanding of the risks of Actemra (tocilizumab) and a report on the distribution and dispensing of Medication Guides.

Your proposed modified REMS, submitted on June 5, 2012, and appended to this letter, is approved.

The revised REMS assessment plan should include but is not limited to the following:

a. Evaluation of healthcare providers' understanding of the serious risks of Actemra (tocilizumab).

b. A summary of all reported serious risks with an analysis of adverse event reporting by prescriber type (e.g., rheumatologist, osteopath, infectious disease specialist, gastroenterologist, hepatologist, internal medicine specialist, hematology-oncology specialist, emergency medicine specialist, family medicine specialist, etc.).

c. Based on the information provided, an assessment and conclusion of whether the REMS is meeting its goals, and whether modification to the REMS are needed.

The timetable for submission of assessments of the REMS will remain the same as that approved on April 15, 2011.

We remind you that assessments of an approved REMS must also include, under section 505-1(g)(3)(B) and (C), information on the status of any post-approval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. With respect to any such post-approval study, you must include the status of such study, including whether any difficulties completing the study have been encountered. With respect to any such post-approval clinical trial, you must include the status of such clinical trial, including whether or not enrollment has begun, the number of participants enrolled, the expected completion date, whether or not any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under subsections (i) and (j) of section 402 of the Public Health Service Act. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 601.70 and including any material or significant updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

In addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of FDCA.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the

assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

BLA 125276 REMS CORRESPONDENCE
(insert concise description of content in bold capital letters, e.g., UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT METHODOLOGY)

Prominently identify the submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

BLA 125276 REMS ASSESSMENT

NEW SUPPLEMENT FOR BLA 125276
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE) FOR BLA 125276
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

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, call Philantha Bowen, Regulatory Project Manager, at (301) 796-2466.

Sincerely,

{See appended electronic signature page}

Sally Seymour, M.D.
Deputy Director for Safety
Division of Pulmonary, Allergy, and Rheumatology Products
Office of Drug Evaluation II

Center for Drug Evaluation and Research

ENCLOSURE(S):
REMS

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

SALLY M SEYMOUR
06/20/2012