DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-356/S-016

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

Dear Ms. Danagher:

Please refer to your supplemental new drug application dated May 6, 2005, received May 9, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for VIREAD (tenofovir disoproxil fumarate) 300 mg Capsules.

We acknowledge receipt of your submissions dated August 5, 2005, November 18, 2005, December 9, 2005, January 17, 2006, February 8, 2006, February 21, 2006, February 24, 2006, February 28, 2006, and March 6, 2006.

This supplemental new drug application provides for the use of VIREAD (tenofovir disoproxil fumarate) 300 mg Capsules in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults.

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.

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

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 21-356/S-016.**" Approval of this submission by FDA is not required before the labeling is used.

We approved this NDA under the regulations at 21 CFR 314 Subpart H for accelerated approval of new drugs for serious or life-threatening illnesses. Approval of this supplement fulfills your commitments made under 21 CFR 314.510.

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 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 the treatment, in combination with other antiretroviral agents, of HIV-1 in pediatric patients ages 2 to 18 years of age.

   Final Report Submission for ages 2 to 18 years of age*:* January 31, 2008

2. Deferred pediatric study under PREA for the use of VIREAD treatment, in combination with other antiretroviral agents, of HIV-1 in pediatric patients ages birth to 2 years of age.

   Due to safety concerns for this age group, we are waiting for completion and review of studies in the 2 to 18 years age group before determining whether it is appropriate to study tenofovir 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 Report Submission for ages birth to 2 years of age: January 31, 2010

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

We remind you of your outstanding postmarketing study commitments. One additional postmarketing study commitment is listed below:

3. Please reassay the 12 virologic failure isolates from Study 934 GS-01-934 *"A Phase III, Randomized, Open-Label, Multicenter Study of the Treatment of Antiretroviral-Naïve, HIV-1 Infected Subjects Comparing Tenofovir Disoproxil Fumarate and Emtricitabine in Combination with Efavirenz versus Combivir (lamivudine/zidovudine) and Efavirenz"* using tenofovir disoproxil fumarate along with several well-characterized tenofovir resistant isolates with a range of susceptibilities to tenofovir to determine if tenofovir or tenofovir disoproxil fumarate is more sensitive in the detection of phenotypic susceptibility.

   Submission Due Date: December 31, 2006

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**."

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
WO 22, Room 4447
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

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}

Jeffery S. Murray, MD, MPH
Deputy Division Director
Division of Antiviral Products
Office of Antimicrobial Products
Office of New Drugs
Center for Drug Evaluation and Research

Enclosure: Final Draft Labeling

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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