

November 29, 1999

Chelsea Laboratories, Inc.  
Attention: Ernest E. Lengle, Ph.D.  
P.O. Box 15686  
8606 Reading Road  
Cincinnati, Ohio 45215-0686

Dear Sir:

This is in reference to your abbreviated new drug application dated September 30, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Ranitidine Tablets USP, 75 mg (OTC).

Reference is also made to the Tentative Approval letter issued by this Office on February 23, 1999, and to your amendments dated May 3 and July 16, 1999.

We have completed the review of this abbreviated application as amended, and have concluded that based upon the information you have presented to date, the drug product is safe and effective for use as recommended in the submitted over-the counter (OTC) labeling. Therefore, the application remains **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.

The listed drug product referenced in your application is subject to periods of patent protection which expire on December 4, 2002, (U.S. Patent No. 4,521,431 [the '431 patent]) and November 13, 2008 (U.S. Patent 4,880,636 [the '636 patent]), respectively. Your application contains patent certifications 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 either of these patents. Section 505(j)(5)(B)(iii) of the Act provides that approval of an abbreviated application shall be made effective immediately unless an action is brought before the expiration of forty-five days from the date the notice

provided under paragraph (2)(B)(I) is received. You have notified FDA that Chelsea Laboratories, Inc. (Chelsea) has complied with the requirements of Section 505(j)(2)(B) of the Act and that no action for patent infringement was brought against Chelsea within the statutory forty-five day period.

In addition, the reference listed drug (RLD) product upon which you have based your application is also subject to a period of market exclusivity. As noted in the current edition of the Agency's publication entitled "Approved Drug Products with Therapeutic Equivalence Evaluations", also known as the "Orange Book", the new strength exclusivity period scheduled to expire on December 19, 1998 was extended under Section 111 of the Food and Drug Administration Modernization Act [21 U.S.C. 355a (1997)] until June 19, 1999.

However, we are unable to approve your application at this time because the Act provides that approval of an abbreviated application that contains a Paragraph IV Certification described in section 505(j)(2)(A)(vii)(IV), and that is for a drug product for which a previous abbreviated application has been submitted which also contains a Paragraph IV Certification, shall be made effective not earlier than one hundred and eighty days after:

- a. the date the Secretary receives notice of the first commercial marketing of the drug under the previous application, or
- b. the date of a decision of a court holding the patent which is the subject of the certification to be invalid or not infringed, whichever event occurs first (Section 505(j)(5)(B)(iv)).

Please note that an abbreviated application for Ranitidine Tablets USP, 75 mg, (OTC) containing a Paragraph IV Certification was accepted for filing by this Office prior to the filing of your application. This application, submitted by Novopharm Limited, received final approval on June 21, 1999. Consequently, Novopharm Limited (Novopharm) is eligible for 180-days of generic drug market exclusivity. Your application will be eligible for final approval beginning one hundred and eighty (180) days after the first commercial marketing of the drug by Novopharm. Novopharm has informed the agency that Novopharm began marketing their approved product on July 19, 1999, thus triggering the 180-day exclusivity period. Therefore, final approval of your application may not be made effective until after the additional 180-day period of marketing exclusivity

awarded to Novopharm has expired, i.e. January 14, 2000. We refer you to the Agency's recently issued guidance document entitled **A180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments** (June 1998), for additional information.

Because the Agency is granting a third tentative approval for this application, please submit an amendment at least 30-days prior to the date you believe your application will be eligible for final approval. This amendment should identify changes, if any, in the conditions under which the drug product was tentatively approved, and should include updated information such as final-printed labeling, chemistry, manufacturing and controls data as appropriate. Alternatively, an amendment should be submitted stating that no changes have been made to the terms of the application since the date of this second tentative approval. This amendment should be designated clearly in your cover letter as a MINOR amendment. In addition to, or instead of this amendment, the Agency may request at any time prior to the date of final approval of this application that you submit an amendment containing the information described above. Failure to submit either or, if requested, both amendments may result in rescission of the tentative approval status of your application, or may result in a delay in the issuance of the final approval letter.

Any changes in the conditions outlined in this abbreviated application as well as changes in 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.

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 before the 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.

Prior to submitting the amendment(s), please contact Kassandra Sherrod, Project Manager, at (301) 827B5849, for further instructions.

Sincerely yours,

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