DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-973/S-016

Eisai, Inc.
Regulatory Affairs Department
Attention: Matthew Biondi, RPh.
Glenpointe Center West
500 Frank W. Burr Blvd.
Teaneck, NJ 07666

Dear Mr. Biondi:

Please refer to your supplemental new drug application dated February 03, 2003, received February 04, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Aciphex® (rabeprazole sodium) Delayed-Release Tablets.

This supplemental new drug application provides for the revision of the *Post-Marketing Adverse Events* section of the package insert.

We completed our review of this application and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text listed below. Accordingly, this application is approved, effective on the date of this letter.

> *Post-Marketing Adverse Events:* Additional adverse events reported from worldwide marketing experience with rabeprazole sodium are: sudden death; coma and hyperammonemia; jaundice; rhabdomyolysis; disorientation and delirium; anaphylaxis; angioedema; bullous and other drug eruptions of the skin; severe dermatologic reactions, including toxic epidermal necrolysis (some fatal), Stevens-Johnson syndrome, and erythema multiforme; interstitial pneumonia; interstitial nephritis; and TSH elevations. In most instances, the relationship to rabeprazole sodium was unclear. In addition, agranulocytosis, hemolytic anemia, leukopenia, pancytopenia, and thrombocytopenia have been reported. Increases in prothrombin time/INR in patients treated with concomitant warfarin have been reported.

The final printed labeling (FPL) must be identical to the submitted labeling (package insert submitted February 03, 2003).

Please submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – NDA (January 1999)*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 20-973/S-016." Approval of this submission by FDA is not required before the labeling is used.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Gastrointestinal and Coagulation Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Melissa Furness, Regulatory Project Manager, at (301)-827-7450.

Sincerely,

{See appended electronic signature page}

Joyce Korvick, M.D., M.P.H.
Deputy Director
Division of Gastrointestinal &
Coagulation Drug Products
Office of Drug Evaluation ODE III
Center for Drug Evaluation and Research

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

/s/

Joyce Korvick
8/1/03 03:39:40 PM