DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 19-384/S-046

Merck & Co., Inc.
Attention: Mary Beth Wigley
Manager, Regulatory Affairs
Sumneytown Pike
P.O. Box 4, BLA-20
West Point, PA 19486

Dear Ms. Wigley:

Please refer to your supplemental new drug application dated March 22, 2006, received March 23, 2006 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for NOROXIN™ (norfloxacin) Tablets, 400 mg.

This "Changes Being Effected" supplemental new drug application provides for additional text in the **PRECAUTIONS**, *Drug Interactions* subsection regarding concomitant administration of quinolones, including norfloxacin, with drugs metabolized by CYP1A2.

The changes were made as follows:
(double underlined text indicates additions/ ~~strikethrough~~ text indicates deletions.)

1. The following text was added as the first paragraph under the **PRECAUTIONS,** *Drug Interactions* subsection:

   Quinolones, including norfloxacin, have been shown *in vitro* to inhibit CYP1A2. Concomitant use with drugs metabolized by CYP1A2 (e.g., caffeine, clozapine, ropinirole, tacrine, theophylline, tizanidine) may result in increased substrate drug concentrations when given in usual doses. Patients taking any of these drugs concomitantly with norfloxacin should be carefully monitored.

2. The following changes were made to the second to the last paragraph under the **PRECAUTIONS,** *Drug Interactions* subsection:

   Some quinolones have also been shown to interfere with the metabolism of caffeine. This may lead to reduced clearance of caffeine and a prolongation of ~~it's~~ the plasma half-life that may lead to accumulation of caffeine in plasma when products containing caffeine are consumed while taking norfloxacin.

We completed our review of this application and it 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).

Submit revised 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. Upon receipt and verification, we will transmit that version to the National Library of Medicine for posting on the DailyMed website.

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 Hyun Son, Pharm. D., Regulatory Project Manager, at (301) 796-1600.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, M.D.
Director
Division of Special Pathogen and Transplant Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure: Package Insert

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

/s/

Renata Albrecht

9/22/2006 11:37:43 AM