ANDA 75-178

May 28, 1999

Apotex Corporation
Attention: Marcy Macdonald
U.S. Agent for: TorPharm
50 Lakeview Parkway, Suite # 127
Vernon Hills, IL 60061

Dear Madam:

This is in reference to your abbreviated new drug application dated July 31, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Enalapril Maleate Tablets USP, 2.5 mg, 5 mg, 10 mg and 20 mg.

Reference is also made to your amendments dated March 12, March 19, March 25, May 4, and May 21, 1999.

We have completed the review of this abbreviated application and have concluded that, based upon the information you have presented to date, the drug is safe and effective for use as recommended in the submitted labeling. Therefore, the application is **tentatively approved**. This determination is based upon information available to the Agency at this time (i.e., information in your application and the status of current good manufacturing practices (CGMPs) of the facilities used in the manufacture and testing of the drug product), and is subject to change on the basis of new information that may come to our attention.

This letter does not address notice issues related to the 180-day exclusivity provisions under section 505(j)(5)(B)(iv) of the Act.

The listed drug product referenced in your application, Vasotec Tablets of Merck Research Laboratories, is subject to a period of patent protection which expires on February 22, 2000, (U.S. Patent No. 4,374,829 [the '829 patent]). Your application contains a patent certification 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 on the '829 patent. Section 505(j)(5)(B)(iii) of the Act provides that approval of an abbreviated application shall be made effective immediately unless an action for patent infringement is brought before the expiration of forty-five days from the date the notice provided under paragraph (2)(B)(i) is received by both the holder of the new drug application (NDA) and the patent holder. You have notified the Agency that TorPharm has complied with the

requirements of Section 505(j)(2)(B) of the Act and that the patent and NDA holder initiated a patent infringement suit against TorPharm in the U.S. District Court for the Northern District of Illinois, Eastern Division, (Merck & Company, Inc. v. Torpharm, Inc., Apotex Corp., and Apotex, Inc., Civil Action No.99-C-2711). Therefore, final approval cannot be granted until:

1. a. The expiration of the 30-month period provided for in section 505(j)(5)(B)(iii) since the date of receipt of the 45-day notice required under section 505(j)(2)(B)(i), unless the court has extended or reduced the period because of the failure of either party to reasonably cooperate in expediting the action; or,

   b. the date of court decision [505(j)(5)(B)(iii) (I), (II), or (III)], which has been interpreted by the Agency to mean the date of the final order or judgement of that court from which no appeal can be or has been taken; or,

   c. the patent has expired; and

2. The Agency is assured there is no new information that would affect whether final approval should be granted.

Because the Agency is granting a tentative approval for this application, please submit an amendment at least 60-days, but not more than 90-days prior to the date you believe that your application will be eligible for final approval. This amendment should be designated clearly in your cover letter as a MINOR amendment and it should identify the circumstances which have occurred that may affect the effective date of final approval. The amendment must also provide:

1. A copy of a final order or judgement from which no appeal may be taken (which might not be the one from the district court), or a settlement agreement between the parties, whichever is applicable, or a licensing agreement between you and the patent holder, or any other relevant information; and

2. a. updated information related to labeling or chemistry, manufacturing and controls data, or any other change in the conditions outlined in this abbreviated application; or

   b. a statement that no such changes have been made to the application since the date of tentative approval.

Any changes in the conditions outlined in this abbreviated application or 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 application will be made.

In addition to, or instead of, the amendments referred to above, the Agency may, at any time prior to the final date of approval, request that you submit amendments containing the information requested above. Failure to submit these amendments may result in rescission of this tentative approval determination, or a delay in issuance of the final approval letter.
The drug product that is the subject of this abbreviated application may not be marketed without final Agency approval under Section 505 of the Act. The introduction or delivery for introduction into interstate commerce of this drug product before the effective final approval date is prohibited under Section 501 of the Act. Also, until the Agency issues the final approval letter, this drug product will not be listed in the Agency's "Approved Drug Products with Therapeutic Equivalence Evaluations" list, commonly referred to as the “Orange Book”.

The amendment submitted in response to this Tentative Approval letter should be clearly designated as a MINOR AMENDMENT in your cover letter. Before you submit the amendment, please contact Bonnie McNeal, Project Manager, at (301) 827-5848, for further instructions.

Sincerely yours,

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