DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-685

Merck & Co. Inc.
Attention: Sandra J. Rattray, Ph.D.
Associate Director, Regulatory Affairs
RY 33-720
P.O. Box 2000
Rahway, NJ 07065

Dear Dr. Rattray:

Please refer to your supplemental new drug application dated April 14, 2003, received April 15, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for CRIXIVAN® (indinavir sulfate) capsules.

This "Changes Being Effected" supplemental new drug application adds information on the increased risk of interstitial nephritis with medullary calcification and cortical atrophy in HIV infected adults receiving CRIXIVAN® who develop asymptomatic severe leukocyturia to the PRECAUTIONS section. Also, "leukocyturia" was included in the ADVERSE REACTIONS section of the label.

We completed our review of this supplemental new drug application, and it is approved, effective on the date of this letter, for use as recommended in the final printed labeling (FPL) submitted on April 14, 2003. However, we request that you revise the following paragraph in the Precautions section at the time of your next printing:

"During post-marketing surveillance of patients treated with indinavir, rare reports of interstitial nephritis with medullary calcification and cortical atrophy have been observed in patients with asymptomatic severe leukocyturia (>100 cells/ high power field). In patients with asymptomatic severe leukocyturia, further evaluation may be warranted."

The paragraph above should be revised to read:

"Reports of interstitial nephritis with medullary calcification and cortical atrophy have been observed in patients with asymptomatic severe leukocyturia (>100 cells/ high power field). Patients with asymptomatic severe leukocyturia should be monitored frequently with urinalyses. In patients with asymptomatic leukocyturia, renal biopsy may be considered."

Please also include an appropriate header for the above paragraph.

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, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Virginia Yoerg, Regulatory Health Project Manager, at (301) 827-2335.

Sincerely,

*{See appended electronic signature page}*

Debra Birnkrant, M.D.
Director
Division of Antiviral Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

Attachments: April 14, 2003 Final Printed Labeling

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

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/s/

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Jeffrey Murray
6/9/03 04:28:51 PM