DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-977/S-017
NDA 20-978/S-020

GlaxoSmithKline
Attention: Martha Anne A. Moore, R.Ph.
Senior Director, Antiviral/Antibacterial US Regulatory Affairs
PO Box 13398
Five Moore Drive
Research Triangle Park, NC 27709-3398

Dear Ms. Moore:

Please refer to your September 20, 2007 supplemental new drug applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ZIAGEN® (abacavir sulfate) Tablets (300 mg) and ZIAGEN® (abacavir sulfate) Oral Solution (20 mg/ml).

Reference is made to your submissions dated November 30, 2007 (2), December 4, 2007, December 5, 2007, December 19, 2007, May 16, 2008, June 6, 2008, June 12, 2008, June 16, 2008, July 11, 2008, and July 16, 2008.

These supplemental new drug applications for ZIAGEN® (abacavir sulfate) Tablets and ZIAGEN® (abacavir sulfate) Oral Solution provide results from the PREDICT-1 (CNA106030) and SHAPE (ABC107442) studies and incorporates language regarding the association of the HLA-B*5701 allele with abacavir-related hypersensitivity reaction (HSR) and recommendation for HLA-B*5701 testing prior to initiation of abacavir into product labeling. In addition, updates were made to reflect the potential increased risk for myocardial infarction with recent ZIAGEN use in response to published data from the D:A:D study [Lancet, 2008].

We completed our review of these applications, as amended. These applications are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indications in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We note that you have fulfilled the pediatric study requirement for all relevant pediatric age groups for this application.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENT

Title IX, Subtitle A, Section 901 of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amends the Federal Food, Drug, and Cosmetic Act (FDCA) to authorize FDA to require the submission of a REMS for an approved drug if the Secretary becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)(2)). This provision took effect on March 25, 2008.

ZIAGEN® (abacavir sulfate) was approved in 1998, for use in combination with other antiretroviral agents for the treatment of HIV-1 infection. Since ZIAGEN's (abacavir sulfate) approval, we have become aware of new safety information indicating that patients who carry the HLA-B*5701 allele are at significantly increased risk of developing abacavir hypersensitivity, which in some cases may be severe or fatal. These patients should not initiate treatment with an abacavir-containing regimen except under exceptional circumstances when the potential benefit outweighs the risk and under close medical supervision. In addition, due to the potential increased risk for myocardial infarction with recent ZIAGEN® (abacavir sulfate) use, patients should inform their doctors if they smoke or have heart disease, high blood pressure, high cholesterol or diabetes. The above information was not available when ZIAGEN® (abacavir sulfate) was granted marketing authorization for use in combination with other antiretroviral agents for the treatment of HIV-1-infection. Therefore, we consider this information to be "new safety information" as defined in FDAAA.

In accordance with section 505-1 of the FDCA, as one element of a REMS, FDA may require the development of a Medication Guide as provided for under 21 CFR Part 208. FDA previously approved a Medication Guide required for distribution with ZIAGEN® (abacavir sulfate) in accordance with 21 CFR Part 208. Pursuant to 21 CFR Part 208, FDA has determined that ZIAGEN® (abacavir sulfate) poses a serious and significant public health concern requiring distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of ZIAGEN® (abacavir sulfate). FDA has determined that ZIAGEN® (abacavir sulfate) is a product that has serious risks of which patients should be made aware because information concerning the risks could affect patients' decisions to use, or continue to use, ZIAGEN® (abacavir sulfate).

This includes the new safety information identified above regarding the use of ZIAGEN® (abacavir sulfate) by patients who carry the HLA-B*5701 allele and the increased risk for development of abacavir hypersensitivity in these patients. In addition, due to the potential increased risk for myocardial infarction with recent ZIAGEN® (abacavir sulfate) use, patients should inform their doctors if they smoke or have heart disease, high blood pressure, high cholesterol or diabetes. The Medication Guide has been revised in response to this new safety information and is now considered to be a part of REMS.

Your proposed REMS, submitted on July 11, 2008 is approved. The REMS consists of the Medication Guide included with this letter and the timetable for submission of assessments of the REMS that was included in your July 10, 2008 submission. The timetable you submitted is as follows:

1st FDAAA assessment:	January 2010 (18 months from approval)
2nd FDAAA assessment:	July 2011 (3 years from approval)
3rd FDAAA assessment:	July 2017 (7 years from approval)

Information needed for assessment of the REMS will include but may not be limited to:

a. A survey of patients' understanding of the risk of hypersensitivity reaction associated with the use of ZIAGEN® (abacavir sulfate)
b. A report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24
c. A report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance.

Use the following designators to prominently label all submissions, including supplements, relating to this REMS:

NDA 20-977/20-978 REMS Assessment
NDA 20-977/20-978 Proposed REMS Modification

Please note that:

- This Medication Guide must be reprinted immediately following the last section of labeling or, alternatively, accompany the prescription drug labeling [21 CFR 201.57(c)(18)] or 21 CFR 201.80(f)(2)];

- You are responsible for ensuring that this Medication Guide is available for distribution to every patient who is dispensed a prescription for this product [21 CFR 208.24];

- The final printed Medication Guide distributed to patients must conform to all conditions described in 21 CFR 208.20, including a minimum of 10 point text; and

- You are responsible for ensuring that the label of each container or package includes a prominent and conspicuous instruction to authorized dispensers to provide a Medication Guide to each patient to whom the drug is dispensed, and states how the Medication Guide is provided [21 CFR 208.24(d)].

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the 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 to the enclosed labeling (text for the package insert, text for the patient package insert). 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 20-977/S-017 and NDA 20-978/S-020.**"

In addition, within 21 days of the date of this letter, amend any pending applications for this NDA with content of labeling in structured product labeling (SPL) format to include the changes approved in these applications.

Marketing the product with FPL that is not identical to the approved labeling text and in the required format may render the product misbranded and an unapproved new drug.

PROMOTIONAL MATERIALS

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 Products and two copies of both the promotional materials and the package insert(s) 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

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
Suite 12B05
5600 Fishers Lane
Rockville, MD 20857

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, please contact Tanima Sinha, M.S., Regulatory Project Manager, at (301) 796-0812.

Sincerely,

{See appended electronic signature page}

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

Enclosure: Final agreed upon label

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
7/18/2008 01:05:53 PM