DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-797/S-003
NDA 21-798/S-003

PRIOR APPROVAL SUPPLEMENT

Bristol-Myers Squibb Pharmaceutical Company
Attention: Joan C. Fung-Tomc, PhD
Director, Global Regulatory Affairs
Bristol-Myers Squibb Company
5 Research Parkway
PO Box 5100
Wallingford, CT 06492

Dear Dr. Fung-Tomc:

Please refer to your supplemental new drug applications dated May 29, 2007, and received May 30, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for BARACLUDE® (entecavir) Tablets and BARACLUDE® (entecavir) Oral Solution.

We acknowledge receipt of your submissions dated June 29, 2007, and received July 2, 2007.

These supplemental new drug applications provide for the use of BARACLUDE® (entecavir) 0.5 mg and 1.0 mg Film-Coated Tablets and BARACLUDE® (entecavir) 0.05 mg/mL Oral Solution for the treatment of chronic hepatitis B virus infection in adults with evidence of active viral replication and either evidence of persistent elevations in serum aminotransferases (ALT or AST) or histologically active disease. These submissions amend the labeling to include safety information related to the use of entecavir (ETV) in patients with human immunodeficiency virus (HIV)/hepatitis B virus (HBV) coinfection who are not receiving simultaneous highly active antiretroviral therapy (HAART). Specifically, a recommendation against the use of BARACLUDE in HIV/HBV co-infected patients who are not also receiving adequate therapy for their HIV is added to the Boxed Warnings and WARNINGS sections. Corresponding changes in PRECAUTIONS: Information for Patients and the Patient Package Insert sections.

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.

Within 21 days of the date of this letter, submit 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 in content to the enclosed submitted labeling dated June 28, 2007. 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 21-797/S-003 and NDA 21-798/S-003.**"

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 June 28, 2007.) These revisions are terms of the approval of these applications.

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 these submissions "**FPL for approved supplement NDA 21-797/S-003 and NDA 21-798/S-003**." Approval of these submissions by FDA is not required before the labeling is used.

We remind you of your postmarketing study commitments in the original NDA approval letter dated March 29, 2005, and in the supplemental (S-001) approval letter dated February 23, 2007.

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

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 this division and two copies of both the promotional materials and the package insert 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
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

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 S. Holloman, BS Pharm, JD, Regulatory Health Project Manager, at (301) 796-0731.

Sincerely,

{See appended electronic signature page}

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

Enclosure: Final agreed-upon package insert and patient package insert

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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

7/24/2007 04:29:08 PM