DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug
Administration
Rockville MD 20857

NDA 21-178

Bristol-Myers Squibb
Attention: Warren C. Randolph
Director, Regulatory Science
P.O. Box 4000
Princeton, NJ 08543-4000

Dear Mr. Randolph:

Reference is made to your correspondence dated May 18, 2001, requesting changes to our letter dated January 31, 2001, Written Request for pediatric studies for Glyburide and Metformin HCl Tablets.

We have reviewed your proposed changes and are amending the below listed section of the Written Request. All other terms stated in our Written Request issued on January 31, 2001, remain the same.

Under **Study Design,** Study 2, the Written Request states that "the maximum titrated dose for each treatment arm will be:

- ≤ 20 mg once a day for the glyburide monotherapy arm.
- ≤ 1000 mg twice a day for the metformin monotherapy arm.
- ≤ 5 mg glyburide/1000 mg metformin twice a day for the fixed combination arm.

Your request to modify the maximum doses in the **Study Design,** Study 2 section is as follows:

- ≤ 5 mg twice a day for the glyburide monotherapy arm.
- ≤ 1000 mg twice a day for the metformin monotherapy arm
- ≤ 2.5 mg glyburide/500 mg metformin twice a day for the fixed combination arm.

Reports of the studies that meet the terms of the Written Request dated January 31, 2001, as amended by this letter must be submitted to the Agency on or before July 15, 2003, in order to possibly qualify for pediatric exclusivity extension under Section 505A of the Act.

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. Please 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 NDA 21-178 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 to the pediatric population.

If you have any questions, please contact Ms. Jena Weber, Regulatory Project Manager, at 301-827-6422.

Sincerely,

{See appended electronic signature page}

David G. Orloff
Division Director Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II
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/

David Orloff

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