



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-356/S-011

Gilead Sciences, Inc  
Attention: Dean Waters  
Associate Director, Regulatory Affairs  
333 Lakeside Drive  
Foster City, CA 94404

Dear Mr. Waters:

Please refer to your supplemental new drug application dated June 4, 2004, received July 13, 2004, submitted under section 505 (b) of the Federal Food, Drug, and Cosmetic Act for Viread® (tenofovir disoproxil fumarate) 300 mg Tablets.

We acknowledge receipt of your submissions dated:

June 4, 2004	April 25, 2005	May 9, 2005
July 13, 2004	April 26, 2005	
March 30, 2005	April 27, 2005	
April 15, 2005	May 2, 2005	
April 19, 2005	May 6, 2005	

This supplemental new drug application provides for the addition of 144-Week clinical data from Study 903 to the Viread® (tenofovir disoproxil fumarate) package insert.

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 and text for the patient package insert) submitted May 9, 2005.

Please submit the FPL electronically 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, in no case more than 30 days after it is printed. Please individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated “**FPL for approved supplement NDA 21-356/S-011**”. Approval of this submission by FDA is not required before the labeling is used.

We remind you of your ongoing postmarketing study commitments. The following additional postmarketing study commitments have been agreed upon:

1. Determine the antiviral activity *in vitro* of tenofovir against multiple HIV-2 isolates in parallel with tenofovir failure isolates randomly selected from naive trials and which fall in the lower quartile of phenotypic susceptibility.

Final Report Submission: June 30, 2006.

2. Provide a summary of all available information related to the interaction between tenofovir DF and didanosine as it affects CD4 cell counts. Evaluate and discuss possible mechanisms for this interaction and further plans to assess the impact on long-term treatment.

Final Report Submission: September 30, 2005

3. Conduct and submit a comprehensive review of the spectrum of renal toxicity reported with the use of tenofovir DF and provide a summary of these events. Discuss any ongoing efforts to identify mechanism of toxicity, important co-factors for developing nephrotoxicity, and how this information could be used to reduce the risk of toxicity in the vulnerable population. This may be submitted with the next Periodic Safety Update Report (PSUR) for NDA 21-356.

Final Report Submission: September 30, 2005

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 this division and two copies of both the promotional materials and package insert directly to:

Division of Drug Marketing, Advertising, and Communication, HFD-42  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD 20857

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, HFD-410  
FDA  
5600 Fishers Lane  
Rockville, MD 20857

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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 Jeff D. O'Neill, Regulatory Health Project Manager, at (301) 827-2362.

Sincerely,

*{See appended electronic signature page}*

Jeffrey Murray, MD, MPH  
Deputy Director  
Division of Antiviral Drug Products  
Office of Drug Evaluation IV  
Center for Drug Evaluation and Research

Enclosure

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**This is a representation of an electronic record that was signed electronically and  
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/s/

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Jeffrey Murray  
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