DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

BLA 125075/96 and 125075/102

OCT 16 2008

Genentech, Inc.
Attention: Sarah Baker
Manager, Regulatory Affairs
Department of Regulatory Affairs
1 DNA Way MS#241B
South San Francisco, CA 94080-4990

Dear Ms. Baker:

Please refer to your supplement to your biologics license application (BLA) dated March 7, 2007, received March 8, 2007 (125075/96), and to your supplement dated September 20, 2007, received September 24, 2007 (125075/102), for RAPTIVA® (efalizumab).

We acknowledge receipt of your amendments to these supplements dated September 24, 2007, May 30, 2008, August 13, 2008, August 22, 2008, and October 9, 2008.

Supplement 125075/96 provides for changes regarding reported adverse events to the WARNINGS, PRECAUTIONS, ADVERSE REACTIONS, REFERENCES, and Patient Information sections of the package insert and the addition of a BOXED WARNING for the risk of serious infections. Supplement 125075/102 provides for changes regarding nonclinical data and pediatric use to the PRECAUTIONS section of the package insert.

We have completed our review of these supplemental applications, as amended, and they are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

RISK EVALUATION AND MITIGATION STRATEGIES (REMS) REQUIREMENTS

Title IX, Subtitle A, Section 901 of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amends the Federal Food, Drug, and Cosmetic Act (FDCA) to authorize FDA to require the submission of a REMS for an approved drug if FDA becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)). This provision took effect on March 25, 2008.

Since RAPTIVA® (efalizumab) was approved on October 27, 2003, for the treatment of chronic moderate to severe plaque psoriasis, we have become aware of an increase in the risk of serious fungal and viral infections reported as postmarketing adverse events. This information was not available when RAPTIVA® (efalizumab) was granted marketing authorization for the treatment

of psoriasis. Therefore, we consider this information to be "new safety information" as defined in FDAAA.

After consideration of this new safety information, we have determined that a REMS is necessary for RAPTIVA® to ensure that the benefits of the drug outweigh the risks. Your REMS, once approved, will create enforceable obligations.

Your proposed REMS must include the following:

Medication Guide: As one element of a REMS, FDA may require the development of a Medication Guide as provided for under 21 CFR Part 208. Pursuant to 21 CFR Part 208, FDA has determined that RAPTIVA® poses a serious and significant public health concern requiring the distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of RAPTIVA®. FDA has determined that RAPTIVA® is a product for which patient labeling could help prevent serious adverse events and that RAPTIVA® has serious risks relative to the benefits of which patients should be made aware because information concerning the risks could affect patients' decisions to use or continue its use. We have determined that your patient package insert should be converted to a Medication Guide. Under 21 CFR 208 and in accordance with 505-1, you are responsible for ensuring that the Medication Guide is available for distribution to patients who are dispensed RAPTIVA®.

Please note that:

- the Medication Guide must be printed immediately following the last section of labeling or, alternatively, accompany the prescription drug labeling [21 CFR 201.57(c)(18)] or 21 CFR 201.80(f)(2)];
- the Medication Guide must conform to all conditions described in 21 CFR 208.20, including a minimum of 10 point text.

Timetable for Assessment: The proposed REMS must include a timetable for assessment of the REMS that shall be no less frequent than by 18 months and 3 years, and in the 7th year after the REMS is initially approved. We recommend that you specify the interval that each assessment will cover and the planned date of submission to the FDA of the assessment. We recommend that assessments be submitted within 60 days of the close of the assessment interval.

Your assessment of the REMS should include an evaluation of:

a. Patients' understanding of the serious risks of RAPTIVA®
b. A report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24
c. A report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance

In accordance with section 505-1, within 30 days of the date of this letter, you must submit a prior-approval supplement containing your proposed REMS and a REMS supporting document.

