DEPARTMENT OF HEALTH & HUMAN SERVICES

ANDA 76-863

Food and Drug Administration
Rockville MD 20857

OCT 14 2004

Barr Laboratories, Inc.
Attention: Nicholas Tantillo
2 Quaker Road
P.O. Box 2900
Pomona, NY 10970-0519

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated October 8, 2003, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Metformin Extended-Release Tablets, 750 mg.

Reference is also made to your amendments dated March 30, April 9, July 12, July 13, August 10, September 2, and October 1, 2004. We also acknowledge receipt of your correspondence dated December 12, and December 24, 2003, and February 23, May 3, July 13, and September 1, 2004, addressing patent and exclusivity issues associated with this drug product.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved. The Division of Bioequivalence has determined your Metformin Hydrochloride Extended-Release Tablets, 750 mg, to be bioequivalent and, therefore, therapeutically equivalent to the listed drug, Glucophage XR Extended-release Tablets of Bristol Myers Squibb Co.

The listed drug product (RLD) referenced in your application, Glucophage XR Extended-release Tablets 750 mg, of Bristol Myers Squibb Company, is subject to periods of patent protection. As noted in the Agency's publication entitled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"), U.S. patents 6,475,521 (the '521 patent) and 6,660,300 (the '300 patent) are each scheduled to expire on March 19, 2018.

Your application contains a paragraph IV certification under section 505(j)(2)(A)(vii)(IV) of the Act to the '521 patent stating that this patent is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Metformin Extended-Release Tablets, 750 mg, under this ANDA. Section 505(j)(5)(B)(iii)[1] of the Act provides that approval of an ANDA shall be made effective immediately unless an action is brought against Barr Laboratories, Inc. (Barr) for infringement of the '521 patent that was the subject of the paragraph IV certification. This action must be brought before the expiration of 45 days from the date the notice you provided under paragraph (2)(B)(i) was received by the NDA/patent holder(s). You have notified the agency that Barr complied with the requirements of section 505(j)(2)(B) of the Act and that no action for infringement of the '521 patent was brought against Barr within the statutory 45-day period.

Subsequently, on December 24, 2003, the '300 patent was listed in the "Orange Book." You amended this application to contain a paragraph IV certification under section 505(j)(2)(A)(vii)(IV) of the Act to the '300 patent stating that the '300 patent is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Metformin Extended-Release Tablets, 750 mg, under this ANDA. You have notified the agency that Barr complied with the requirements of section 505(j)(2)(B)[2] of the Act with respect to the '300 patent and that no action for patent infringement was brought against Barr within the statutory 45-day period.

Regarding 180-day generic drug exclusivity, we note that with respect to Metformin Extended-Release Tablets, 750 mg, the Agency has concluded that Barr was the first ANDA applicant to submit a substantially complete ANDA with paragraph IV certifications to both the '521 and '300 patents. Therefore, with this approval, Barr is eligible for 180-days of market exclusivity for Metformin Hydrochloride Extended-release Tablets, 750 mg. This exclusivity, which is provided for under

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[1] Because information on the '521 patent was submitted before August 18, 2003, this reference is to a section of the Act as in effect prior to December 8, 2003, when the Medicare Prescription Drug, Improvement and Modernization Act (MMA) (Public Law 108-173) was enacted. See MMA § 1101(c)(3).

[2] Because information on the '300 patent was submitted *after* August 18, 2003, this reference is to a section of the Act as in effect after December 8, 2003, when the MMA was enacted. See MMA § 1101(c)(2).

section 505(j)(5)(B)(iv) of the Act[3], will begin to run from the date of first commercial marketing of your Metformin Hydrochloride Extended-release Tablets, 750 mg. Please submit correspondence to this application informing the Agency of the date of first commercial marketing of the product.

Your dissolution testing should be incorporated into the stability and quality contol program using the same method proposed in your application. The "interim" dissolution specifications are as follows:

(b)(4)

The "interim" dissolution test(s) and tolerances should be finalized by submitting dissolution data from the first three production size batches. These data should be submitted as a "Special Supplement - Changes Being Effected" if there are no revisions to the "interim" specifications or when the final specifications are tighter than the "interim" specifications. In all other instances, the information should be submitted in the form of a Prior Approval Supplement.

Under section 506A of the Act, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

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[3] Because your ANDA was filed before the date of enactment of the MMA on December 8, 2003, this reference is to a section of the Act as in effect prior to December 8, 2003. See MMA § 1102(b)(1). Note that because in this case there is no possibility of a court decision (see section 505(j)(5)(B)(iv)(II) as in effect prior to December 8, 2003), first commercial marketing is the only action by which exclusivity can begin to run.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert(s) directly to:

Food and Drug Administration
Division of Drug Marketing, Advertising, and
Communications (HFD-42)
5600 Fishers Lane
Rockville, MD 20857

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-40) with a completed Form FDA 2253 at the time of their initial use.

Sincerely yours,

(b)(6)

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research