CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER 21-165

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-165

Schering Corporation
2000 Galloping Hill Road
Kenilworth, New Jersey 07330

DEC 21 2001

Attention: Joseph F. Lamendola, Ph.D.
Vice President, U.S. Regulatory Affairs

Dear Dr. Lamendola:

Please refer to your new drug application (NDA) dated October 20, 1999, received October 21, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Clarinex (desloratadine) Tablets.

We acknowledge receipt of your submissions dated November 26 (2), 1999, February 14, and, 17, March 20 (2), and 31, April 19, May 18, June 19, and 29, July 28, August 2, and 16, September 14, and 29, October 3, 4, 9 (2), 13, 19, 20, 25, 27,and 31, November 1, 2, and 10, and December 18, 2000, January 18, and 31, February 13, March 5, and 16, April 18, May 22, July 20, August 3 and 15, September 17, November 5, and December 5 (2), 10, 14, 17, 18 (2), 19, 20 and 21, 2001. Your submission of December 5, 2001, constituted a complete response to our January 19, 2001, action letter.

This new drug application provides for the use of Clarinex (desloratadine) Tablets for the relief of the nasal and non-nasal symptoms of seasonal allergic rhinitis in patients 12 years of age and older.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed-upon labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert, immediate container and carton labels submitted December 18, 2001). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be

designated "FPL for approved NDA 21-165." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your Postmarketing Study commitment specified in your submission dated October 30, 2000. You agreed to submit a final report of the ongoing mouse carcinogenicity study within three years of NDA approval.

Submit the study final report to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(vii), you should include a status summary of the commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, and any changes in plans since the last annual report. All submissions, including supplements, relating to this postmarketing study commitment should be prominently labeled **"Postmarketing Study Final Report", or "Postmarketing Study Correspondence."**

We also remind you of your agreement, dated December 20, 2001, to clarify or revise, as needed, the stability procedures to ensure appropriate identification and labeling of
in stability batches by Februrary 2002, and to review all stability data generated at Las Piedras to ensure proper identification of degradants by January 15, 2002.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). We note that you have not fulfilled the requirements of 21 CFR 314.55 (or 601.27). We are waiving the pediatric study requirements for this action for this application for pediatric patients ages 0 to 6 months. We are deferring submission of your pediatric studies for patients ages 6 months to 12 years, until December 7, 2002. You have fulfilled the pediatric study requirement at this time for pediatric patients ages 12 years to 16 years.

Please submit your pediatric drug development plans within 120 days from the date of this letter unless you believe a waiver is appropriate. Within approximately 120 days of receipt of your pediatric drug development plan, we will review your plan and notify you of its adequacy.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will notify you within 120 days of receipt of your response whether a waiver is granted. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov/cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" (PPSR) in addition to your plans for pediatric drug development described above. We recommend that

you submit a Proposed Pediatric Study Request within 120 days from the date of this letter. If you are unable to meet this time frame but are interested in pediatric exclusivity, please notify the division in writing. FDA generally will not accept studies submitted to an NDA before issuance of a Written Request as responsive to a Written Request. Sponsors should obtain a Written Request before submitting pediatric studies to an NDA. If you do not submit a PPSR or indicate that you are interested in pediatric exclusivity, we will review your pediatric drug development plan and notify you of its adequacy. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please send one copy to the Division of Pulmonary and Allergy Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Anthony M. Zeccola, Regulatory Management Officer, at 301-827-1058.

Sincerely,

/S/

{See appended electronic signature page}

John K. Jenkins, M.D.
Director
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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US Regulatory Affairs

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We have completed the review of this application, as amended, and it is approvable. Before this application may be approved it will be necessary to resolve the following deficiencies.

1. During recent inspections of the Union, New Jersey, and Las Piedras, Puerto Rico, manufacturing facilities for your NDA, a number of CGMP deficiencies were noted. Satisfactory inspections will be required before this application may be approved.

2. Submit draft labeling revised as indicated in the attached marked-up labeling.

We acknowledge your correspondence dated January 10, 2001, withdrawing the Schering Kenilworth, New Jersey, facility from this application. If you choose to resubmit this site to this application, a satisfactory inspection will be required before this application may be approved.

Within 10 days after the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action, FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

The drug product may not be legally marketed until you have been notified in writing that the application is approved.

If you have any questions, call Gretchen Trout, Project Manager, at (301) 827-1058.

Sincerely yours,

/s/

{See appended electronic signature page}
John K. Jenkins, M.D.
Director
Office of Drug Evaluation II
Center for Drug Evaluation and Research

14 pages redacted from this section of the approval package consisted of draft labeling