DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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

Our Reference No. 96-0350

June 18, 1996

M. David MacFarlane, Ph.D.
Genentech, Inc.
460 Point San Bruno Blvd.
South San Francisco, CA 94080

Dear Dr. MacFarlane:

Your request to supplement your product license application for Alteplase to include an indication for the management of acute ischemic stroke in adults, for improving neurological recovery, and reducing the incidence of disability has been approved.

We acknowledge your commitments to conduct phase 4 studies and to provide additional clinical information as detailed in your letter of June 14, 1996. These commitments are summarized as follows:

1. To continue the ongoing study to evaluate the safety and efficacy of Alteplase treatment in patients treated more than three hours after stroke onset.

2. To conduct a prospectively designed uncontrolled clinical study, in patients treated within three hours of stroke onset, to identify patient characteristics that may be associated with an increased risk from treatment.

3. To provide the electronic dataset and additional safety analyses from The European Cooperative Acute Ischemic Stroke Study (ECASS).

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). These requirements became effective on December 27, 1994. 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 (FDA Form 2567) with completed implementation information. In addition, please submit a label transmittal form with three copies of advertising and promotional labeling at the time of use

to the Center for Biologics Evaluation and Research, Advertising and Promotional Labeling Staff, HFM-202, 1401 Rockville Pike, Rockville, MD 20852-1448. You may also wish to submit these items in draft for comment. 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.

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

Sincerely yours,

Karen D. Weiss, M.D.
Director
Division of Clinical Trial
Design and Analysis
Office of Therapeutics
Research and Review
Center for Biologics
Evaluation and Research