



NDA 20-977/S-011  
NDA 20-978/S-013

GlaxoSmithKline  
Attention: Martha Anne A. Moore, R.Ph.  
Antiviral/Antibacterial US Regulatory Affairs  
PO Box 13398  
Five Moore Drive  
Research Triangle Park, NC 27709

Dear Ms. Moore:

Please refer to your supplemental new drug applications dated June 13, 2003, received June 16, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ZIAGEN® (abacavir sulfate) tablets and oral solution.

We acknowledge receipt of your submissions dated:

June 13, 2003	December 17, 2003 (2)	April 07, 2004
July 01, 2003	January 16, 2004	April 08, 2004
September 05, 2003	March 02, 2004	April 12, 2004
November 07, 2003	March 11, 2004	April 13, 2004
November 10, 2003	April 02, 2004	April 14, 2004

These supplemental applications provide information to fulfill the accelerated approval commitments as required under CFR 314.510. Specifically, these supplemental new drug applications provide for the use of ZIAGEN® (abacavir sulfate) tablets and oral solution in combination with other antiretroviral agents for the treatment of HIV-1 infection.

We have completed the review of these applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text. Accordingly, this application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, text for the medication guide). Marketing the products with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

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, these

submissions should be designated "FPL for approved supplement NDA 20-977/S-011 and NDA 20-978/S-013." Approval of these submissions 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 note that you have fulfilled the pediatric study requirements for these applications.

We remind you of your postmarketing study commitments in your submission dated April 14, 2004. These commitments are listed below. Please address each as stated.

1. Submit revised text to update labeling, including medication guide and Warning Card for abacavir products.

Labeling supplement submission date: within 2 months of this letter.

2. Study and report on available information on the management of abacavir-associated rash developing in patients who are being treated with multiple antiretroviral agents and other commonly used HIV-related drugs.

Labeling supplement submission date: within 2 months of this letter.

3. Submit a final report on abacavir use in adolescent patients in study PACTG 1018.

Report submission date: within 12 months of this letter.

4. Provide information on the status and outcome of study ACTG 321 to evaluate abacavir in neonates.

Status and outcome submission date: within 12 months of this letter.

5. Provide an updated summary of the clinical pharmacology, safety, and efficacy of abacavir in pediatric patients.

Summary submission date: within 12 months of this letter.

6. Submit HIV-1 viral resistance and cross-resistance data for abacavir in the Agency requested format for the agreed completed studies along with revised labeling.

Report submission date: within 2 months of this letter

7. Provide data on the *in vitro* susceptibility of NNRTI resistant HIV-1 isolates to abacavir and data on the *in vitro* susceptibility of abacavir resistant HIV-1 isolates to the FDA approved NNRTIs.

Report submission date: within 18 months of this letter

8. Conduct and submit a meta-analysis of data from abacavir clinical trials to assess the rate of psychiatric events (including depression, worsening depression, suicidal ideation/attempt, and acute psychosis) on the abacavir versus control arms.

Analysis plan submission date:	within 6 months of this letter
Final report submission date:	within 18 months of this letter

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 Protocol”**, **“Postmarketing Study Final Report”**, or **“Postmarketing Study Correspondence.”**

In addition, submit three copies of the introductory promotional materials that you propose to use for these products. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Antiviral Drug Products and two copies of both the promotional materials and the package insert(s) directly to:

Division of Drug Marketing, Advertising, and Communications, 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

Please submit one market package of the drug product when it is available.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

NDA 20-977/S-011

NDA 20-978/S-013

Page 4

If you have any questions, please contact Tanim Sinha, M.S., Regulatory Project Manager, at (301) 827-2335.

Sincerely yours,

*{See appended electronic signature page}*

Debra Birnkrant, M.D.  
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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Debra Birnkrant  
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NDA 20-978, 20-977