DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-445/S-011

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

Dear Dr. DiDomenico:

Please refer to your supplemental new drug application submitted March 4, 2005, under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zetia (ezetimibe) Tablets, 10 mg.

This "Changes Being Effected" supplemental new drug application provides for

1. To the Package Insert (PI), under **ADVERSE REACTIONS**, *Postmarketing Experience*, "myalgia; increased CPK; elevations in liver transaminases; hepatitis; thrombocytopenia; and very rarely, myopathy/rhabdomyolysis (see PRECAUTIONS, *Skeletal Muscle*)".

2. To the Patient Package Insert (PPI), under **What are the possible side effects of ZETIA?**, addition of "muscle aches; alterations in some laboratory blood tests; liver problems…"

   "Very rarely, patients have experienced severe muscle problems while taking ZETIA, usually when ZETIA was added to a statin drug. If you experience unexplained muscle pain, tenderness, or weakness while taking ZETIA, contact your doctor immediately. You need to do this promptly, because on rare occasions, these muscle problems can be serious, with muscle breakdown resulting in kidney damage."

3. To the PI, additional text to **CLINICAL PHARMACOLOGY**, *Drug Interactions*, **PRECAUTIONS**, and **Adverse Reactions**, *Postmarketing Experience* sections.

We have completed our review of this application. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert and text for the patient package insert).

Please submit the FPL electronically according to the guidance for industry titled "*Providing Regulatory Submissions in Electronic Format – NDA"*. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 21-445/S-011." Approval of this submission by FDA is not required before the labeling is used.

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, HFD-410
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 Valerie Jimenez, Regulatory Project Manager, at (301) 827-9090.

Sincerely,

{See appended electronic signature page}

David Orloff, M.D.
Director
Division of Metabolic and Endocrine Drug Products, HFD-510
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/

Mary Parks
3/22/05 11:48:54 AM
for Dr. Orloff