DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-687/S-019

Merck & Co., Inc., Agent for
MSP Singapore Company, LLC
Attention: Sandra Mackenzie, B.Sc., Director, Regulatory Affairs
126 E. Lincoln Avenue, PO Box 2000, RY33-208
Rahway, NJ 07065-0900

Dear Ms. Mackenzie:

Please refer to your supplemental new drug application dated November 17, 2006, received November 20, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vytorin (ezetimibe/simvastatin) Tablets.

We acknowledge receipt of your submission dated December 21, 2006.

This "Changes Being Effected" supplemental new drug application provides for labeling revisions to the Vytorin package insert regarding the molecular mechanism of action and a text change on the non-caucasian population for ezetimibe.

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

> 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.

To the **CLINICAL PHARMACOLOGY**, Special Populations, Race, *Ezetimibe* subsection, the paragraph has been changed to read:

> Based on a meta-analysis of multiple-dose pharmacokinetic studies, there were no pharmacokinetic differences between Black and Caucasian subjects. Studies in Asian subjects indicated that the pharmacokinetics of ezetimibe were similar to those seen in Caucasian subjects.

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.

In addition, submit three copies of the introductory promotional materials that you propose to use for these products. 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
Food and Drug Administration
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 PI #9619608
PPI #9621004

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
5/16/2007 09:04:39 AM
Eric Colman for Mary Parks