DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-445/S-016

Schering Corporation, Agent for
MSP Singapore Co., LLC
Attention: Patricia Kay-Mugford DVM, MSc
Senior Manager, Global Regulatory Affairs
2000 Galloping Hill Road
Kenilworth, N.J. 07033

Dear Dr. Kay-Mugford:

Please refer to your supplemental new drug application dated May 8, 2006, received May 9, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zetia (ezetimibe) Tablets.

We acknowledge receipt of your submissions dated September 25, and October 19, 2006.

This supplemental new drug application provides for labeling revisions to the package insert concerning the molecular mechanism of action of ezetimibe.

To the **CLINICAL PHARMACOLOGY,** *Mode of Action* subsection, a new sentence has been added to the third paragraph to read:

> The molecular target of ezetimibe has been shown to be the sterol transporter, Niemann-Pick C1-Like 1 (NPC1L1), which is involved in the intestinal uptake of cholesterol and phytosterols.

To the **CLINICAL PHARMACOLOGY,** *Mode of Action* subsection, the fourth paragraph, second sentence has been changed to read:

> Instead, ezetimibe localizes at the brush border of the small intestine and inhibits the absorption of cholesterol, leading to a decrease in the delivery of intestinal cholesterol to the liver.

We completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text. Submit content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/oc/datacouncil/spl.html, that is identical in content to the enclosed labeling text which you submitted on October 19, 2006. Upon receipt and verification, we will transmit that version to the National Library of Medicine for posting on the DailyMed website.

The final printed labeling (FPL) must be identical to the enclosed draft labeling.

Please submit either an electronic version or 20 paper copies of the FPL as soon as it is available (no more than 30 days after it is printed). If paper copies are submitted, individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved supplement NDA 21-445/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 this division and two copies of both the promotional materials and the package insert directly 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

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
Food and Drug Administration
WO 22, Room 4447
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

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 Margaret Simoneau, M.S., R.Ph., Regulatory Project Manager, at (301) 796-1295.

Sincerely,

{See appended electronic signature page}

Mary H. Parks, M.D.
Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure

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

/s/

Eric Colman
11/2/2006 11:37:49 AM
Eric Colman for Mary Parks