ANDA 74-845 September 15, 1999

Keller & Heckman
Attention: John Dubeck
U.S. Agent for: Biovail Corporation International
Suite 500 West
1001 G Street, N.W.
Washington, DC 20001

Dear Sir:

This is in reference to your abbreviated new drug application dated January 31, 1996, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Diltiazem Hydrochloride Extended-release Capsules USP, 60 mg, 90 mg, and 120 mg (Twice a Day Dosage).

Reference is also made to your amendments dated April 7, and December 30, 1997; February 12, and March 26, 1998; and January 4, January 14, and August 24, 1999.

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 Diltiazem Hydrochloride Extended-release Capsules USP, 60 mg, 90 mg, and 120 mg, to be bioequivalent, and therefore therapeutically equivalent to the listed drug, (Cardizem® SR Capsules, 60 mg, 90 mg, and 120 mg, respectively,) of Hoechst Marion Roussel, Inc.).

Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application. The dissolution testing should be conducted in 900 mL of phosphate buffer, pH 6.5, at 37^{o} C using USP 23 apparatus 1 (basket) at 100 rpm. Your Diltiazem Hydrochloride Extended-release Capsules should meet the following "interim" dissolution specifications:

> Not more than at 1 hour, at 6 hours, at 9 hours, and not less than at 24 hours, of the labeled amount of diltiazem are dissolved.

The "interim" dissolution test and tolerances should be finalized by submitting dissolution data for the first three production size batches in a supplemental application. The supplemental application should be submitted under 21 CFR 314.70 (c)(1) when there are no revisions to the “interim” specifications or the final specifications are tighter than the “interim” specifications. In all other instances the supplement should be submitted under 21 CFR 314.70(b)(2)(ii).

The listed drug referenced in your application, Cardizem SR Capsules of Hoechst Marion Roussel, Inc., is subject to a period of patent protection which expires on January 26, 2005 (patent 4,721,619 [the ‘619 patent]). Your application contains a patent certification to the ‘619 patent under Section 505(j)(2)(A)(vii)(IV) of the Act stating that your manufacture, use, or sale of this drug product will not infringe this patent. Section 505(j)(5)(B)(iii) of the Act provides that approval of your application shall be made effective immediately, unless an action is brought for infringement of the patent which is the subject of the certification before the expiration of forty-five days from the date the notice provided under paragraph (2)(B)(i) is received. You have notified the FDA that Biovail Corporation International (Biovail) has complied with the requirements of Section 505(j)(2)(B) of the Act and that no action for patent infringement was brought against Biovail within the statutory forty-five day period.

Under 21 CFR 314.70, 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.

We request that you submit, in duplicate, any proposed advertising or promotional copy that you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-40). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

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 FD-2253 at the time of their initial use.

Sincerely yours,

Douglas L. Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research