DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-973/S-015

Eisai Medical Research, Inc.
Attention: Charles Callaghan
Associate Director, Regulatory Affairs
Glenpointe Center West
500 Frank W. Burr Blvd.
Teaneck, NJ 07666-6741

Dear Mr. Callaghan:

Please refer to your supplemental new drug application dated May 30, 2002, received May 31, 2002, 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 a new formulation of the 20 mg tablets and related changes.

We have completed the 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. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted labeling (package insert) submitted May 30, 2002.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, 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 would also like to make a clarification regarding the approval letter sent regarding NDA 20-973/S-014 on 09/23/02. The letter stated that the following labeling text had been approved by our division:

Pharmacokinetics and Metabolism
ACIPHEX® delayed-release tablets are enteric-coated to allow rabeprazole sodium, which is acid labile, to pass through the stomach relatively intact. After oral administration of 20 mg ACIPHEX®, peak plasma concentrations (C_{max}) of rabeprazole occur over a range of 2.0 to 5.0 hours (T_{max}). The rabeprazole C_{max} and AUC are linear over an oral dose range of 10 mg to 40 mg. There is no appreciable accumulation when doses of 10 mg to 40 mg are administered every 24 hours; the pharmacokinetics of rabeprazole are not altered by multiple dosing. The plasma half-life ranges from 1 to 2 hours. ~~Whe(b r(b)~~

Absorption: Absolute bioavailability for a 20 mg oral tablet of rabeprazole (compared to intravenous administration) is approximately 52%. When rabeprazole is administered with a high fat meal, its T_{max} is variable and (b) - may delay its absorption up to 4 hours or longer, however, the C_{max} and the extent of rabeprazole absorption (AUC) are not altered. Thus rabeprazole may be taken without regard to timing of meals.
(b)

One word, "significantly", was inadvertently left out of the approved labeling text that was sent to you regarding NDA 20-973/S-014. The text should have read as follows (this omitted word has been bolded below for clarification purposes):

Pharmacokinetics and Metabolism
ACIPHEX® delayed-release tablets are enteric-coated to allow rabeprazole sodium, which is acid labile, to pass through the stomach relatively intact. After oral administration of 20 mg ACIPHEX®, peak plasma concentrations (C_{max}) of rabeprazole occur over a range of 2.0 to 5.0 hours (T_{max}). The rabeprazole C_{max} and AUC are linear over an oral dose range of 10 mg to 40 mg. There is no appreciable accumulation when doses of 10 mg to 40 mg are administered every 24 hours; the pharmacokinetics of rabeprazole are not altered by multiple dosing. The plasma half-life ranges from 1 to 2 hours. Whe(b (b) -

Absorption: Absolute bioavailability for a 20 mg oral tablet of rabeprazole (compared to intravenous administration) is approximately 52%. When rabeprazole is administered with a high fat meal, its T_{max} is variable and (b) - may delay its absorption up to 4 hours or longer, however, the C_{max} and the extent of rabeprazole absorption (AUC) are not **significantly** altered. Thus rabeprazole may be taken without regard to timing of meals.
(b)

We remind you that you must comply with the requirements for an approved NDA set forth under 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}

Robert L. Justice, M.D., M.S.
Division 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
9/30/02 03:03:37 PM
for Dr. Robert Justice