DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

Our STN: BL 103767/5094

OCT 15 2008

Eisai Medical Research, Inc.
Attention: Ray Lubecki, RPh
Senior Director, US Regulatory Affairs
55 Challenger Road
Ridgefield Park, NJ 07660

Dear Mr. Lubecki:

Your request to supplement your biologics license application for Ontak® (denileukin diftitox) to verify the clinical benefit of Ontak for the treatment of patients with persistent or recurrent cutaneous T-cell lymphoma has been approved.

This application was approved under the regulations for accelerated approval of new drugs for serious or life-threatening illnesses, specifically, 21 CFR 601.41. At the time of approval, you committed to:

> *"Granting of this approval is contingent upon completion of the blinded, placebo-controlled study, Protocol 93-04-11 with amendments as submitted on February 2, 1999 and submission of the results within 12 months of entry of the last patient, as outlined in your commitment of February 3, 1999. An amended protocol will be submitted within one month of February 5, 1999. Please submit annual updates on accrual and progress of the ongoing study. It is understood that, to fulfill the requirements of accelerated approval, these studies must be conducted with due diligence and must verify that clinical benefit is associated with the surrogate endpoint."*

We have concluded that the requirements established in 21 CFR 601.41 are no longer necessary for the safe and effective use of Ontak (denileukin, diftitox) because the clinical benefit has been verified.

This fulfills your commitment to complete study protocol 93-04-11 as stated in the February 5, 1999 approval letter.

We acknowledge your written commitments as described in your correspondence of October 15, 2008 as outlined below:

Postmarketing Study Commitments not subject to reporting requirements of 21 CFR 601.70.

1. To establish a quantitative lower limit for the amount of polysorbate 20 in the final drug product. The new specification and the data supporting the specification will be submitted by December 31, 2008.

2. To provide the performance characteristics of a validated assay(s) that detects [redacted], by December 31, 2009.

Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to your BLA STN BL 103767. 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.

The final printed labeling (FPL) must be identical to the enclosed labeling. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

We note your October 14, 2008 submission included final content of labeling [CFR 601.14(b)] in structured product labeling (SPL) format; we will transmit it to the National Library of Medicine for public dissemination. Within 21 days of the date of this letter, amend any pending supplement(s) for this BLA with content of labeling in SPL format to include the changes approved in this supplement.

You may submit draft copies of the proposed introductory advertising and promotional labeling with a cover letter requesting advisory comments to the Food and Drug Administration, Center for Drug Evaluation and Research, Division of Drug Marketing, Advertising and Communication, 5901-B Ammendale Road, Beltsville, MD 20705-1266. Final printed advertising and promotional labeling should be submitted at the time of initial dissemination, accompanied by a FDA Form 2253.

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence to support that claim.

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

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