DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-972/S-029
NDA 21-360/S-016

Bristol-Myers Squibb Company
Attention: Lori DeVore
Associate Director, Global Regulatory Science
5 Research Parkway
P.O. Box 5100
Wallingford, CT 06492-7660

Dear Ms. DeVore:

Please refer to your supplemental new drug application dated July 21, 2006, received July 24, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Sustiva® (efavirenz) 50mg, 100mg and 200mg capsules and Sustiva® (efavirenz) 600mg tablets.

We acknowledge receipt of your submissions dated August 21, 2006 and January 22, 2007.

These supplemental new drug applications provide for the inclusion of drug-drug interaction information regarding co-administration of efavirenz with rifampin, diltiazem, itraconazole, voriconazole, atorvastatin, pravastatin, simvastatin, pimozide, and bepredil.

We completed our review of these applications, as amended. These applications are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

Please refer to the January 8, 2007, teleconference during which we stated the literature references provided in this application did not support dosing recommendations for the co-administration of efavirenz and rifampin. As agreed, the current language in the package insert is retained with the following added text (depicted in bold type):

> "Clinical significance of reduced efavirenz concentrations is unknown. **Dosing recommendations for concomitant use of SUSTIVA and rifampin have not been established."**

We consider dosing recommendations for the co-administration of efavirenz and rifampin to be an important global public health issue; therefore, we would like to further discuss the development of a formal drug-drug interaction study with efavirenz and rifampin.

The final printed labeling (FPL) must be identical to the submitted labeling (package insert submitted January 22, 2007, patient package insert submitted January 22, 2007).

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 20-972/S-029, NDA 21-360/S-016**." Approval of this submission by FDA is not required before the labeling is used.

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
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

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 Jaewon Hong, Regulatory Project Manager, at (301) 796-2013.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, M.D.
Division Director
Division of Antiviral Products
Office of Antimicrobial 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/

Jeffrey Murray

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