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