DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

ANDA 76-969

JUL 31 2006

Sandoz Inc.
Attention: Dietrich Bartel, B.S.
Director, Regulatory Affairs
4700 Sandoz Drive
Wilson, NC 27893

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated December 18, 2003, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Metoprolol Succinate Extended-Release Tablets USP, 25 mg, 50 mg, 100 mg and 200 mg.

Reference is also made to your amendments dated May 13, 2005; March 28, June 1, and June 19, 2006. We acknowledge receipt of your correspondences dated February 11, and April 2, 2004; April 20, and July 21, 2005; and January 23, 2006, addressing the patent and exclusivity issues associated with this ANDA.

We have completed the review of this ANDA and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. However, because of the 180-day generic drug exclusivity issue explained below, at this time we are unable to grant final approval to your Metoprolol Succinate Extended-Release Tablets USP, 50 mg, 100 mg and 200 mg. Therefore, only your Metoprolol Succinate Extended-Release Tablets USP, 25 mg is approved. Your Metoprolol Succinate Extended-Release Tablets USP, 50 mg, 100 mg and 200 mg strengths are tentatively approved and will not be eligible for final approval until the 180-day generic drug exclusivity period associated with these strengths has expired.

The referenced listed drug (RLD) upon which you have based your ANDA, Toprol-XL® Extended-Release Tablets of AstraZeneca LP (AstraZeneca), is subject to periods of patent protection. The following patents and expiration dates are currently listed in

the Agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"):

U.S. Patent Number	Expiration Date
4,927,640 (the '640 patent)	May 22, 2007
4,957,745 (the '745 patent)	September 18, 2007
5,001,161 (the '161 patent)	September 18, 2007
5,081,154 (the '154 patent)	September 18, 2007

Your ANDA contains paragraph IV certifications to each of the patents 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 Sandoz complied with the requirements of section 505(j)(2)(B) of the Act, and that litigation for infringement of the '161 and '154 patents was initiated against Sandoz in the United States District Court for the District of Delaware, then transferred and consolidated in the Eastern District of Missouri [Astrazeneca AB, Aktiebolaget Hassle & AstraZeneca LP, v Eon Labs Inc., Civil Action No. 04-CV-0205]. You have also notified the agency that the court decided that '161 and '154 patents are invalid and unenforceable. Therefore, under section 505(j)(5)(B)(iii) your ANDA is eligible for approval.

I. Approval of Metoprolol Succinate Extended-Release Tablets USP, 25 mg

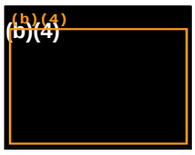
The Division of Bioequivalence has determined your Metoprolol Succinate Extended-Release Tablets USP, 25 mg, to be bioequivalent and, therefore, therapeutically equivalent to the referenced listed drug, Toprol-XL of AstraZeneca.

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:

Apparatus:	(b)(4)
Speed:	
Medium:	
Volume:	

Specifications:

1 hr:
4 hrs:
8 hrs:
20 hrs:



The "interim" dissolution test(s) and tolerances should be finalized by submitting dissolution data for the first three production size batches. Data should be submitted as a Special Supplement - Changes Being Effected when 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.

With respect to 180-day generic drug exclusivity for Metoprolol Succinate Extended-Release Tablets USP, 25 mg, Sandoz was the first ANDA applicant to submit a substantially complete ANDA for Metoprolol Succinate Extended-Release Tablets USP, 25 mg, with a paragraph IV certification to the four patents listed above. Therefore, with this approval, Sandoz may be eligible for 180 days of generic drug exclusivity for Metoprolol Succinate Extended-Release Tablets USP, 25 mg. Generic drug exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the Act, begins to run from the date of commercial marketing identified in section 505(j)(5)(B)(iv). Please submit correspondence to this ANDA informing the agency of the date commercial marketing begins. The agency notes that Sandoz failed to obtain tentative approval of this ANDA within 30 months after the date on which the ANDA was filed. See section 505(j)(5)(D)(i)(IV) of the Act. However, the agency is not making a formal determination at this time of Sandoz's eligibility for 180-day generic drug exclusivity. It will do so only if another applicant becomes eligible for approval within 180 days after Sandoz begins commercial marketing of Metoprolol Succinate Extended-Release Tablets USP, 25 mg.

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.

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 Metoprolol Succinate Extended-Release Tablets USP, 25 mg.

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
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 materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications with a completed Form FDA 2253 at the time of their initial use.

II. Tentative Approval of Metoprolol Succinate Extended-Release Tablets USP, 50 mg, 100 mg and 200 mg.

We are unable to grant final approval to your Metoprolol Succinate Extended-Release Tablets USP, 50 mg, 100 mg and 200 mg, at this time because other ANDAs providing for the 50 mg, 100 mg, and 200 mg strengths and containing paragraph IV certifications to the patents listed in the Orange Book were submitted to the agency prior to the submission of your ANDA. Other ANDAs, therefore, are entitled to 180-day generic drug exclusivity for Metoprolol Succinate Extended-Release Tablets USP, 50 mg, 100 mg, and 200 mg. Accordingly, your Metoprolol Succinate Extended-Release Tablets USP, 50 mg, 100 mg and 200 mg will be eligible for final approval on the date that is 180 days after the agency receives notice, with respect to the other ANDAs, of the earlier of the commercial marketing or court decision dates identified in section 505(j)(5)(B)(iv) of the Act.[1]

---

[1] Because the other ANDAs, unlike yours, were 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).

Our tentative approval of your Metoprolol Succinate Extended-Release Tablets USP, 50 mg, 100 mg and 200 mg, is based upon information currently available to the agency, i.e., data in your ANDA and the status of current good manufacturing practices (cGMPs) of the facilities used in the manufacture and testing of the drug product. This decision is subject to change on the basis of new information that may come to our attention.

To reactivate this ANDA to provide for final approval of the 50 mg, 100 mg and 200 mg strengths, please submit a "Supplemental Application - Expedited Review Requested" 90 days prior to the date you believe that these products will be eligible for final approval. Your supplement must provide a summary of the legal basis upon which you believe the ANDA should be approved, as well as:

1. updated information related to final-printed labeling or chemistry, manufacturing and controls data, or any other change in the conditions outlined in this ANDA, or
2. a statement that no such changes have been made to the ANDA since the date of tentative approval.

Any changes in the conditions outlined in this ANDA and the status of the manufacturing and testing facilities' compliance with current good manufacturing practices (cGMPs) are subject to agency review before final approval of the 50 mg, 100 mg and 200 mg strengths will be made. Such changes should be categorized as representing either "major" or "minor" changes, and they will be reviewed according to OGD policy in effect at the time of receipt.

In addition to the supplement requested above, the agency may request at any time prior to the final date of approval that you submit an additional supplement containing the requested information. Failure to submit either supplement may result in rescission of this tentative approval determination, or delay in issuance of the final approval letter.

Your Metoprolol Succinate Extended-Release Tablets USP, 50 mg, 100 mg and 200 mg, may not be marketed without final agency approval under section 505 of the Act. The introduction or delivery for introduction into interstate commerce of a drug before the effective final approval date is prohibited under section 501 of the Act. Also, until the agency issues the final

approval letter, the 50 mg, 100 mg, 200 mg strengths will not be listed in the "Orange Book."

For further information on the status of this ANDA, or prior to submitting a supplement providing for the final approval of your Metoprolol Succinate Extended-Release Tablets USP, 50 mg, 100 mg and 200 mg, please contact Cheryl Wiseman, Project Manager, at 301-827-5806.

Sincerely yours,

Robert Lee Lest /for

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