DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-445/S-013

Schering Corporation, Agent for
MSP Singapore Co., LLC
Attention: Beth DiDomenico, Ph.D, M.B.A.
Senior Manager, Global Regulatory Affairs
2000 Galloping Hill Road
Kenilworth, N.J. 07033

Dear Dr. DiDomenico:

Please refer to your supplemental new drug application dated July 26, 2005, received July 27, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zetia (ezetimibe) Tablets.

We acknowledge receipt of your submissions dated October 17, and December 13, 2005, and March 1, 13, and 23, April 26, and 28, and May 11 (email), 2006.

This supplemental new drug application provides for a new indication for Zetia to be administered in combination with fenofibrate, as adjunctive therapy to diet for the reduction of elevated total-C, LDL-C, Apo B, and non-HDL-C in patients with mixed hyperlipidemia.

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 agreed-upon labeling text.

We remind you of your July 26, 2005, plan to obtain additional information for reports of biliary adverse experiences associated with use of ZETIA (with or without concomitant fenofibrate use) by means of mailings and, for serious unlabeled events, telephone calls to the reporting health care provider.

The final printed labeling (FPL) must be identical to the submitted draft labeling [package insert submitted May 11 (email), 2006](copy enclosed).

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA.* Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. 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-013**." Approval of this submission by FDA is not required before the labeling is used.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and

effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving the pediatric study requirement for children less than 10 years of age for this indication and for children aged 10 to 17 years for homozygous familial hypercholesterolemia. We are deferring pediatric studies for children 10 years to less than 18 years of age for the treatment of patients with mixed hyperlipidemia for this application.

Your deferred pediatric study required under section 2 of the Pediatric Research Equity Act (PREA) is considered a required postmarketing study commitment. The status of this postmarketing study shall be reported annually according to 21 CFR 314.81. This commitment is listed below.

1. Deferred pediatric study under PREA for Zetia to be administered in combination with fenofibrate in pediatric patients ages 10 years to less than 18 years of age.

   Final Report Submission: December 31, 2011

Submit the final study report to this NDA. For administrative purposes, all submissions related to this pediatric postmarketing study commitment must be clearly designated "**Required Pediatric Study Commitment**".

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.
Acting 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
5/23/2006 04:11:18 PM
Eric Colman for Mary Parks