DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

IND 56,897

Bristol-Myers Squibb Company
Attention: Louis M. Ferrara
Director, Regulatory Science
5 Research Parkway
Wallingford, CT 06492

Dear Mr. Ferrara:

Reference is made to your telephone facsimile submitted to IND 56,897 on June 7, 2001, for atazanavir (BMS-232632). In addition, please refer to the Division of Antiviral Drug Products' telephone facsimile dated June 18, 2001 stating that it plans to issue a pediatric Written Request.

To obtain needed pediatric information on the use of atazanavir, the Food and Drug Administration (FDA) is hereby making a formal Written Request, pursuant to Section 505A of the Federal Food, Drug, and Cosmetic Act (the Act), that you submit information from the following studies:

Type of study:
Multiple-dose pharmacokinetic, safety, and activity study of atazanavir in combination with other antiretroviral agents in HIV-infected pediatric patients.

Indication to be studied: Treatment of HIV-1 infection.

Age group in which studies will be performed: HIV-infected pediatric patients from three months to 16 years.

Drug Information
Dosage form: 200 mg capsules and age-appropriate formulation
Route of administration: oral
Regimen: to be determined by development program

Drug specific safety concerns:
- Indirect hyperbilirubinemia
- Metabolic disturbances
- PR & QT interval prolongation

Statistical information, including power of study and statistical assessments:

- Descriptive analyses of multiple-dose pharmacokinetic, safety and activity data in HIV-infected pediatric patients.

- Study should include an adequate number of patients to characterize pharmacokinetics over the age range studied, taking into account inter-subject and intra-subject variability. The number of subjects should be uniformly distributed across the age range studied.

Study Endpoints:

Pharmacokinetics

Parameters such as C_{max}, C_{min}, $T_{max,}$ $t_{1/2}$, AUC

Safety and tolerability

All pediatric patients enrolled should be followed for safety for a minimum of six months at the recommended dose. Please submit plans for long-term safety monitoring in HIV-infected pediatric patients who have received atazanavir.

Activity

Assessment of changes in plasma HIV RNA levels and in CD4 cell counts.

Labeling that may result from the study:

Information regarding dosing, safety, and activity in HIV-infected pediatric population and information regarding dosing and safety.

Format of reports to be submitted:

Full study reports not previously submitted to the Agency addressing the issues outlined in this request with full analysis, assessment, and interpretation. Please include other information as appropriate.

Timeframe for submitting reports of the study:

Reports of the above studies must be submitted to the Agency on or before August 2003. Please note that pediatric exclusivity only extends existing patent protection or exclusivity that has not expired or been previously extended at the time you submit your reports of the studies in response to this Written Request.

Please submit protocols for the above studies to an investigational new drug application (IND) and clearly mark your submission "**PEDIATRIC PROTOCOL SUBMITTED FOR PEDIATRIC EXCLUSIVITY STUDY**" in large font, bolded type at the beginning of the cover letter of the submission. Please notify us as soon as possible if you wish to enter into a written agreement by submitting a proposed written agreement. Clearly mark your submission "**PROPOSED WRITTEN AGREEMENT FOR PEDIATRIC STUDIES**" in large font, bolded type at the beginning of the cover letter of the submission.

Reports of the studies should be submitted as a supplement to your approved NDA or as a new drug application, as appropriate, with the proposed labeling changes you believe would be warranted based on the data derived from these studies. When submitting the reports, please

clearly mark your submission "**SUBMISSION OF PEDIATRIC STUDY REPORTS – PEDIATRIC EXCLUSIVITY DETERMINATION REQUESTED"** in large font, bolded type at the beginning of the cover letter of the submission and include a copy of this letter. Please also send a copy of the cover letter of your submission, via fax (301-594-0183) or messenger to the Director, Office of Generic Drugs, HFD-600, Metro Park North II, 7500 Standish Place, Rockville, MD 20855-2773.

If you wish to discuss any amendments to this Written Request, please submit proposed changes and the reasons for the proposed changes to your application. Submissions of proposed changes to this request should be clearly marked "**PROPOSED CHANGES IN WRITTEN REQUEST FOR PEDIATRIC STUDIES"** in large font, bolded type at the beginning of the cover letter of the submission. You will be notified in writing if any changes to this Written Request are agreed upon by the Agency.

We hope you will fulfill this pediatric study request. We look forward to working with you on this matter in order to develop additional pediatric information that may produce health benefits in the pediatric population.

If you have any questions, please contact Karen A. Young at 301-827-2335.

Sincerely yours,

M. Dianne Murphy, M.D.
Director
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Dianne Murphy
8/2/01 04:09:59 PM