Dear Dr. Takaki:

Please refer to your supplemental new drug applications dated March 31, 2009, received April 1, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Sustiva® (efavirenz) 50 mg and 200 mg capsules, and Sustiva® (efavirenz) 600 mg tablets. We acknowledge receipt of your submission dated September 15, 2009.

These Prior Approval supplemental new drug applications provide for the following revisions to the package insert (PI):

- Additions to the Drug Interaction and Clinical Pharmacology sections based on the results of the two drug-drug interaction studies (efavirenz with atazanavir, a protease inhibitor of HIV-1, and efavirenz with an oral contraceptive)
- Addition of information from postmarketing reports of contraceptive failure in a few patients who were treated with efavirenz while on an implantable hormonal contraceptive
- Addition of information based on a literature review of the interaction of immunosuppressants metabolized by CYP3A4 (cyclosporine, sirolimus, tacrolimus) and inducers of the CYP3A4 isozyme

In addition, the following revisions were made to the patient package insert:

- Reyataz was added to “The following medicines may need to be replaced with another medicine when taken with Sustiva;” section.
The immunosuppressant medicines cyclosporine (Gengraf, Neoral, Sandimmune and others) Prograf (tacrolimus) and Rapamune (sirolimus) were added to “The Following medicines may require a change in the dose of either SUSTIVA or other medicine,” section.

We have 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.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the package insert and patient package insert enclosed. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, “SPL for approved NDA 20-972/S-033 and NDA 21-360/S-021.

LABELING

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert and text for the patient package insert).

PROMOTIONAL MATERIALS

All promotional materials for your drug product that include representations about your drug product must be promptly revised to make it consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions to your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the following address or by facsimile at 301-847-8444:

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

In addition, as required under 21 CFR 314.81(b)(3)(i), you must submit your updated final promotional materials, and the package insert(s), at the time of initial dissemination or
publication, accompanied by a Form FDA-2253, directly to the above address. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

**LETTERS TO HEALTH CARE PROFESSIONALS**

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 Sherly Abraham, R.Ph., Regulatory Project Manager, at (301)796-3198.

Sincerely,

{See appended electronic signature page}

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

Enclosures:  
Package Insert  
Patient Package Insert
<table>
<thead>
<tr>
<th>Application Type/Number</th>
<th>Submission Type/Number</th>
<th>Submitter Name</th>
<th>Product Name</th>
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<tr>
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<td>SUPPL-33</td>
<td>BRISTOL MYERS SQUIBB CO</td>
<td>SUSTIVA</td>
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<tr>
<td>NDA-21360</td>
<td>SUPPL-21</td>
<td>BRISTOL MYERS SQUIBB PHARMA CO</td>
<td>SUSTIVA (EFAVIRENZ) 300/600MG TABLETS</td>
</tr>
</tbody>
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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.

/s/

KENDALL A MARCUS
09/23/2009