DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 76-640

KV Pharmaceutical Company
Attention: David Jesperson
Vice President of Regulatory Affairs
2503 South Hanley Road
St. Louis, MO 63144-2555

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated January 15, 2003, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Metoprolol Succinate Extended-release Tablets USP, 100 mg and 200 mg.

Reference is also made to your amendments dated October 3, 2003; April 14, May 7, and July 30, 2004; July 22 and October 28, 2005; February 13, March 8, March 27, June 26 (two submissions), October 18, November 21 (two submissions), and December 15, 2006; and March 8, March 21, April 3, April 11, and May 17, 2007. We also acknowledge receipt of your correspondence dated April 16, August 13, and September 2, 2003; December 2, 2005; and January 19, and February 24, 2006.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the ANDA is approved, effective on the date of this letter. The Division of Bioequivalence has determined your Metoprolol Succinate Extended-release Tablets USP, 100 mg and 200 mg, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Toprol-XL Extended-release Tablets,100 mg and 200 mg, respectively, of AstraZeneca, LP.

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

Dissolution testing should be conducted in 900 mL of pH 6.8 phosphate buffer with 0.2% Triton X-100, at 37°C, using USP apparatus II (paddle), at 50 rpm.

Your Metoprolol Succinate Extended-release Tablets USP, 100 mg and 200 mg should meet the following *interim* specifications:

Time (hours)	Percent Dissolved
1	NMT --%
4	-----
8	-----%
20	NLT --%
24	NLT --%

These "interim" dissolution test(s) and tolerances should be finalized by submitting dissolution data from the first three production size batches for each strength. These data should be submitted as a "Special Supplement – Changes Being Effected" (CBE-30) when there are no revisions to be made to the "interim" specifications or if 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 RLD upon which you have based your ANDA, AstraZeneca's Toprol-XL Extended-release Tablets, 100 mg and 200 mg, is subject to periods of patent protection. The following patents and expiration dates (with pediatric exclusivity added) are currently listed in the Agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book") for this drug product:

U.S. Patent Number	Expiration Date
4,927,640 (the '640 patent)	November 22, 2007
4,957,745 (the '745 patent)	March 18, 2008
5,001,161 (the '161 patent)	March 18, 2008
5,081,154 (the '154 patent)	March 18, 2008
5,246,714 (the '714 patent)	March 21, 2011

To each of these patents your ANDA contains paragraph IV certifications under section 505(j)(2)(A)(vii)(IV) of the Act stating that the patents are invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Metoprolol Succinate Extended-release Tablets USP, under this ANDA. You

have notified the agency that KV Pharmaceuticals Company (KV) complied with the requirements of section 505(j)(2)(B) of the Act, and that no litigation for infringement of the '640 or '714 patents was initiated against KV. However, litigation for infringement of the '161, '154, and '745 patents was initiated against KV in the United States District Court for the Eastern District of Missouri [AstraZeneca AB, Aktiebolaget Hassle, and AstraZeneca LP v. KV Pharmaceutical Company, Civil Action No. 03-CV-00592]. You have also notified the agency that the court decided that the '161 and '154 patents are invalid and unenforceable, and that the case involving the '745 patent was dismissed with prejudice. Therefore, under section 505(j)(5)(B)(iii) your ANDA is eligible for approval.

With respect to 180-day generic drug exclusivity, we note that KV was the first ANDA applicant to submit a substantially complete ANDA with a paragraph IV certification to the patents listed above for Metoprolol Succinate Extended-release Tablets USP, 100 mg and 200 mg. Therefore, with this approval, KV is eligible for 180-days of generic drug exclusivity for Metoprolol Succinate Extended-release Tablets USP, 100 mg and 200 mg. This exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the Act, will begin to run from the earlier of the commercial marketing or court decision dates identified in section 505(j)(5)(B)(iv).[1] Please submit correspondence to this ANDA 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.

Postmarketing 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

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[1]Because your ANDA was filed before the date of enactment of the Medicare Prescription Drug, Improvement and Modernization Act (MMA) (Public Law 108-173) 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).

applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Division of Drug Marketing, Advertising, and Communications with a completed Form FDA 2253 at the time of their initial use.

Sincerely yours,

{See appended electronic signature page}

Gary Buehler
Director
Office of Generic Drugs
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/

Robert L. West
5/18/2007 11:04:56 AM
for Gary Buehler