CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-937

APPROVAL LETTER(S)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-937

Gilead Sciences, Inc
Attn: Pamela S. Danagher, MS
Associate Director, Regulatory Affairs
333 Lakeside Drive
Foster City, CA 94404

Dear Ms. Danagher:

Please refer to your new drug application (NDA) dated April 25, 2006, received April 26, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ATRIPLA (efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg) Tablets.

We acknowledge receipt of your submissions dated January 13, 2006, March 24, 2006, March 31, 2006, April 5, 2006, April 14, 2006, April 18, 2006, April 27, 2006, June 26, 2006, June 30, 2006, July 3, 2006, July 5, 2006, July 6, 2006, and July 10, 2006.

This new drug application provides for the use of ATRIPLA (efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg) Tablets for use alone as a complete regimen or in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults.

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 final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, text for the patient package insert, and immediate container and carton labels). Marketing the 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*. 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 NDA 21-937.**" 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 deferring submission of your pediatric studies for ages from birth to 18 years of age.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of these

postmarketing studies shall be reported annually according to 21 CFR 314.81. These commitments are listed below.

1. Deferred pediatric study under PREA for use of ATRIPLA alone as a complete regimen or in combination with other antiretroviral agents for the treatment of HIV-1 infection in pediatric subjects ages from 2 to 18 years of age.

   Pediatric studies are ongoing for the individual products, SUSTIVA (efavirenz) and VIREAD (tenofovir disoproxil fumarate).

   SUSTIVA Final Study Report Submission for ages 3 months to 3 years of age: January 31, 2008
   VIREAD Final Report Submission for ages 2 to 18 years of age: January 31, 2008

   After submission of these studies, we will determine whether additional studies for ATRIPLA will be required. Should pediatric studies for ATRIPLA be required, the timeline for completion is as follows:

   Final Study Report Submission for ages 2 to 18 years: January 31, 2011

2. Deferred pediatric study under PREA for the use of ATRIPLA alone as a complete regimen or in combination with other antiretroviral agents for the treatment of HIV-1 infection in pediatric subjects ages birth to 2 years of age.

   Due to safety concerns for this age group, we are waiting for completion and review of studies of VIREAD in the 2 to 18 years age group before determining whether it is appropriate to study VIREAD or ATRIPLA in the birth to 2 years age group. Should further pediatric studies in this age group be required, the timeline for completion is as follows:

   Final Study Report Submission for ages birth to 2 years of age: January 31, 2011

Submit final study reports to this NDA. For administrative purposes, all submissions related to this/these pediatric postmarketing study commitment(s) must be clearly designated "**Required Pediatric Study Commitments.**"

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 product. Submit all proposed materials in draft or mock-up form, not final print. Send

one copy to the Division of Antiviral Products 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

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

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 Marsha Holloman, Regulatory Health Project Manager, at (301) 796-0731.

Sincerely,

{See appended electronic signature page}

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

Enclosure: Final Agreed Upon Labeling (text for the package insert, text for the patient package insert, and immediate container and bottle labels)

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
7/12/2006 11:06:16 AM