DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-991/S-001

Merck & Co., Inc.
Attention: Randi Albin, Ph.D.
Director, Regulatory Affairs
P.O. Box 2000
RY33-204
Rahway, NJ 07065

Dear Dr. Albin:

Please refer to your supplemental new drug application dated and received May 9, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zolinza (vorinostat) Capsules, 100 mg.

This supplemental new drug application provides for changes to the CLINICAL PHARMACOLOGY, Pharmacokinetics section of the package insert to include the results from the P-glycoprotein transport studies conducted as a postmarketing commitment.

We 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).

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 21-991/S-001**." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your postmarketing study commitments in your submission dated October 4, 2006. These commitments are listed below.

Commitment 1:
Merck commits to provide updates of the exposure and safety data (adverse experiences leading to dose interruption, dose modification, or dose discontinuation) collected for CTCL patients who initially received vorinostat on Protocol 001 and continued to receive vorinostat on Protocol 007. A report will be provided annually starting in October 2007 and will continue until the final CTCL patient discontinues from Protocol 007 or for a maximum of 3 years.

First Report Submission: October 2007
Final Report Submission: October 2009

Commitment 2:
Merck agrees to conduct a pharmacokinetic study in cancer patients with hepatic impairment. Merck will submit the protocol to the agency prior to conduct of the study for agreement with the study design. Merck will conduct this pharmacokinetic study in the advanced cancer patient population with mild to moderate hepatic insufficiency, according to the Child-Pugh classification or the NCI criteria. Pharmacokinetic sample collection will occur after single-dose administration. The minimum target sample size will be approximately 4. If the study cannot be fully enrolled, the study will be closed after completion of the moderate impairment cohort.

Protocol Submission Date: April 1, 2007
Study Start (study enrollment open): October 1, 2007
Final Report Submission: October 2012

Commitment 3:
Merck agrees to study the effect of vorinostat on the ECG QT interval in the advanced cancer patient population. Intensive ECG monitoring, as well as pharmacokinetic sampling, will occur at baseline and after single-dose administration. The target sample size will be approximately 18.

Protocol Submission Date: January 1, 2007
Study Start (study enrollment open): April 1, 2007
Final Report Submission: April 2009

Commitment 4:
Merck commits to assess safety and laboratory monitoring data from ongoing Merck studies in patients treated concomitantly with vorinostat and warfarin. A report will be submitted annually starting October 2007 and will continue until data has been analyzed for 40 patients or for a maximum of three years.

First Report Submission Date: October 2007
Final Report Submission: October 2009

Commitment 5:
Merck commits to submit all adverse experiences reported as vorinostat-drug interactions in the post-marketing environment as expedited (15-day) reports. Each adverse experience from Merck clinical trials which meets the criteria of serious according to the regulatory definition and is considered to be a result of a vorinostat-drug interaction will be submitted as an expedited (15-day) report. A summary of these adverse experiences will be submitted annually starting in October 2007 and will continue for three years.

First Report Submission Date: October 2007
Final Report Submission: October 2009

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled

"**Postmarketing Study Commitment Protocol**", "**Postmarketing Study Commitment Final Report**", or "**Postmarketing Study Commitment Correspondence**."

In addition, submit three copies of the introductory promotional materials that you propose to use for this 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
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
Suite 12B05
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 Paul Zimmerman, Regulatory Project Manager, at 301-796-1489.

Sincerely,

{See appended electronic signature page}

Robert Justice, M.D.
Director
Division of Drug Oncology Products
Office of Oncology Drug Products
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/

Robert Justice

7/22/2008 06:19:28 PM