We suggest that your proposed REMS submission include two parts: a "Proposed REMS" and a "REMS Supporting Document." Attached is a template for the Proposed REMS that you should complete with concise, specific information about RAPTIVA® (see Appendix A). Include information in the template that is specific to your proposed REMS for RAPTIVA®. Once FDA finds the content acceptable, we will include this document as an attachment to the approval letter that includes the REMS. The REMS, once approved, will create enforceable obligations.

The REMS Supporting Document should be a document explaining the rationale for each of the elements of the REMS. It should include the following sections:

1. Background Section
2. Goals Section
3. Rationale and Description of Proposed REMS Section
    a. Additional Potential REMS Elements (Sec 505-1(e)) - Medication Guide
    b. Timetable for Assessment of the REMS Section (505-1(d))
4. Information Needed for Assessments

Use the following designator at the top of the first page of the proposed REMS submission in bold, capital letters:

NEW SUPPLEMENT FOR BLA 125075
PROPOSED REMS

For subsequent submissions related to the proposed REMS, prominently identify the submission by including the following designator in bold, capital letters at the top of the first page of the submission:

SUPPLEMENT [assigned #]
PROPOSED REMS–AMENDMENT

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 (text for the package insert). 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 125075/96 and STN BL 125075/102". In addition, within 14 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.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) to:

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

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 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 www.fda.gov/cder/ddmac.

LETTERS TO HEALTH CARE PROFESSIONALS

If you issue a letter communicating important safety related information about this 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
Food and Drug Administration
HFD-001, Suite 5100
5515 Security Lane
Rockville, MD 20852

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
(HFD-330) Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Biological product deviations sent by courier or overnight mail should be addressed to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Compliance
Division of Compliance Risk Management and Surveillance
(HFD-330) Montrose Metro 2
11919 Rockville Pike
Rockville, MD 20852

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at www.fda.gov/medwatch/report/mmp.htm.

If you have any questions, call Catherine Carr, Regulatory Project Manager, at (301) 796-2110.

Sincerely,

Susan J. Walker, M.D., F.A.A.D.
Director
Division of Dermatology and Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure

Appendix A

REMS Template

Application number TRADE NAME (DRUG NAME)

Class of Product as per label

Applicant name
Address
Contact Information

PROPOSED RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL(S):

List the goals and objectives of the REMS.

II. REMS ELEMENTS:

A. Medication Guide or PPI

A Medication Guide will be dispensed with each [drug name] prescription. [Describe in detail how you will comply with 21 CFR 208.24.]

B. Communication Plan

[Applicant] will implement a communication plan to healthcare providers to support implementation of this REMS.

List elements of communication plan. Append the printed material and web shots to the REMS Document

C. Elements To Assure Safe Use

List elements to assure safe use included in this REMS. Elements to assure safe use may, to mitigate a specific serious risk listed in the labeling, require that:
A. Healthcare providers who prescribe [drug name] have particular training or experience, or are specially certified. Append any enrollment forms and relevant attestations/certifications to the REMS;

B. Pharmacies, practitioners, or healthcare settings that dispense [drug name] are specially certified. Append any enrollment forms and relevant attestations/certifications to the REMS ;

C. [Drug name] may be dispensed to patients only in certain healthcare settings (e.g., hospitals);

D. [Drug name] may be dispensed to patients with documentation of safe-use conditions;

E. Each patient using [drug name] is subject to certain monitoring. Append specified procedures to the REMS; or

F. Each patient using [drug name] be enrolled in a registry. Append any enrollment forms and other related materials to the REMS Document.

D. Implementation System

Describe the implementation system to monitor and evaluate implementation for, and work to improve implementation of, Elements to Assure Safe Use (B),(C), and (D), listed above .

E. Timetable for Submission of Assessments

Specify the timetable for submission of assessments of the REMS. The timetable for submission of assessments shall include an assessment by 18 months, 3 years, and in the 7th year after the REMS is initially approved, with dates for additional assessments if more frequent assessments are necessary to ensure that the benefits of the drug continue to outweigh the risks.