DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
1401 Rockville Pike
Rockville MD 20852-1448

Our Reference No.: 97-0244

November 26, 1997

M. David MacFarlane, Ph.D.
Genentech, Inc.
1 DNA Way
South San Francisco, CA 94080-4990

Dear Dr. MacFarlane:

Your biologics license application for Rituximab is approved effective this date. Genentech, Inc., South San Franciso, California, is hereby authorized to manufacture and ship for sale, barter, or exchange in interstate and foreign commerce Rituximab under Department of Health and Human Services Biologics License No. 1048.

Rituxumab is indicated for the treatment of patients with relapsed or refractory low-grade or follicular, B-cell non-Hodgkin's lymphoma.

Under this authorization, you are approved to manufacture Rituximab utilizing Formulated Bulk Rituximab (For Further Manufacturing Use) manufactured by IDEC Pharmaceuticals Corp. (Biologics License No. 1235) under a shared manufacturing arrangement. Any addition or deletion of establishments involved in the shared manufacturing arrangement will require the submission of appropriate supporting data in order to ensure continued compliance with the approved standards for the manufacture of Rituximab.

In accordance with approved labeling, your product will bear the tradename RITUXAN and will be marketed in 10 mL and 50 mL fill sizes.

You are not currently required to submit samples of future lots of this product to the Center for Biologics Evaluation and Research (CBER) for release by the Director, CBER, under 21 CFR 610.2. FDA will continue to monitor compliance with 21 CFR 610.1 requiring assay and release of only those lots that meet release specifications.

The dating period for this product shall be 24 months from the date of manufacture when stored at 2-8°C. The date of manufacture shall be defined as the date of final sterile filtration of the product. Results of ongoing stability studies should be submitted throughout the dating period as they become available including the results of stability studies from the first three production lots.

We acknowledge your written commitments of October 17, 1997 to: :

1. Submit the results of your study evaluating the time and temperature specifications for the transport of Rituximab Formulated Bulk and filled vials between buildings to CBER upon completion.

2. Submit the results of the environmental monitoring survey to CBER by January 31, 1998.

3. Include Lot E9054A in your ongoing Rituximab stability program.

4. Establish a maximum fill duration for 500 mg Rituximab in 50 mL vials, supported by media fill data.

Any changes in the supplier of the Formulated Bulk Rituximab (For Further Manufacturing Use), or in the manufacture, packaging or labeling of the product or in the manufacturing facilities will require the submission of information to your biologics license application for our review and written approval consistent with 21 CFR 601.12.

It is requested that adverse experience reports be submitted in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80) and that distribution reports be submitted as described (21 CFR 600.81). All adverse experience reports should be prominently identified according to 21 CFR 600.80 and be submitted to the Center for Biologics Evaluation and Research, HFM-210, Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852-1448.

Please submit three copies of all final printed labeling at the time of use and include part II of the label transmittal form with completed implementation information. In addition, you may wish to submit draft copies of the proposed introductory advertising and promotional labeling with an FDA Form 2567 to the Center for Biologics Evaluation and Research, Advertising and Promotional Labeling Staff, HFM-202, 1401 Rockville Pike, Rockville, MD 20852-1448. Final printed advertising and promotional labeling should be submitted at the time of initial dissemination, accompanied by an FDA Form 2567. All promotional claims must be consistent with and not contrary to approved labeling. No comparative promotional claim or claim of superiority over other similar products should be made unless data to support such claims are submitted to and approved by the Center for Biologics Evaluation and Research.

Sincerely yours,

Jay P. Siegel, M.D., FACP
Director
Office of Therapeutics
Research and Review
Center for Biologics