DEPARTMENT OF HEALTH & HUMAN SERVICES

ANDA 76-378

Food and Drug Administration
Rockville MD 20857

APR 26 2005

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 March 21, 2002, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Niacin Extended-release Tablets, 500 mg and 750 mg.

Reference is also made to the Tentative Approval letter issued by this office on June 13, 2003, and to your amendments dated December 13, 2002; and January 28, March 4, March 11, and April 5, 2005. We also refer to your correspondence dated April 2, August 23, and September 17, 2004; and January 28, and March 4, 2005, addressing the patent issues noted below.

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 Niacin Extended-release Tablets, 500 mg and 750 mg, to be bioequivalent and, therefore, therapeutically equivalent to the listed drug Niaspan® Extended-release Tablets, 500 mg, and 750 mg, respectively, of KOS Pharmaceuticals, Inc. Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application. The "interim" dissolution specifications are as follows:

> The dissolution testing should be conducted in (b)(4) of water at (b)(4), using (b)(4). The test product should meet the following "interim" dissolution specifications:

Time (hours)	Percent Dissolved
1	(b)(4)
3	
6	
9	
12	
20	

The "interim" dissolution tests 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 be made 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.

The referenced listed drug product (RLD) upon which you have based your application, Niaspan® Extended-release Tablets, 500 mg and 750 mg of KOS Pharmaceuticals, Inc. (KOS), is subject to multiple periods of patent protection. The following U.S. patents with their expiration dates are currently listed in the Agency's publication entitled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"):

Patent Number	Expiration Date
6,080,428 (the '428)	May 27, 2017
6,129,930 (the '930)	September 20, 2013
6,406,715 (the '715)	October 31, 2017
6,676,967 (the '967)	September 20, 2013
6,746,691 (the '691)	September 20, 2013
6,818,229 (the '229)	February 15, 2014

Your application contains paragraph IV certifications to each of these patents under section 505(j)(2)(A)(vii)(IV) of the Act stating that the claims of these patents are invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of the Niacin Extended-release Tablets, 500 mg and 750 mg, under this ANDA. As noted in our tentative approval letter dated June 13, 2003, you informed the agency that KOS initiated a patent infringement suit against you in the United States District Court for the Southern District of New York (KOS Pharmaceuticals v. Barr Laboratories, Inc., [KOS III] Consolidated Civil Action No. 02-CV-1683) to the '428, '930, and

'715 patents. The agency recognizes that the 30-month period identified in section 505(j)(5)(B)(iii) of the Act, during which time FDA was precluded from approving your application with respect to these three patents expired on March 30, 2005. Furthermore, you have notified the agency that no actions for patent infringement involving the '691 patent or the '229 patent were brought against Barr Laboratories, Inc. (Barr) within the statutory 45-day periods. In addition, we note that although KOS initiated litigation against Barr for infringement of the '967 patent [Civil Action No. 04-CV-2403], the '967 patent information was submitted to FDA on February 11, 2004, which is both after the applicable August 18, 2003 effective date of the Medicaid Modernization Act (MMA) and after the date of submission of your ANDA. Therefore, there is no 30-month stay of approval under section 505(j)(5)(B)(iii)[1] with respect to your paragraph IV certification to the '967 patent. See MMA § 1101(c)(3).

We acknowledge that Barr was the first ANDA applicant to submit a substantially complete ANDA with paragraph IV certifications to the patents listed above for Niacin Extended-release Tablets, 500 mg and 750 mg. Therefore, with this approval Barr is eligible for 180 days of market exclusivity for Niacin Extended-release Tablets, 500 mg and 750 mg. This exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the Act,[2] will begin to run from the earlier of the commercial marketing or court decision dates identified in section 505(j)(5)(B)(iv). Please submit correspondence to this application informing the agency of the date the exclusivity begins to run.

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

---

1 Because information on the '428, '930, and '715 patents was submitted to FDA before August 18, 2003, references to section 505(j)(5)(B)(iii) with respect to those patents are to that 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. However, information on the '967, '691, and '229 patents was submitted to FDA after submission of your ANDA and after August 18, 2003, so references to section 505(j)(5)(B)(iii) with respect to those patents are to that section of the Act as in effect after December 8, 2003. See MMA § 1101(c)(3).

2 Because your ANDA was filed before the date of enactment of the MMA on December 8, 2003, this reference to the 180-day exclusivity provision is to the section of the Act as in effect prior to December 8, 2003. See MMA § 1102(b)(1).

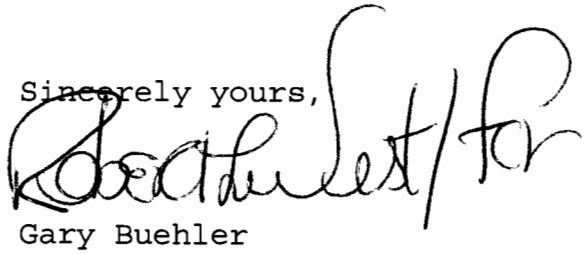
Post-marketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

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,



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