DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-937/S-007 **CBE SUPPLEMENT**

Gilead Sciences, Inc.
ATTN: Dara Wambach, MA
Manager, Regulatory Affairs
333 Lakeside Drive
Foster City, CA 94404

Dear Ms. Wambach:

Please refer to your supplemental new drug application dated May 25, 2007, and received May 29, 2007, 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.

This "Changes Being Effected" supplemental new drug application revises ATRIPLA labeling to include changes incorporated in the May 21, 2007 approved TRUVADA package insert. In addition, the following changes are proposed:

1. Addition of the letter "s" to **WARNINGS** section and minor word changes to the Black Box Warning for clarification.

2. Addition of **INDICATION and USAGE** to the reference in the first sentence, **MICROBIOLOGY: Resistance: Efavirenz, emtricitabine, and tenofovir disoproxil fumarate** section, second paragraph.

3. In the **CLINICAL PHARMACOLOGY: Drug Interactions: Emtricitabine and tenofovir disoproxil fumarate** section, a grammatical correction. Editorial change to present information in alphabetical order.

4. Changes to the **WARNINGS: Patients with HIV and HBV Coinfection** section that rearrange some words and delete others in order to clarify the section.

5. Changes to the **WARNINGS: Coadministration with Related Drugs** section that add the generic names immediately following the brand names of the listed drugs.

6. Changes to the **WARNINGS: Renal Impairment** section that delete outdated information and include new information about creatinine clearance and serum phosphorus in patients at risk for renal impairment.

7. Changes to the **PRECAUTIONS: Liver Enzymes** section that move "Coinfected" from the end of the reference to the middle.

8. Changes to the **PRECAUTIONS: Bone Effects** section that add information about cases of osteomalacia.

9. Changes to the **PRECAUTIONS: Emtricitabine and tenofovir disoproxil fumarate** section:

    - Editorial change to present information in alphabetical order;
    - Addition the brand names of didanosine (Videx, Videx EC); and
    - Information about cases of suppression of CD4 cell counts when tenofovir disoproxil fumarate is coadministered with didanosine at a dose of 400 mg daily.

10. Changes to the **ADVERSE REACTIONS: Clinical Trials** section that correct a typographical error in the units for Fasting Cholesterol value (mg/dL instead of mg/mL) in Table 10. Also, editorial change to add the letter "s" to the last two entries (Neutrophils and Fasting Triglyceride).

11. Grammatical changes to the **ADVERSE REACTIONS: Post Marketing Experience** section to clarify the first sentence.

12. Changes to the **ADVERSE REACTIONS: Post Marketing Experience** section that add the following events that have been identified during post-approval use of tenofovir disoproxil fumarate:

    - SKIN AND SUBCUTANEOUS TISSUE DISORDERS: Rash
    - MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS: Myopathy, Osteomalacia (both associated with proximal renal tubulopathy)
    - RENAL AND URINARY DISORDERS: Addition of the word "Interstitial" before nephritis "and (including acute cases)" after.
    - GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS: Asthenia.

13. Changes in the effective date of the labeling changes for the package insert and the patient package insert.

14. Addition of generic names to the **Patient Package Insert, MEDICINES YOU SHOULD NOT TAKE WITH ATRIPLA** section, bullet one.

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

Within 14 days of the date of this letter, submit content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical in content to the enclosed labeling. 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 21-937**." In addition, amend any pending applications for Atripla [redacted] with content of labeling in SPL format to include the changes approved in this application.

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

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 Elizabeth Thompson, MS, Regulatory Project Manager, at (301) 796-0824.

Sincerely,

{See appended electronic signature page}

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

Enclosure: Final Agreed-Upon Labeling

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

/s/

Debra Birnkrant
2/28/2008 01:41:04 PM
NDA 21-937