CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-762

APPROVAL LETTER(S)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-762

Merck & Co., Inc.
Attention: Michele R. Flicker, M.D., Ph.D.
Director, Regulatory Affairs
P.O. Box 2000, Mail Drop: RY 33-200
Rathway, NJ 07065

Dear Dr. Flicker:

Please refer to your new drug application (NDA) dated and received May 24, 2004 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Fosamax Plus D (alendronate sodium 70 mg & 2800 I.U. vitamin D_3) Tablets.

We acknowledge receipt of your submissions dated June 4, July 27, August 4, September 24, and November 11, 2004, and January 19, February 18, 22, 24, and 25, March 17 (2 submissions), 21, and 31, and April 6, 2005.

This new drug application provides for the use of Fosamax Plus D (alendronate sodium 70 mg & 2800 I.U. vitamin D_3) Tablets for the treatment of osteoporosis in postmenopausal women and the treatment to increase bone mass in men with osteoporosis.

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

The stability data reviewed supports an 18-month expiry in all package presentations.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for package insert and patient package insert submitted March 31, 2005, and immediate carton labels submitted February 18, 2005). Marketing this product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug. Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – NDA*. In addition, submit the content of labeling in electronic format as described in 21 CFR 314.50(l)(5) and in the format described at the following website: http://www.fda.gov/oc/datacouncil/spl.html. For administrative purposes, designate this submission "**FPL for approved NDA 21-762**." Approval of this submission by FDA is not required before the labeling is used.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving the pediatric study requirement for this application.

We remind you of your postmarketing study commitments in your submission dated March 31, 2005. These commitments are listed below.

1. In support of approval of a new alendronate/vitamin D_3 combination tablet containing a higher weekly dose of vitamin D_3, a commitment to conduct a dissolution study comparing the dissolution profile of the current Fosamax Plus D tablet to the new proposed tablet.

Submission of protocol for study	June 30, 2005
Completion of the dissolution study	September 30, 2005
Submission of the study results	December 30, 2005

2. Commitment to complete the extension phase of Protocol 227 in which patients received either the current strength combination tablet alone or the current strength tablet plus additional vitamin D_3.

Submission of protocol	Completed
Completion of study	Completed
Submission of final study report	December 30, 2005

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."**

We also acknowledge your April 6, 2005, agreement to work with the Agency to address the Agency's request to develop final acceptance criteria and acceptable in vitro dissolution methodology for the vitamin D_3 component of the current combination tablet.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. 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:

Division of Drug Marketing, Advertising,
And Communications, HFD-42
Food and Drug Administration
5600 Fishers Land
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, please call Randy Hedin, R.Ph., Senior Regulatory Management Officer, at (301) 827-6392.

Sincerely,

{See appended electronic signature page}

David G. Orloff, M.D.
Director
Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure: