DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20977/S-027
NDA 20978/S-031

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENTS

ViiV Healthcare Company
Attention: Vicki Horton, DVM, Ph.D., DABT
Director, Global Regulatory Affairs
Five Moore Drive, PO Box 13398
Research Triangle Park, NC 27709

Dear Dr. Horton:

Please refer to your Supplemental New Drug Applications (sNDAs) dated and received May 23, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for ZIAGEN (abacavir sulfate) 300 mg scored tablets and 20 mg per mL oral solution.

We acknowledge receipt of your amendments dated June 20, 2014, July 29, 2014, August 29, 2014, September 5, 2014, September 22, 2014, October 10, 2014, December 10, 2014, February 26, 2015, March 4, 2015, March 13, 2015, March 19, 2015, March 20, 2015, and March 23, 2015.

These "Prior Approval" supplemental new drug applications provide for once-daily dosing in pediatric patients 3 months of age and older in combination with other antiretroviral agents for the treatment of HIV-1 infection.

APPROVAL & LABELING

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

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert and Medication Guide), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

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 indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

This product is appropriately labeled for use in ages 3 months to 17 years for this indication. Therefore, no additional studies are needed in this pediatric group.

FULFILLMENT OF POSTMARKETING REQUIREMENTS

These Prior Approval Supplements were also submitted to fulfill the following PREA postmarketing requirements:

426-1	Deferred pediatric study under PREA for the treatment of HIV-1 infection in pediatric patients ages 3 months to 17 years.
1545-1	Deferred pediatric study under PREA for the treatment of HIV-1 infection in pediatric patients ages 3 months to 17 years.

The approval of these supplemental new drug applications fulfills these postmarketing requirements.

This completes all of your postmarketing requirements and postmarketing commitments acknowledged in our August 4, 2004 and the September 21, 2009, approval letters.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

Since ZIAGEN (abacavir sulfate) was approved on December 17, 1998, we have become aware of substitutions in reverse transcriptase, K65R, L74V, M184V/I and Y115F, that confer reduced susceptibility to abacavir and substitution M184V/I that confers high level reduced susceptibility to lamivudine. We consider this information to be "new safety information" as defined in section 505-1(b)(3) of the FDCA.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to identify the unexpected serious risk of the emergence of resistance-associated substitutions in HIV-1 isolates from subjects who fail to respond to the treatment regimen.

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA will not be sufficient to assess this serious risk.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

Clinical Virology

2890-1 Analyze the emergence of resistance-associated substitutions in HIV-1 isolates from subjects who fail to respond to the treatment regimen in the ARROW trial. Conduct genotypic analyses of the isolates to identify and characterize HIV-1 mutants with, but not limited to, the substitutions K65R, L74V, M184V/I, and Y115F in reverse transcriptase. Include in the submission the ARROW trial resistance data and plots of viral load from virologic failure subjects.

The timetable you submitted on March 4, 2015, states that you will conduct this study according to the following schedule:

Final Report Submission: 05/31/2015

Submit the protocol to your IND 63468, with a cross-reference letter to this NDA. Submit all final report(s) to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **"Required Postmarketing Protocol Under 505(o)", "Required Postmarketing Final Report Under 505(o)", "Required Postmarketing Correspondence Under 505(o)".**

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii), requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

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 Victoria Tyson, Regulatory Project Manager, at (301) 796-0827.

Sincerely,

{See appended electronic signature page}

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

ENCLOSURE:
Content of 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 B BIRNKRANT
03/23/2015